

### PURPOSE

Selected samples seized from the United States Southwest border are submitted to the Center for Forensic Science Research and Education (CFSRE) for testing for research purposes of qualitative and quantitative testing. The purpose of this report is provide information on an atypical batch of counterfeit tablets that was received and tested which contained multiple complex drug mixtures representing a significant health threat.

### BACKGROUND

Seized tablets and powders suspected of containing fentanyl are analyzed at CFSRE using a workflow that includes microscopic imaging of tablets using the MiScope® Megapixel MP3, qualitative analysis by both gas chromatography mass spectrometry (GC/MS) as well as liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS) for identification of novel substances, and quantitative analysis using Waters® Acquity UPLC coupled with a Waters Xevo® TQ-S micro.

### Images of Six Different Counterfeit Tablets in a Single Atypical Case



Figure 1. The tablets pictured were differentiated from each other based on differing colors and/or monogramming. The “30” marking on Exhibits 4 and 5 appear to be similar, but were differentiated based on color comparison and diagonal of M square measurement, which for Exhibit 4 was 4.95 mm and for Exhibit 5 was 5.85 mm. Exhibits 5 and 6 differed in the height of “0” measurement for the “30” monogram portion of the tablet. The height of zero measurement for Exhibit 5 was 1.50 mm and for Exhibit 6 was 2.21 mm. Exhibit 3 differed from the other exhibits because it appeared degraded and the monogramming could not be visually compared to the rest of the exhibits.

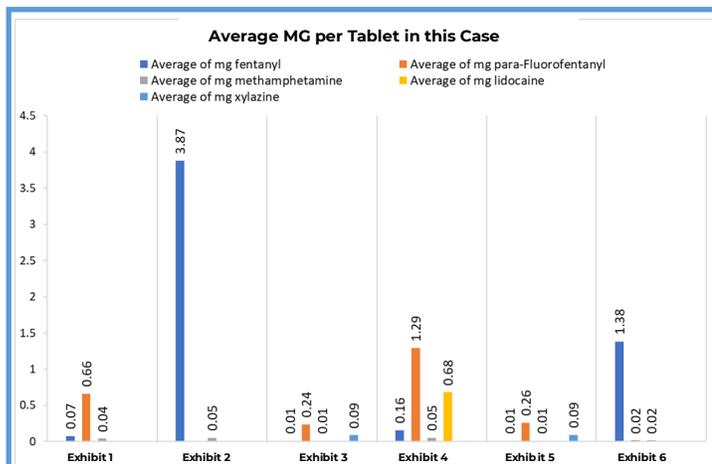
### Combined Qualitative GC/MS and LC-QTOF-MS Results for All Exhibits Tested

	Fentanyl	Metamizole	Para-fluoro fentanyl	Acetaminophen	Methamphetamine	Fluoro phenethyl 4-ANPP	Despropionyl para-fluorofentanyl	4-ANPP	Xylazine	Pentobarbital	Levamisole	Lidocaine
Exhibit 1	X	X	X		X	X	X					
Exhibit 2	X	X		X	X			X				
Exhibit 3	X	X	X	X		X	X		X	X		
Exhibit 4	X	X	X	X	X	X	X				X	X
Exhibit 5	X	X	X	X	X	X	X					
Exhibit 6	X	X	X	X				X	X	X		

CFSRE received a case involving suspected counterfeit tablets seized at the US Southwest Border. It consisted of six separate exhibits containing a total of 40 counterfeit tablets. One tablet was tested from Exhibits 1-3, ten tablets were tested from Exhibit 4, twelve tablets were tested from Exhibit 5, and fifteen tablets were tested from Exhibit 6.

All 40 tablets contained fentanyl and the banned analgesic metamizole. The fentanyl analog para-fluorofentanyl was present in 5 of the exhibits. Other substances present in the tablets were the psychoactive substances methamphetamine, xylazine (a veterinary sedative) and pentobarbital (a veterinary euthanasia agent). The samples also contained other adulterants including acetaminophen, lidocaine the banned anti-worming agent levamisole, and chemical reaction by-products and precursors from illicit fentanyl manufacture.

**NOTE: Although 2 mg is frequently considered a lethal fentanyl dose even in tolerant individuals, and the majority of cases analyzed contained less than 2 mg of fentanyl, almost all of these cases can still be considered potentially lethal due to the toxic and synergistic effects of adulterants such as para-fluorofentanyl, metamizole, xylazine, levamisole, methamphetamine, and pentobarbital. Much lower doses of fentanyl can also be lethal in individuals with less tolerance.**



Ex	GC/MS Findings
1	Fentanyl, para-Fluorofentanyl, Methamphetamine, Metamizole Despropionyl para-fluorofentanyl, para-Fluorophenethyl 4-ANPP
2	Fentanyl, Methamphetamine Acetaminophen, Metamizole 4-ANPP
3	Fentanyl, para-Fluorofentanyl, Pentobarbital Acetaminophen, Metamizole Despropionyl para-fluorofentanyl, para-Fluorophenethyl 4-ANPP
4	Fentanyl, para-Fluorofentanyl, Methamphetamine Acetaminophen, Metamizole, Lidocaine, Levamisole 4-ANPP, Despropionyl para-fluorofentanyl, para-Fluorophenethyl 4-ANPP
5	Fentanyl, para-Fluorofentanyl, Methamphetamine, Pentobarbital Acetaminophen, Metamizole, Xylazine Despropionyl para-fluorofentanyl, para-Fluorophenethyl 4-ANPP
6	Fentanyl, para-Fluorofentanyl Acetaminophen, Metamizole 4-ANPP

A total of 40 tablets were quantitatively tested for all six exhibits. The average mg of para-fluorofentanyl was greater than the average mg of fentanyl for 4 out of the 6 exhibits (exhibits 1, 3, 4, and 5). The average mg of acetaminophen per tablet was greater than 60% for exhibits 2-5.

Fentanyl and metamizole were detected in every exhibit to a greater or lesser extent. In exhibits 1,3,4 and 5 however, the analog para-fluorofentanyl was the predominant opioid. Cutting agents highlighted in yellow can make the individual pills more potent and lethal.

## Information Regarding Adulterants Effects on Human Health

<b>Acetaminophen</b>	An over the counter analgesic which is used to reduce pain and fever. Overdose can result in acute liver failure. Symptoms of a possible acetaminophen overdose also includes loss of appetite, nausea, vomiting, extreme tiredness, sweating, unusual bleeding or bruising, yellowing of skin or eyes, and pain in the abdomen (especially in the upper right side). Acetaminophen was detected in 5 out of the 6 exhibits.
<b>Levamisole</b>	A de-worming drug that is used for veterinary practice. It is most commonly used as a cutting agent in cocaine to modify the stimulant effects of the drug. Adverse effects of levamisole use include unexplained fever and agranulocytosis (lowering of white blood cells), unexplained vasculitis (damage to blood vessels) with purple skin lesions over ear lobes, legs and thighs, persistent or recurrent fever and chills, worsening or persistent sore throat, worsening swollen glands. Levamisole may also increase the toxic effects of opioids.
<b>Lidocaine</b>	A local anesthetic drug approved for human use, lidocaine is added to drug samples as a filler so that not as much actual drug product is added. Because it produces a numbing effect, like cocaine, lidocaine is added to minimize the discomfort that injection or snorting of drugs usually comes with. Lidocaine toxicity can manifest as cardiotoxicity which includes symptoms of abnormal heart rhythms, low blood pressure, or altered mental status. It can also manifest as methemoglobinemia for which symptoms include, cyanosis, low blood oxygen, distressed breathing, headache, dizziness, delirium, and seizures.
<b>Metamizole</b>	A non-opioid analgesic that is used in Europe, South America, and Asia today to combat pain, fever, and muscle spasms. It is also commonly known as dipyrone. Metamizole was removed from the medical drug market in the United States due to frequency of agranulocytosis. Other adverse effects include nausea, vomiting, abdominal pain, diarrhea, headache, dizziness, renal dysfunctions, and others. Less common effects are aplastic anemia and anaphylaxis. Metamizole may increase toxic effects of opioids and affect naloxone ability to reverse overdose
<b>Pentobarbital</b>	A barbiturate belonging to a class of sedative-hypnotic, seizure drugs which is widely used as a euthanasia agent in veterinary medicine. It has historically been used in humans as a medication used to treat or manage seizures, intracranial pressure control, and insomnia. Adverse effects of pentobarbital include altered mental status, agitation, confusion, drowsiness, respiratory depression, bradycardia, hypotension, cardiovascular collapse, dizziness, hallucinations, headache, insomnia, nausea, vomiting, hepatotoxicity. Symptoms of pentobarbital toxicity include airway compromise, cardiovascular collapse, coma, and death.
<b>Xylazine</b>	Xylazine is a veterinary sedative used in animal surgery and sedation. It has never been approved in the US for human use due to its adverse effects. It is one of the most common adulterants in fentanyl powders in the eastern and midwestern United States. Xylazine can be dangerous when taken in combination with illicit drugs. Its toxicity symptoms include CNS depression, sedation, respiratory depression, bradycardia, skin lesions, and slowed wound healing. While naloxone can reverse opioid effects it does not reverse the contribution to sedation from xylazine.

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