B17 Analyzing Designer Fentanyl Analogs Using a Fentanyl Classifier

Arun S. Moorthy, PhD, National Institute of Standards and Technology, Gaithersburg, MD 20899; Anthony Kearsley, PhD, National Institute of Standards and Technology, Gaithersburg, MD 20899-8910; W. Gary Mallard, PhD, Teal Consulting, Chevy Chase, MD 20815; William E. Wallace, PhD, National Institute of Standards and Technology, Gaithersburg, MD 20899-8362*

Learning Overview: After attending this presentation, attendees will have learned how mass spectral similarity mapping, as implemented in the Fentanyl Classifier, can be used to generate putative identifications of fentanyl analogs not contained in a reference library.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by informing attendees that drug screening with the Fentanyl Classifier has the potential to greatly reduce false negative presumptive identifications of fentanyl analogs that differ from fentanyl by up to two modifications by leveraging the increased information content available through mass spectral similarity mapping.

Fentanyl is a highly addictive synthetic narcotic originally developed for treating severe pain. Growth in abuse of fentanyl, fueled in part by designer fentanyl analogs, has led to an unprecedented rise in overdose deaths. The large and rapidly evolving number of these drugs presents a challenge to chemical identification. Mass spectral similarity mapping is a natural extension of traditional mass spectral similarity searching. In both processes, a query mass spectrum of an analyte is searched against a library of reference spectra. Whereas a traditional similarity search provides an analyst with a hit list—a high-confidence way of identifying an analyte with a replicate spectrum in the library—similarity mapping provides a map that is informative even for analytes that are not in the reference library, such as new designer drugs.

A library of mass spectra that included fentanyl and Type I fentanyl analogs was collected. Here, *Type* indicates the number of modification sites by which an analog differs from the standard fentanyl scaffold. Mass spectral similarity maps can be generated using query spectra and the fentanyl library. These maps can be scrutinized to classify the query based on the likely site of modification and, in some instances, propose a complete structure for the query. An open-source implementation of mass spectral similarity mapping applied to fentanyl analogs, referred to as the National Institute of Standards and Technology (NIST) Fentanyl Classifier (NFC), is available at https://github.com/asm3-nist/FentanylClassifier. The NFC was tested using several example spectra, including replicate spectra of fentanyl, replicate spectra of the Type I fentanyl analogs contained in the library, spectra of Type I fentanyl analogs not represented in the library, spectra of Type II analogs, and spectra of non-fentanyl compounds. As expected, the NFC correctly localized modification sites for fentanyl analogs that differ from fentanyl by modification on, at most, two sites (i.e., Type I and Type II fentanyl analogs). In cases where the query was a Type II fentanyl analog with *composing cognates* contained in the library, the NFC was able to accurately identify the query short of positional isomers.

Fentanyl, GC/MS, Screening