SOFT 2021
Abstract Submission Form

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*****Do not exceed 600 words including tables and charts.*****

Title: Examining the Evidence on Fluorofentanyl – Multidisciplinary Evaluation of this Emerging Drug with a Focus on Forensic Toxicology Investigations

AUTHOR(S) AND AFFILIATION(S): *Alex J Krotulski, PhD[1], Donna M Papsun, MS, D-ABFT[2], Barry K Logan, PhD, F-ABFT[1,2]*
[1]Center for Forensic Science Research and Education, Fredric Rieders Family Foundation, Willow Grove, PA
[2]NMS Labs, Horsham, PA

ABSTRACT:

Background/Introduction:

Around 2008, fentanyl began infiltrating the recreational heroin market in the United States (US), becoming dominant by the late 2010s. Today, fentanyl related deaths and incidental positivity continue to increase. Fentanyl maintains a strong hold on the recreational opioid market, fueled by illicit manufacture and distribution within North America. The recent emergence/re-emergence of fluorofentanyl raises the prospect of fentanyl being displaced as the primary illicit opioid in the US, at least potentially in some regions and/or drug supplies. Fluorofentanyl exists in three isomeric forms: *ortho*-, *meta*-, and *para*-fluorofentanyl.

Objectives:

Fentanyl manufacture can be studied via the analysis of precursors and/or byproducts from clandestine synthesis (i.e., signature analysis or chemical fingerprint). Our laboratory implemented sample-mining and data-mining approaches in 2018 to track emerging and evolving drug trends. The objective herein was to evaluate comprehensive toxicology data to determine positivity, prevalence, and important epidemiological factors with respect to fluorofentanyl. The goal of this presentation is to provide a multidisciplinary look at fluorofentanyl and how associated aspects mimics fentanyl, but not other NPS.

Methods:

Biological samples, extracts, and seized drug materials from forensic and clinical toxicology investigations were obtained for comprehensive toxicology testing. Non-targeted acquisition using a SCIEX TripleTOF® 5600+ quadrupole time-of-flight mass spectrometer (LC-QTOF-MS) was employed. The library database included more than 900 traditional drugs, NPS, metabolites, and other relevant analytes. Confirmation of *ortho*- vs. *meta*- vs. *para*-fluorofentanyl was conducted using a Waters Xevo TQ-S micro tandem mass spectrometer (LC-QQQ-MS).

Results:

Fluorofentanyl "re-emerged" in the recreational drug supply in late 2020 and continues to increase exponentially in positivity (of total cases: Q3 2020: 0%, Q4 2020: 0.4%, Q1 2021: 4.0%). Fluorofentanyl is the first fentanyl analogue to gain traction in the US drug supply since the enactment of core structure scheduling of fentanyl related substances in 2018. Confirmatory analysis identified *para*-fluorofentanyl as the most commonly encountered isomer of this analogue. *para*-Fluorofentanyl was routinely found in combination with fentanyl. Concentrations of *para*-fluorofentanyl in blood ranged from less than 0.1 ng/mL to greater than 20 ng/mL. Analysis of drug materials showed varying ratios of *para*-fluorofentanyl to fentanyl (<0.1 to >25), and some counterfeit opioid tablets contained *para*-fluorofentanyl only. Signature analysis in both toxicology samples and drug materials uncovered the presence of byproducts related to fluorofentanyl (e.g., fluoro-4-ANPP, fluoro-phenethyl-4-ANPP). These byproducts matched those related to fentanyl from illicit synthetic routes. *In vitro* activity data for fluorofentanyl shows the *para*- isomer to be similar in potency to fentanyl; however, the *ortho*- isomer is significantly more potent, stressing the need for differentiation during analytical testing. Cases involving fluorofentanyl originated from more than 30 states, spanning all regions of the US. This finding is dissimilar from other emerging synthetic opioids which were localized around the Midwest, before proliferating to other regions.

Conclusion/Discussion:

The distribution of fluorofentanyl in forensic casework is increasingly similar to that of fentanyl in the US. Data show that fluorofentanyl is widespread in the opioid supply, both in combination with fentanyl and increasingly being found on its own. Byproducts detected in toxicology samples and drug materials suggest that the route of illicit manufacture is the same as that for fentanyl, but from different synthetic precursors. Unlike the recent emergence of NPS opioids (e.g., isotonitazene, brorphine), the appearance of fluorofentanyl seems to be linked to drug scheduling actions involving inactive precursors used to synthesize fentanyl (e.g., 4-AP) rather than the final drug itself. Overall, this trend may mark a new turning point in the illicit opioid landscape which can have significant impacts on forensic toxicology practice.