Department of Defense
Drug Demand Reduction Program

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DoD Drug Testing Enterprise

NDSL = Navy Drug Screening Laboratory
FTDTL = Forensic Toxicology Drug Testing Laboratory (ARMY)
AFDTL = Air Force Drug Testing Laboratory
SFTDTL = Special Forensic Toxicology Drug Testing Laboratory at the Armed Forces Medical Examiner System (AFMES)
Achieving Agility

• Agility model used by the Drug Demand Reduction Program (DDRP)
  ➢ Central, tri-Service governance body: Biochemical Testing Advisory Board
    ▪ Assess: perpetual SWOT analysis
      o Expanded Quality Assurance and surveillance programs
    ▪ Decide: ends, ways, and means analysis to move forward
      o Capital resource investments: common, new technologies, infrastructure
      o Expanded testing panel (e.g., fentanyl, LSD, delta-8-THC)
    ▪ Implement: decisions acted upon
      o Enabling policies
      o Standardized, coordinated
      o Centralized development, decentralized execution
    ▪ Assure: via measures of effectiveness
      o Compliance monitoring
      o Oversight
      o Reporting
Agility #1: Introduction of Rapid Fire-Mass Spectrometry Screening

**LSD**
- Resurgence of LSD use among the military population; reintroduced to the DoD drug panel in December 2020.
- Only one commercially available IA kit; poor specificity
- Developed a MS adjunct drug screening method.

**Synthetic Cannabinoids (SYCANS)**
- Developed a primary MS screening method; 3 current panel analytes (JWH-018, JWH-073, and MAM-2201).

**Amphetamines/Designer Amphetamines**
- Current confirmation rates across all 5 labs are extremely low.
- Developed an adjunct MS screening method.
RapidFire-MS/MS Workflow
Agility #1: Introduction of Rapid Fire-Mass Spectrometry Screening

Methods:

✓ Solid phase extraction (SPE) methods were developed and optimized for a RapidFire-365 high-throughput system coupled to an Agilent 6460 triple quadrupole mass spectrometer.

✓ LSD method targets 2-oxo-3-hydroxy LSD (OHLSD), the primary metabolite of LSD.

✓ SYCAN method targets JWH-018, JWH-073, and MAM-2201.

✓ AMPS method targets amphetamine (AMP), methamphetamine (METH), 3,4-methylenedioxyamphetamine (MDA), and 3,4-methylenedioxymethamphetamine (MDMA).

✓ Each method uses a single, appropriate, deuterated internal standard.

✓ Validation: precision, accuracy, linearity, and stability.
Agility #1: Introduction of Rapid Fire-Mass Spectrometry Screening

Methods – LSD
Automated sample preparation and plating on the Hamilton MicroLab STAR

1. Aliquot 4 µL urine to 96 well plate
2. Add 1 mL diluent (10 pg/mL LSD-d3 in 10 mM ammonium carbonate)
3. Seal plate and mix on heater/shaker deck for 5 minutes
4. Transfer to RapidFire/MS/MS for analysis (19 s/sample)

2-oxo-3-hydroxy-LSD
Agility #1: Introduction of Rapid Fire-Mass Spectrometry Screening

Methods – LSD

OHLSD had $R^2$ values $>0.995$. Limits were not pushed to failure since the methods are meant for screening purposes only.

$$y = 0.3058x + 0.0063$$

$$R^2 = 0.9955$$

OHLSD standard curves in urine had excellent linearity within the measured range of 0.25-0.8 ng/mL.
Agility #1: Introduction of Rapid Fire-Mass Spectrometry Screening

Methods – Synthetic Cannabinoids
Automated sample preparation and plating using a Hamilton MicroLab STAR

Aliquot 20 µL urine to 96 well plate
↓
Add 1 mL diluent (250 pg/ml d5 JWH-073 n-butanoic acid in H₂O/MeOH/Formic Acid (50:50:0.1%))
↓
Seal plate and mix on heater/shaker deck for 5 minutes
↓
Transfer to RapidFire/MS/MS for analysis (19 s/sample)

JWH-018
JWH-073
MAM-2201
Agility #1: Introduction of Rapid Fire-Mass Spectrometry Screening

Methods – SYCANS

All analytes had $R^2$ values greater than 0.995. Limits were not pushed to failure since the methods are meant for screening purposes only.

- JWH-018: $y = 1.0102x + 0.16$
  $R^2 = 0.9995$
- JWH-073: $y = 0.9972x + 0.56$
  $R^2 = 0.9995$
- MAM-2201: $y = 1.0464x - 0.53$
  $R^2 = 0.9985$
Agility #1: Introduction of Rapid Fire-Mass Spectrometry Screening

Methods – Amphetamines
Automated sample preparation and plating using a Hamilton MicroLab STAR

1. Aliquot 1 µL urine to 96 well plate
2. Add 1 mL diluent (2 ng/mL methamphetamine-d14 in water)
3. Seal plate and mix on heater/shaker deck for 5 minutes
4. Transfer to RapidFire/MS/MS for analysis (14.6 s/sample)

Chemical structures:
- Amphetamine
- Methamphetamine
- MDA
- MDMA
Agility #1: Introduction of Rapid Fire-Mass Spectrometry Screening

Methods – Amphetamines

All analytes had $R^2$ values >0.995. Limits were not pushed to failure since the methods are meant for screening purposes only.

AMP/METH standard curves in urine had excellent linearity within the measured range of 50-150 ng/mL

$$y = 0.0006x - 0.0009$$  
$$R^2 = 0.9986$$

$$y = 0.0004x + 0.0008$$  
$$R^2 = 0.9986$$

AMP/METH standard curves in urine had excellent linearity within the measured range of 250-750 ng/mL

$$y = 0.0002x - 0.0003$$  
$$R^2 = 0.9998$$

$$y = 0.0002x - 0.0018$$  
$$R^2 = 0.9989$$

MDMA/MDA standard curves in urine had excellent linearity within the measured range of 250-750 ng/mL

$$y = 0.0002x - 0.0018$$  
$$R^2 = 0.9989$$

$$y = 0.0002x - 0.0003$$  
$$R^2 = 0.9998$$
Agility #1: Introduction of Rapid Fire-Mass Spectrometry Screening

Testing Results – LSD, Dec 2020 – Sep 2021

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of specimens screened with IA for LSD</td>
<td>214,460</td>
</tr>
<tr>
<td>Number of non-negative specimens from IA</td>
<td>10,051</td>
</tr>
<tr>
<td>Number of “presumptive positive” specimens from RF</td>
<td>288</td>
</tr>
<tr>
<td>Percentage of specimens sent to confirmation after RF</td>
<td>2.8%</td>
</tr>
<tr>
<td>Number of specimens confirmed positive</td>
<td>77</td>
</tr>
<tr>
<td>Reduction in confirmation workload</td>
<td>97.2%</td>
</tr>
<tr>
<td>Confirmation rate</td>
<td>26.7%</td>
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</tbody>
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Way Forward for RF-MS/MS

• Adjunct AMPS methods nearly online – programming LIMS.

• Reevaluating SYCAN screening on the RF-MS/MS.
  • Updating the testing panel to address more prevalent SYCANS.
  • Targeting common transitions rather than unique analytes.

• Fentanyl adjunct method.
The DDRP began seeing an “interferent” in its cannabinoid cases in April 2019.

The Problem
Urine sample containing a partially-resolved interference.
• Integrated peak (blue peak) is Δ9-THC-COOH.
• Presence of Δ8-THC-COOH can cause false negative results for Δ9-THC-COOH because of chromatographic interference.
• Must report out Δ9-THC-COOH as negative due the peak not meeting acceptance criteria (resolution).

The Solution
Urine sample showing the isomeric differentiation of Δ8-THC-COOH and Δ9-THC-COOH.
• The integrated peak (blue peak) is Δ8-THC-COOH.
• DDRP now has the ability to differentiate between Δ9-THC-COOH and Δ8-THC-COOH and can report results for both.
Agility #2: Recent Addition of Delta-8-THC

- Delta-8-THC is controlled under the CSA as a “tetrahydrocannabinol”.
- Delta-8-THC is considered to be a synthetic derivative of THC. Even though delta-8 is naturally occurring at low levels, the amounts found in the commercially available hemp, CBD and delta-8 products can only be achieved through a chemical reaction.
- Testing requires long run times ranging from 11 to 20 minutes.
- Cannabinoid testing to date: 66% delta-9 only, 18% delta-8 only, 15% delta-9 and delta-8 (cutoff 15 ng/mL).
Conclusions

• Using our agility model has allowed the DDRP to quickly adjust to emerging drug threats new technologies.

• The LSD confirmation workload is reduced substantially with the addition of RF-MS/MS as an adjunct screening technique.

• The DDRP is seeing a large number of delta-8-THC positives – 18% of those positives are delta-8-THC alone!