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Trace Detection of Fentanyl-related Substances in Screening Environments

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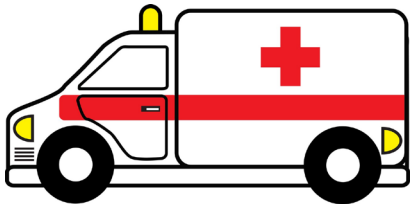
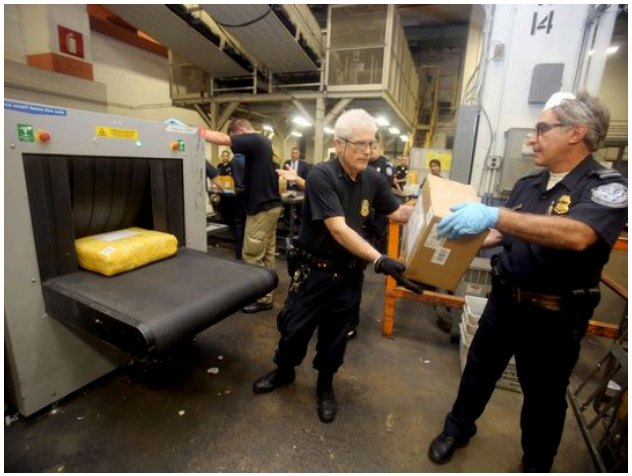
Screening Environments

- Emergency Medical



- Law Enforcement

- Mail/Packages

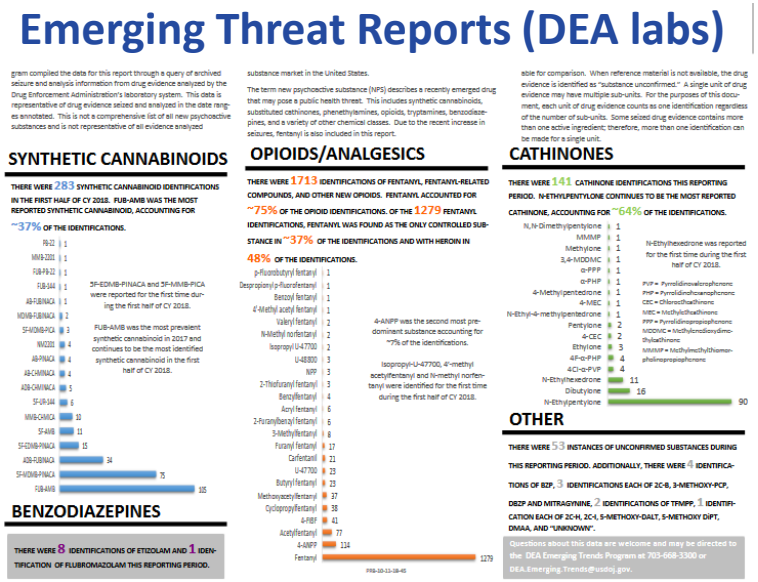


Detect to Protect and…

- **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)

gram compiled the data for this report through a query of archived seizure and analysis information from drug evidence analyzed by the Drug Enforcement Administration's laboratory system. This data is representative of drug evidence seized and analyzed in the date ranges annotated. This is not a comprehensive list of all new psychoactive substances and is not representative of all evidence analyzed

substance market in the United States.

The term new psychoactive substance (NPS) describes a recently emerged drug that may pose a public health threat. This includes synthetic cannabinoids, substituted cathinones, phenethylamines, opioids, tryptamines, benzodiazepines, and a variety of other chemical classes. Due to the recent increase in seizures, fentanyl is also included in this report.

able for comparison. When reference material is not available, the drug evidence is identified as "substance unconfirmed." A single unit of drug evidence may have multiple sub-units. For the purposes of this document, each unit of drug evidence counts as one identification regardless of the number of sub-units. Some seized drug evidence contains more than one active ingredient; therefore, more than one identification can be made for a single unit.

SYNTHETIC CANNABINOIDS

THERE WERE 283 SYNTHETIC CANNABINOID IDENTIFICATIONS IN THE FIRST HALF OF CY 2018. FUB-AMB WAS THE MOST REPORTED SYNTHETIC CANNABINOID, ACCOUNTING FOR ~37% OF THE IDENTIFICATIONS.

PB-22 1
MMB-2201 1
FUB-PB-22 1
FUB-144 1
AB-FUBINACA 1
MDMB-FUBINACA 2
5F-MDMB-PICA 3
MN2201 4
AB-PINACA 4
AB-CHMINACA 4
ADB-CHMINACA 5
5F-UR-144 6
MMB-CHMICA 10
5F-AMB 11
5F-EDMB-PINACA 15
ADB-FUBINACA 34
5F-MDMB-PINACA 76
FUB-AMB 135

5F-EDMB-PINACA and 5F-MMB-PICA were reported for the first time during the first half of CY 2018.

FUB-AMB was the most prevalent synthetic cannabinoid in 2017 and continues to be the most identified synthetic cannabinoid in the first half of CY 2018.

OPIOIDS/ANALGESICS

THERE WERE 1713 IDENTIFICATIONS OF FENTANYL, FENTANYL-RELATED COMPOUNDS, AND OTHER NEW OPIOIDS. FENTANYL ACCOUNTED FOR ~75% OF THE OPIOID IDENTIFICATIONS. OF THE 1279 FENTANYL IDENTIFICATIONS, FENTANYL WAS FOUND AS THE ONLY CONTROLLED SUBSTANCE IN ~37% OF THE IDENTIFICATIONS AND WITH HEROIN IN 48% OF THE IDENTIFICATIONS.

p-Fluorobutyryl fentanyl 1
Despropionyl-p-fluorofentanyl 1
Benzoyl fentanyl 1
4'-Methyl acetyl fentanyl 1
Valeryl fentanyl 2
N-Methyl norfentanyl 2
Isopropyl U-47700 2
U-48800 3
NPP 3
2-Thiofuranyl fentanyl 3
Benzylfentanyl 4
Acryl fentanyl 6
2-Furanylbenzyl fentanyl 6
3-Methylfentanyl 8
Furanyl fentanyl 17
Carfentanil 21
U-47700 23
Butyryl fentanyl 23
Methoxyacetylfentanyl 37
Cyclopropylfentanyl 38
4-PIBP 41
Acetylfentanyl 77
4-ANPP 114
Fentanyl 1279

4-ANPP was the second most predominant substance accounting for ~7% of the identifications.

Isopropyl-U-47700, 4'-methyl acetylfentanyl and N-methyl norfentanyl were identified for the first time during the first half of CY 2018.

CATHINONES

THERE WERE 141 CATHINONE IDENTIFICATIONS THIS REPORTING PERIOD. N-ETHYLPENTYLONE CONTINUES TO BE THE MOST REPORTED CATHINONE, ACCOUNTING FOR ~64% OF THE IDENTIFICATIONS.

N,N-Dimethylpentylone 1
MMMP 1
Methylone 1
3,4-MDDMC 1
α-PPP 1
α-PVP 1
4-Methylpentedrone 1
4-MEC 1
N-Ethyl-4-methylpentedrone 1
Pentylone 2
4-CEC 2
Ethylone 3
4F-α-PHP 4
4-Cl-α-PVP 4
N-Ethylhexedrone 11
Dibutylone 16
N-Ethylpentylone 90

N-Ethylhexedrone was reported for the first time during the first half of CY 2018.

PVP = Pyrrolidinovalerophenone
PHP = Pyrrolidinohexanophenone
CEC = Chlorocathinone
MEC = Methylcathinone
PPP = Pyrrolidinopropiophenone
MDDMC = Methylenedioxydimethylcathinone
MMMP = Methylmethylthiomethcathinopropiophenone

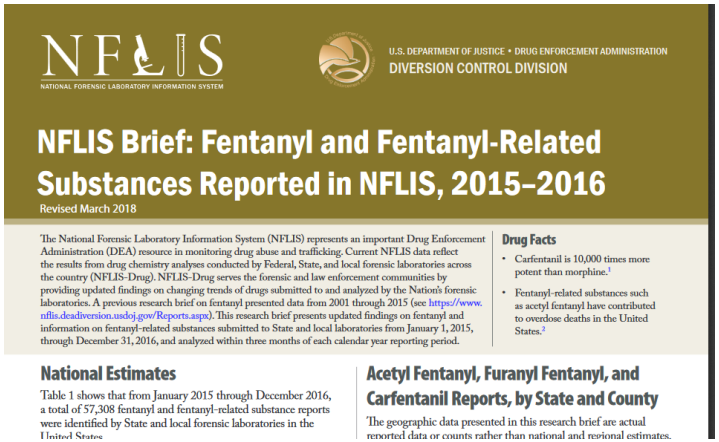
BENZODIAZEPINES

THERE WERE 8 IDENTIFICATIONS OF ETIZOLAM AND 1 IDENTIFICATION OF FLUBROMAZOLAM THIS REPORTING PERIOD.

OTHER

THERE WERE 53 INSTANCES OF UNCONFIRMED SUBSTANCES DURING THIS REPORTING PERIOD. ADDITIONALLY, THERE WERE 4 IDENTIFICATIONS OF BZP, 3 IDENTIFICATIONS EACH OF 2C-B, 3-METHOXY-PCP, DBZP AND MITRAGYNINE, 2 IDENTIFICATIONS OF TFMPP, 1 IDENTIFICATION EACH OF 2C-H, 2C-I, 5-METHOXY-DALT, 5-METHOXY DIPT, DMAA, AND "UNKNOWN".

Questions about this data are welcome and may be directed to the DEA Emerging Trends Program at 703-668-3300 or DEA.Emerging.Trends@usdoj.gov.



NFLIS
NATIONAL FORENSIC LABORATORY INFORMATION SYSTEM

U.S. DEPARTMENT OF JUSTICE • DRUG ENFORCEMENT ADMINISTRATION
DIVERSION CONTROL DIVISION

NFLIS Brief: Fentanyl and Fentanyl-Related Substances Reported in NFLIS, 2015–2016

Revised March 2018

The National Forensic Laboratory Information System (NFLIS) represents an important Drug Enforcement Administration (DEA) resource in monitoring drug abuse and trafficking. Current NFLIS data reflect the results from drug chemistry analyses conducted by Federal, State, and local forensic laboratories across the country (NFLIS-Drug). NFLIS-Drug serves the forensic and law enforcement communities by providing updated findings on changing trends of drugs submitted to and analyzed by the Nation's forensic laboratories. A previous research brief on fentanyl presented data from 2001 through 2015 (see https://www.nflis.deadiversion.usdoj.gov/Reports.aspx). This research brief presents updated findings on fentanyl and information on fentanyl-related substances submitted to State and local laboratories from January 1, 2015, through December 31, 2016, and analyzed within three months of each calendar year reporting period.

Drug Facts

- Carfentanil is 10,000 times more potent than morphine.[1]
- Fentanyl-related substances such as acetyl fentanyl have contributed to overdose deaths in the United States.[2]

National Estimates

Table 1 shows that from January 2015 through December 2016, a total of 57,308 fentanyl and fentanyl-related substance reports were identified by State and local forensic laboratories in the United States

Acetyl Fentanyl, Furanyl Fentanyl, and Carfentanil Reports, by State and County

The geographic data presented in this research brief are actual reported data or counts rather than national and regional estimates.

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

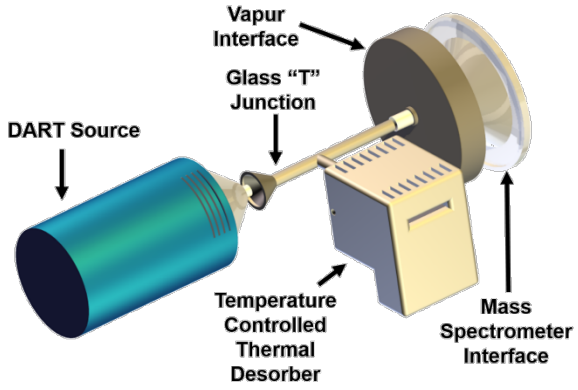
Immunoassay

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



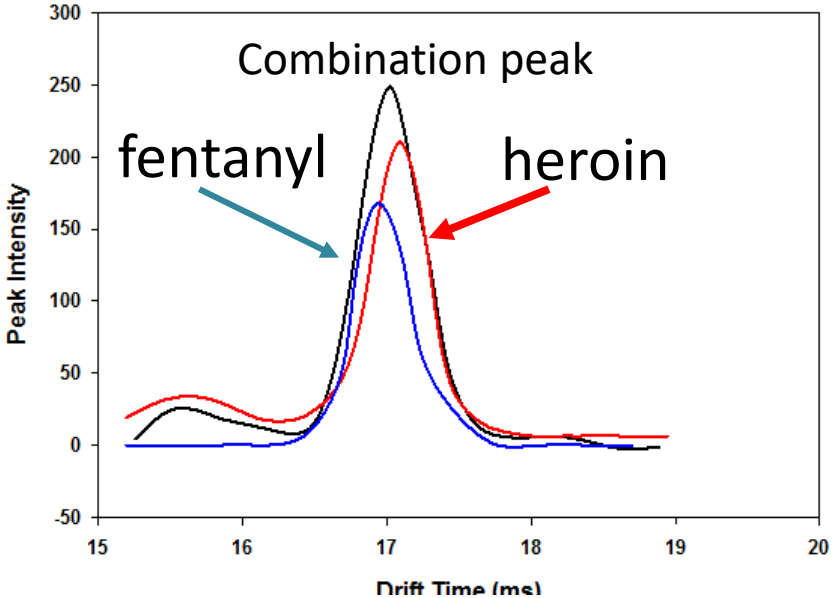
Results from Initial Study

- 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

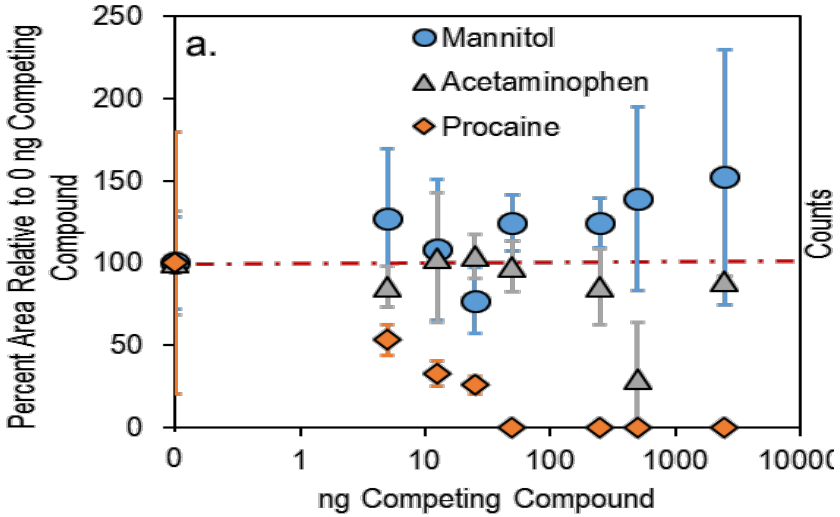
Resolution

- 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

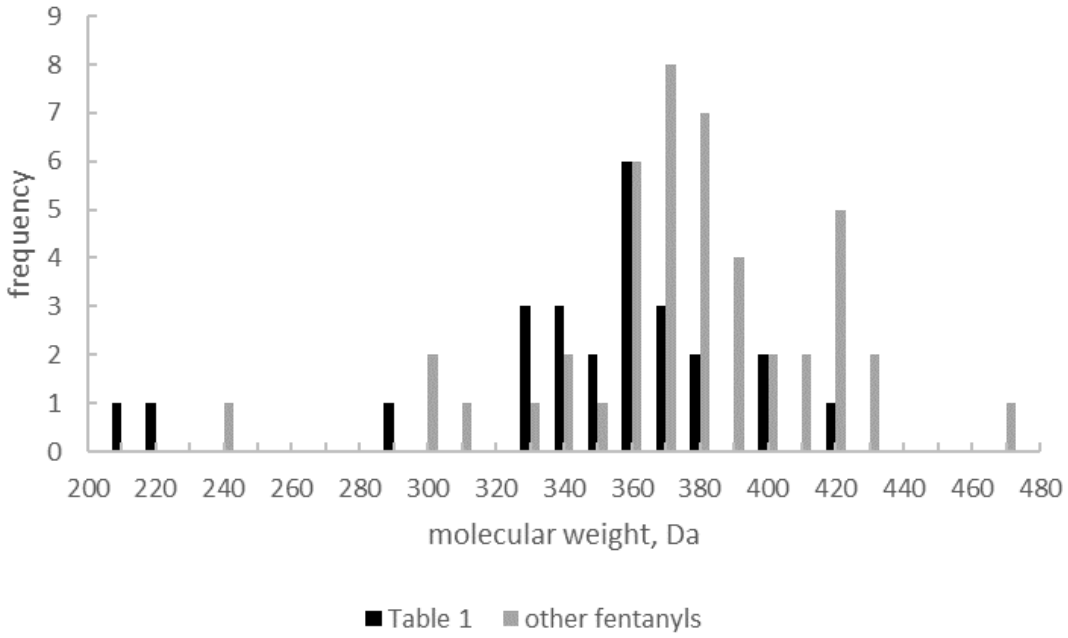
- **6 Commercial IMS Detectors**
  - Potential repurposing of retired explosives detectors
- **Tested to common sample set**
  - Selection of analogs
  - Excipients and ratios
- **Evaluate selectivity and sensitivity**
  - Pure
  - Mixtures with heroin
  - Mixtures with excipients
- **Exercised specific 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

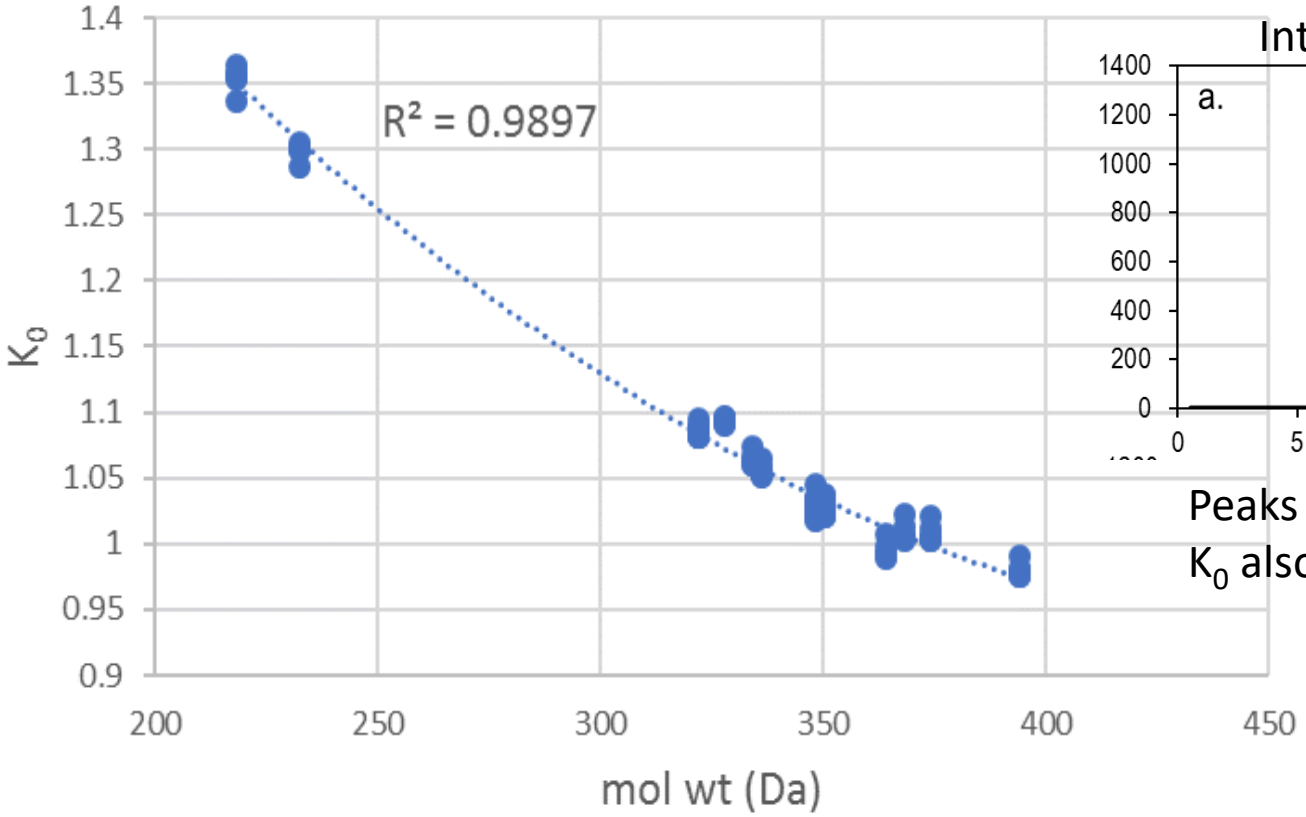
- Could entrain residual vapors
- Testing involved repeated doses of many different fentanyls

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

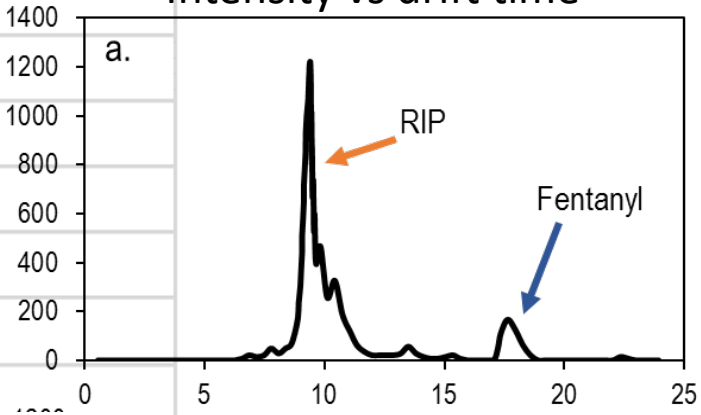
Air flow after sampling

All Compounds Detected by All Instruments

Reduced Mobility (K_0) vs Molecular Weight



Intensity vs drift time



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

K_0 also affected by structure

Compound	measured K_0 avg (std)
U-47700	1.093 (0.003)
Acetyl fentanyl	1.086 (0.005)
Benzylfentanyl	1.086 (0.003)
Acryl fentanyl	1.065 (0.005)
Fentanyl	1.056 (0.005)
THC	1.051 (0.006)
Heroin	1.042 (0.006)
Cyclopropylfentanyl	1.034 (0.006)
trans-3-Methylfentanyl	1.028 (0.006)
Butyryl fentanyl	1.026 (0.006)
Crotonyl fentanyl	1.024 (0.006)
p-FIBF	1.009 (0.007)
Furanyl fentanyl	1.008 (0.007)
Valeryl fentanyl	0.995 (0.007)
Carfentanil	0.980 (0.006)
(Buprenorphine)	~0.91

- Averages and uncertainties over all 6 instruments
- Within instrument uncertainty can be much lower

K_0 Used in Detection Libraries

For detection algorithm, window will be set about library value of K_0 (or drift time)

Fentanyl K_0	Inst. 1	Inst. 2	Inst. 3	Inst. 4	Inst. 5	Inst. 6
average	1.0523	1.0518	1.0583	1.0563	1.0645	1.0516
1 stdev	0.0001	0.0019	0.0005	0.0036	0.0025	0.0002

- The uncertainties in peak position (K_0) will influence size of detection windows
- Smallest detection windows typically ± 0.003

Additional components can change K_0

Mixtures	Δ k0 relative to pure fentanyl					
10:1 heroin	-0.0044	-0.0081	-0.0002	-0.0011	0.0001	-0.0137
100:1 heroin	-0.0044	-0.0076	0.0008	0.0030	-0.0057	-0.0015
100:1 procaine	-0.0009	-0.0067	0.0002	np	np	-0.0007
100:1 quinine	-0.0018	0.0029	-0.0027	0.0044	-0.0153	-0.0016

All Instruments Sensitive to Nanograms

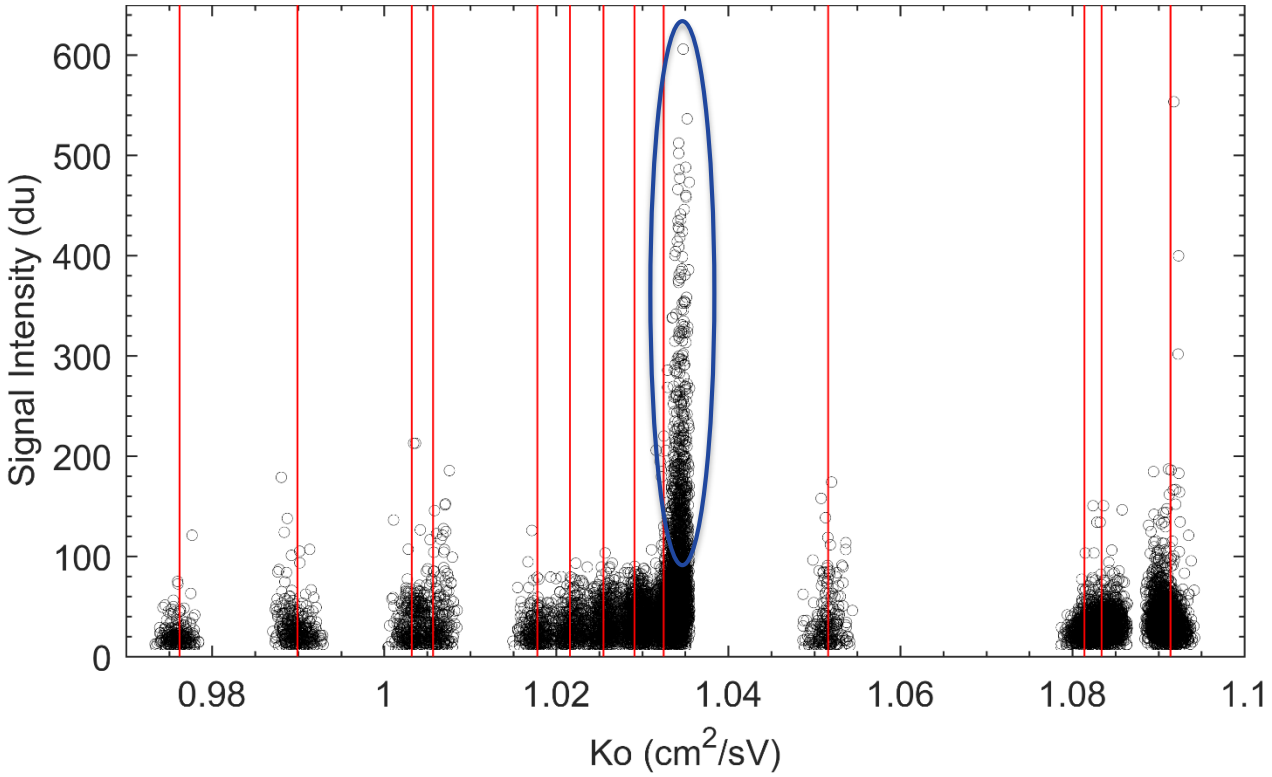
Limit of Detection (LOD) and Upper Confidence Limits (UCL) in nanograms

Fentanyl	Inst. 1	Inst. 2	Inst. 3	Inst. 4	Inst. 5	Inst. 6
LOD 90	51.7	0.6	7.0	2.3	24.2	1.4
90% UCL LOD	87.5	1.0	13.5	4.5	49.1	2.0
Benzylfentanyl						
LOD 90	34.6	0.5	10.8	1.2	17.7	0.8
90% UCL LOD	63.9	0.9	16.5	2.3	29.1	1.2

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

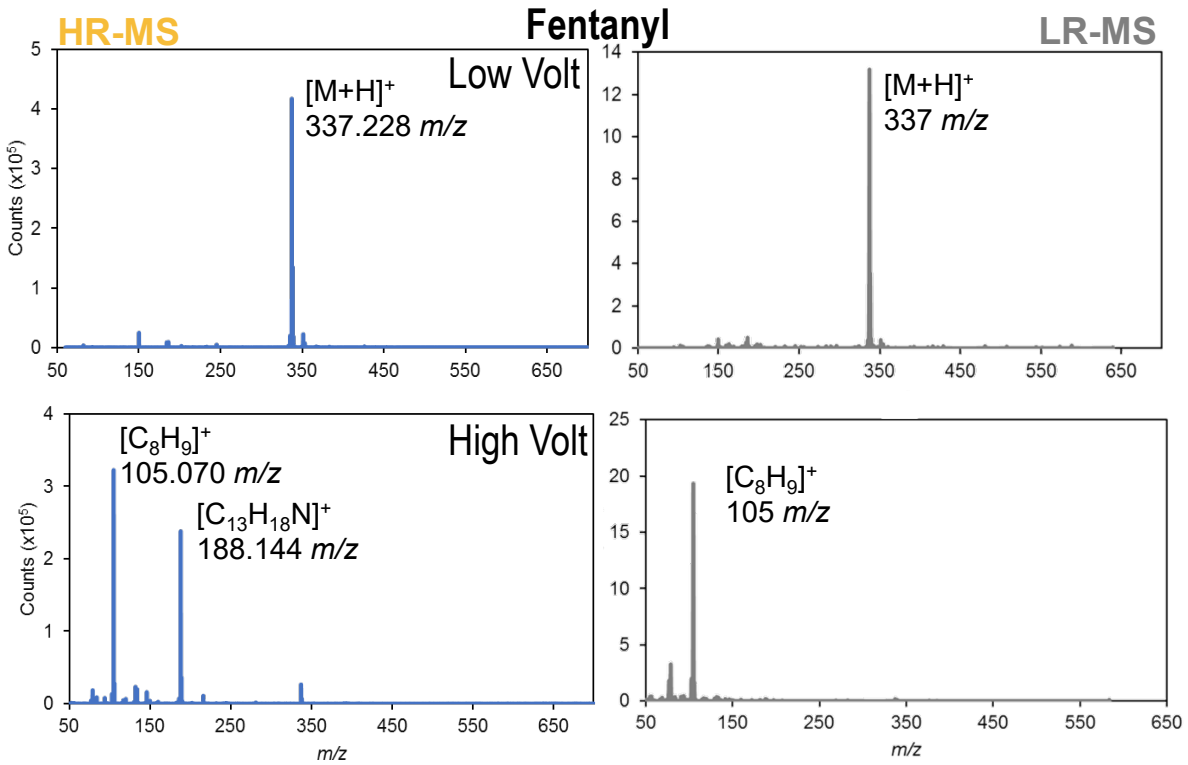
- Background from deployed condition (vehicle screening) o.k.

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