Table S1. Target analytes and corresponding internal standards.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Internal Standard</th>
</tr>
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<tbody>
<tr>
<td>Methamphetamine</td>
<td>Methamphetamine-d8</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>Amphetamine-d8</td>
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<tr>
<td>3,4-Methylenedioxymethamphetamine</td>
<td>3,4-Methylenedioxymethamphetamine-d5</td>
</tr>
<tr>
<td>3,4-Methylene-dioxyamphetamine</td>
<td>3,4-Methylene-dioxyamphetamine -d5</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Ketamine-d4</td>
</tr>
<tr>
<td>Norketamine</td>
<td>Norketamine-d4</td>
</tr>
<tr>
<td>6-Acetylmorphine</td>
<td>6-Acetylmorphine-d6</td>
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<tr>
<td>Morphine</td>
<td>Morphine-d3</td>
</tr>
<tr>
<td>Codeine</td>
<td>Codeine-d6</td>
</tr>
<tr>
<td>Methadone</td>
<td>Methadone-d9</td>
</tr>
<tr>
<td>2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine</td>
<td>2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine-d3</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Cocaine-d3</td>
</tr>
<tr>
<td>Benzoylecgonine</td>
<td>Benzoylecgonine-d3</td>
</tr>
<tr>
<td>Cathinone</td>
<td>Cathinone-d5</td>
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<tr>
<td>Mephedrone</td>
<td>Mephedrone-d3</td>
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<tr>
<td>p-Methoxymethamphetamine</td>
<td>p-Methoxymethamphetamine-d3</td>
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<td>Benzylpiperazine</td>
<td>Benzylpiperazine-d7</td>
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<td>1-(3-chlorophenyl) Piperazine</td>
<td>1-(3-chlorophenyl) Piperazine-d8</td>
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<td>3-Trifluoromethylphenylpiperazine-d4</td>
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<td>4-Iodo-2,5-Dimethoxyphenethylamine</td>
<td>4-Iodo-2,5-Dimethoxyphenethylamine-d3</td>
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<td>Tramadol</td>
<td>Tramadol-13C-d3</td>
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<td>Fentanyl</td>
<td>Fentanyl-d5</td>
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<td>Methylone</td>
<td>Methylone-d3</td>
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<td>3,4-Methylenedioxypyrovalerone</td>
<td>3,4-Methylenedioxypyrovalerone-d8</td>
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Figure S1. The elution gradient of mobile phase B (MeOH).
Figure S2. Chromatogram of 24 analyzed substances (a) and their corresponding deuterated (b).
Table S2. MS parameters (quantifier and qualifier ions), declustering potential, collision energy and retention time.

<table>
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<tr>
<th>Analyte</th>
<th>Retention time (min)</th>
<th>Precursor Ion (m/z)</th>
<th>Declustering Potential (V)</th>
<th>Quantifier</th>
<th>Qualifier</th>
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<th>enantiomer purity (%)</th>
<th>Alkylation Position</th>
<th>Sample Preparation</th>
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<td>163.0</td>
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<td>158.1</td>
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<td>342.3</td>
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<td>268.4</td>
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<td>58.1</td>
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<td>Methylone-d3</td>
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<td>4.68</td>
<td>211.3</td>
<td>50</td>
<td>162.9</td>
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<td>284.1</td>
<td>80</td>
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Table S3. Method validation parameters: recovery, matrix effect, repeatability, reproducibility, LOD, LOQ and procedure bank.

<table>
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<tr>
<th>Analyte</th>
<th>Recovery 400 ng/L (n = 3) (%)</th>
<th>Matrix 10 μg/L (n = 5) (RSD %)</th>
<th>Repeatability</th>
<th>Reproducibility</th>
<th>LOD *</th>
<th>LOQ *</th>
<th>Procedure Bank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methamphetamine</td>
<td>92.2 ± 4.2</td>
<td>−5.5 ± 8.8</td>
<td>2.3</td>
<td>4.3</td>
<td>0.2</td>
<td>0.8</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>98.7 ± 5.5</td>
<td>−2.1 ± 0.9</td>
<td>5.8</td>
<td>8.8</td>
<td>2.0</td>
<td>4.0</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Ketamine</td>
<td>97.6 ± 5.5</td>
<td>−3.0 ± 2.3</td>
<td>4.3</td>
<td>5.8</td>
<td>0.2</td>
<td>0.8</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Norketamine</td>
<td>98.2 ± 6.2</td>
<td>4.9 ± 5.8</td>
<td>2.5</td>
<td>3.9</td>
<td>2.0</td>
<td>0.8</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Morphine</td>
<td>95.6 ± 13.6</td>
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<td>6.1</td>
<td>0.5</td>
<td>2.0</td>
<td>&lt;LOD</td>
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<tr>
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<td>95.3 ± 6.2</td>
<td>0.2 ± 10.0</td>
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<td>9.1</td>
<td>0.5</td>
<td>2.0</td>
<td>&lt;LOD</td>
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<tr>
<td>6-Acetylmorphine</td>
<td>83.6 ± 10.1</td>
<td>17.2 ± 7.3</td>
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<td>3.6</td>
<td>0.5</td>
<td>0.8</td>
<td>&lt;LOD</td>
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<td>95.1 ± 8.2</td>
<td>−4.2 ± 2.0</td>
<td>4.8</td>
<td>5.5</td>
<td>0.2</td>
<td>0.8</td>
<td>&lt;LOD</td>
</tr>
<tr>
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<td>96.1 ± 3.6</td>
<td>−6.3 ± 1.3</td>
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<td>3.7</td>
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<td>3.3</td>
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<td>−1.2 ± 5.5</td>
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<td>5.1</td>
<td>0.2</td>
<td>0.8</td>
<td>&lt;LOD</td>
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<tr>
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<td>104.9 ± 3.8</td>
<td>0.6 ± 4.1</td>
<td>3.9</td>
<td>4.0</td>
<td>0.2</td>
<td>0.8</td>
<td>&lt;LOD</td>
</tr>
<tr>
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<td>−10.3 ± 3.5</td>
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<td>6.4</td>
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<td>−0.4 ± 3.6</td>
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<td>6.7</td>
<td>0.2</td>
<td>0.8</td>
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<td>0.2</td>
<td>0.8</td>
<td>&lt;LOD</td>
</tr>
</tbody>
</table>

* LOD—limit of detection; b LOQ—limit of quantification; c RSD—relative standard deviation.
Table S4. The human excretion factors of the target drugs, molecular weight ratio of parent and metabolite and typical dose.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Selected Biomarker</th>
<th>Excretion Factor (%)</th>
<th>MW_p/MW_m</th>
<th>Typical Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methamphetamine</td>
<td>Methamphetamine</td>
<td>43[1]</td>
<td>1.00</td>
<td>30 [2]</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Ketamine</td>
<td>16 b[2,3]</td>
<td>1.00</td>
<td>75 [2]</td>
</tr>
<tr>
<td>MDMA</td>
<td>MDMA</td>
<td>26 [4]</td>
<td>1.00</td>
<td>100 [1]</td>
</tr>
<tr>
<td>Codeine</td>
<td>Codeine</td>
<td>30 [5]</td>
<td>1.00</td>
<td>38 [3]</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Tramadol</td>
<td>30 [2]</td>
<td>1.00</td>
<td>50 [2]</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Benzoylcegonine</td>
<td>29 [6]</td>
<td>1.05</td>
<td>100 [1]</td>
</tr>
<tr>
<td>Morphine</td>
<td>Morphine</td>
<td>77.7 [7]</td>
<td>1.00</td>
<td>20 d[8]</td>
</tr>
</tbody>
</table>

MW_p/MW_m—molecular weight ratio of parent and metabolite; Mean excretion factor; MDMA—3,4-Methylenedioxyamphetamine; d Assume the typical dose is same to heroin based on the similar structures.

Table S5. Number of drug dependents of amphetamine-type stimulants and opiates in Malaysia from 2013–2017 [10].

<table>
<thead>
<tr>
<th>Year</th>
<th>Opiates</th>
<th>Methamphetamine</th>
<th>Amphetamine-type stimulants tablets *</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>16041</td>
<td>3008</td>
<td>476</td>
</tr>
<tr>
<td>2014</td>
<td>14502</td>
<td>5356</td>
<td>1774</td>
</tr>
<tr>
<td>2015</td>
<td>16616</td>
<td>8807</td>
<td>1309</td>
</tr>
<tr>
<td>2016</td>
<td>16985</td>
<td>12738</td>
<td>3395</td>
</tr>
<tr>
<td>2017</td>
<td>10154</td>
<td>14785</td>
<td>5130</td>
</tr>
</tbody>
</table>

* Includes methamphetamine, ecstasy type (MDMA) and amphetamine.

References:


