Trace Detection of Fentanyl-related Substances in Screening Environments

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Screening Environments

• Emergency Medical

• Law Enforcement

• Mail/Packages
Detect to Protect and...

• Emergency Medical
  – *Treat*

• Law Enforcement
  – *Presumptive identification*

• Mail/packages
  – *Interdict*
Many Fentanyl-Related Compounds

- 25 reported fentanyl-related substances 2015-2018
  - Fentanyl + fentanyl analogs + metabolites
  - Precursors (4-ANPP etc.)
  - Other synthetic opioids (U-47700, etc.)

Emerging Threat Reports (DEA labs)
Sample Purity

• **Street Level, Southern Border**
  
  – Average 6.5 % for 300 fentanyl powder exhibits (2017)$^1$
  
  – Average 1.1 mg/tablet, or ~ 1.5 to 0.1 %$^2$
  
  – Commonly mixed with heroin, other drugs
  
  – Excipients: procaine, acetaminophen, quinine, caffeine, mannitol, sucrose, etc.

• **Mail/Packages**
  
  – Relatively pure
  
  – Could be novel analogs/compounds

$^1$US DOJ, DEA, Fentanyl Briefing Guide 2017
$^2$US DOJ, DEA Intelligence Brief DCT-DB-003-18, 2018
EMS Detection Requirements

• **Visible powders**
  – Samples likely street level (impure)

• **Rapid response**
  – No reachback for technical assistance

• **Portable**
  – Battery powered

• **Detect the threat**
  – Detect to treat down the road
Law Enf. Detection Requirements

• **Visible powders**
  – Samples likely street level (impure)

• **Rapid response**
  – Limited reachback for technical assistance

• **Portable**
  – Battery powered

• **Presumptive ID**
Mail Detection Requirements

- **No visible powders**
  - Sealed bags, possibly opaque
  - Novel compounds

- **Intermediate response time**
  - Reachback for technical assistance

- **Table-top**

- **Presumptive ID**
Existing Toolkit

Purity, sample amounts
Optical – IR, Raman

Selectivity
IMS

Cost, time, size
MS, GC-MS

Purity, selectivity
Colorimetrics

Analog specific
Immunoassay
IMS and TD-DART-MS

E. Sisco, J. Verkouteren, J. Staymates, J. Lawrence “Rapid detection of fentanyl, fentanyl analogues, and opioids for on-site or laboratory based drug seizure screening using thermal desorption DART-MS and ion mobility spectrometry” *Forensic Chemistry* 4, **2017**, 108-115.

**Ion Mobility Spectrometry**

**Thermal desorption-Direct Analysis in Real Time – Mass Spectrometry**

FORENSICS @ NIST

#NISTForensics
Results from Initial Study

• Detection of fentanyl and 16 analogues is possible using both TD-DART-MS and IMS.

• Fentanyl can be detected in the presence of 1000× heroin with no signal reduction.

• Fentanyl and heroin can be detected in the presence of background matrices.

• Nanogram quantities can be detected by sampling residues off a plastic bag.
Issues with IMS

Resolution

• Fentanyl and heroin not resolved
• Characteristic peak shift indicates fentanyl

Competitive Ionization

• Procaine suppresses fentanyl response
• No issues with other excipients

Excipients investigated: acetaminophen, caffeine, mannitol, quinine, and procaine
Background contaminants: dirt, sebum, plastic bag
Follow-up IMS Study

- **6 Commercial IMS Detectors**
  - Potential repurposing of retired explosives detectors

- **Tested to common sample set**
  - Selection of analogs
  - Excipients and ratios

- **Evaluate selectivity and sensitivity**
  - Pure
  - Mixtures with heroin
  - Mixtures with excipients

- **Exercised specific safety controls**
Selection of Analogs

Most Frequently Reported
Top 11 out of 25
Fentanyl
Furanyl fentanyl
Acetyl fentanyl
4-FIBF
Carfentanil
4-ANPP
Butyryl fentanyl
Acryl fentanyl
3-methyl fentanyl
U-47700
Cyclopropyl fentanyl

Included for experimental reasons:
• THF fentanyl (high molecular weight)
• Acetyl norfentanyl (low molecular weight)
Studies Conducted in Hood

All IMS have countercurrent airflow that can exhaust towards operator after sampling
• Could entrain residual vapors
• Testing involved repeated doses of many different fentanyls

• Samples desorbed by internal heater/oven
• Sample vapors drawn toward inward towards ionization region

Air flow after sampling
All Compounds Detected by All Instruments

Reduced Mobility ($K_0$) vs Molecular Weight

Peaks are typically $[M+H]^+$

$K_0$ also affected by structure

$R^2 = 0.9897$

Intended vs drift time

Peaks are typically $[M+H]^+$

$K_0$ also affected by structure
<table>
<thead>
<tr>
<th>Compound</th>
<th>measured $K_0$ avg (std)</th>
</tr>
</thead>
<tbody>
<tr>
<td>U-47700</td>
<td>1.093 (0.003)</td>
</tr>
<tr>
<td>Acetyl fentanyl</td>
<td>1.086 (0.005)</td>
</tr>
<tr>
<td>Benzylfentanyl</td>
<td>1.086 (0.003)</td>
</tr>
<tr>
<td>Acryl fentanyl</td>
<td>1.065 (0.005)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>1.056 (0.005)</td>
</tr>
<tr>
<td>THC</td>
<td>1.051 (0.006)</td>
</tr>
<tr>
<td>Heroin</td>
<td>1.042 (0.006)</td>
</tr>
<tr>
<td>Cyclopropylfentanyl</td>
<td>1.034 (0.006)</td>
</tr>
<tr>
<td>trans-3-Methylfentanyl</td>
<td>1.028 (0.006)</td>
</tr>
<tr>
<td>Butyryl fentanyl</td>
<td>1.026 (0.006)</td>
</tr>
<tr>
<td>Crotonyl fentanyl</td>
<td>1.024 (0.006)</td>
</tr>
<tr>
<td>p-FIBF</td>
<td>1.009 (0.007)</td>
</tr>
<tr>
<td>Furanyl fentanyl</td>
<td>1.008 (0.007)</td>
</tr>
<tr>
<td>Valeryl fentanyl</td>
<td>0.995 (0.007)</td>
</tr>
<tr>
<td>Carfentanil</td>
<td>0.980 (0.006)</td>
</tr>
<tr>
<td>(Buprenorphine)</td>
<td>~0.91</td>
</tr>
</tbody>
</table>

- Averages and uncertainties over all 6 instruments
- Within instrument uncertainty can be much lower
**K₀ Used in Detection Libraries**

For detection algorithm, window will be set about library value of K₀ (or drift time)

<table>
<thead>
<tr>
<th>Fentanyl K₀</th>
<th>Inst. 1</th>
<th>Inst. 2</th>
<th>Inst. 3</th>
<th>Inst. 4</th>
<th>Inst. 5</th>
<th>Inst. 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>average</td>
<td>1.0523</td>
<td>1.0518</td>
<td>1.0583</td>
<td>1.0563</td>
<td>1.0645</td>
<td>1.0516</td>
</tr>
<tr>
<td>1stdev</td>
<td>0.0001</td>
<td>0.0019</td>
<td>0.0005</td>
<td>0.0036</td>
<td>0.0025</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

- The uncertainties in peak position (K₀) will influence size of detection windows
- Smallest detection windows typically ± 0.003

Additional components can change K₀

<table>
<thead>
<tr>
<th>Mixtures</th>
<th>Δ k₀ relative to pure fentanyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:1 heroin</td>
<td>-0.0044 -0.0081 -0.0002 -0.0011 0.0001 -0.0137</td>
</tr>
<tr>
<td>100:1 heroin</td>
<td>-0.0044 -0.0076 0.0008 0.0030 -0.0057 -0.0015</td>
</tr>
<tr>
<td>100:1 procaine</td>
<td>-0.0009 -0.0067 0.0002 np np -0.0007</td>
</tr>
<tr>
<td>100:1 quinine</td>
<td>-0.0018 0.0029 -0.0027 0.0044 -0.0153 -0.0016</td>
</tr>
</tbody>
</table>
All Instruments Sensitive to Nanograms

Limit of Detection (LOD) and Upper Confidence Limits (UCL) in nanograms

<table>
<thead>
<tr>
<th></th>
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<th>Inst. 3</th>
<th>Inst. 4</th>
<th>Inst. 5</th>
<th>Inst. 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fentanyl</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LOD 90</td>
<td>51.7</td>
<td>0.6</td>
<td>7.0</td>
<td>2.3</td>
<td>24.2</td>
<td>1.4</td>
</tr>
<tr>
<td>90% UCL LOD</td>
<td>87.5</td>
<td>1.0</td>
<td>13.5</td>
<td>4.5</td>
<td>49.1</td>
<td>2.0</td>
</tr>
<tr>
<td><strong>Benzylfentanyl</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LOD 90</td>
<td>34.6</td>
<td>0.5</td>
<td>10.8</td>
<td>1.2</td>
<td>17.7</td>
<td>0.8</td>
</tr>
<tr>
<td>90% UCL LOD</td>
<td>63.9</td>
<td>0.9</td>
<td>16.5</td>
<td>2.3</td>
<td>29.1</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Determined using ASTM E2677 Web-based Standard Test Method for Limits of Detection (LOD)
https://www-s.nist.gov/loda/
Background Study of Deployed Detector

- Commercial IMS deployed for vehicle screening at NIST, explosives detection
- Evaluate positive ion (drug) background data from archived spectra (true negatives)
- Determine minimum intensity thresholds to obtain desired true/false positive rates

Background signal relevant to detection of fentanyls

High intensities in heroin channel
Bottom Line

- Extensive ongoing studies to evaluate performance of IMS detectors for fentanyl detection
- Multiple (~ 15) fentanyl compounds can be simultaneously detected
  - Not all differentiated
  - Some issues with heroin
  - Instrument manufacturers will customize software/hardware
- Nanogram-level detection (safe sampling)
- Minimal conflict with detection of other common drugs
- Existing detectors used for explosives detection will work
- Background from deployed condition (vehicle screening) o.k.
Also Looking at Fieldable DART

- Similar responses for HR-MS & LR-MS

DART-QDa

35” by 16” footprint
1 Da resolution (LR-MS)

Some analog-analog competition may occur in LR-MS not seen in HR-MS
Conclusions

• Will need many tools to solve the problem

• Combinations of tools

• Standard methodology for testing