New Psychoactive Substances - Are We Doing Enough?

July 2014

Science for a safer world

LGC Classification: NOT PROTECTIVELY MARKED
Background
New Psychoactive Substances (NPS)

NPS (often called legal highs) cover a wide range of substances:

1. Products with names which give no indication of what they contain, Vertex Pirate Edition
2. Named and specific substances which are designed to be similar chemically and/or pharmacologically to known specific controlled drugs, for example many synthetic cannabinoids
3. Substances related to medicines, such as 2-MeO-2-deschloroketamine
4. Herbal and fungal materials or their extracts, salvia
Increasing Prevalence

- New psychoactive substances reported are increasing (EMCDDA)
Legal Status of Legal Highs

- Legislation is slow to react to new drugs
- Many NPS are not controlled
- Fast track system – ‘Temporary Class Drugs’ in place to cover supply of most serious compounds
  - Issued for benzofury (5/6 APB), NBOMe compounds and methoxetamine
Hot of the press:- Queen’s Speech in UK at opening of new parliament

- New UK government approach to Legal Highs

The main elements of the Bill are:

- The Bill would make it an offence to produce, supply, offer to supply, possess with intent to supply, import or export psychoactive substances; that is, any substance intended for human consumption that is capable of producing a psychoactive effect. The maximum sentence would be seven years’ imprisonment.
Risks

• Legal does **NOT** mean safe
• Most (excl prescription) not tested in humans
• Health risks (short and long term) are often not understood
• Impairment outcomes are often not understood
• Not guaranteed that you are taking what you think you are - hence possible unexpected consequences
Traditional Techniques

• Workplace drug testing
• Screened on clinical analysers or using point of care tests (POCT) using immunoassay
• Limited panel of substances
• High throughput
• Cheap
• New reagents can take a while to develop
Alternative Approach

- High resolution accurate mass (HRAM) LCMS to cover much broader range of analytes.
- Quick and easy to update analyte coverage
- Expensive capital purchase
- Requires high level of technical expertise
Findings

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City Centre Study

‘Night time’ economy study:
1. Pooled urine samples from urinals
2. Taken from night clubs and city centre
3. Alternative approach as opposed to self reporting
4. HRAM screening
5. 164 different substances found, including synthetic steroids, drugs of abuse, prescription and over the counter medication, and NPS
<table>
<thead>
<tr>
<th>Compounds detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,4 methoxyphenylpiperazine</td>
</tr>
<tr>
<td>4 methylethcathinone</td>
</tr>
<tr>
<td>4-ethylmethcathinone</td>
</tr>
<tr>
<td>4-fluoroephedrine</td>
</tr>
<tr>
<td>4-methylmethcathinone</td>
</tr>
<tr>
<td>5/6-APB</td>
</tr>
<tr>
<td>Ambroxol</td>
</tr>
<tr>
<td>Amisulpiride</td>
</tr>
<tr>
<td>Amitriptyline</td>
</tr>
<tr>
<td>Amphetamine</td>
</tr>
<tr>
<td>Amphetamine</td>
</tr>
<tr>
<td>Arecoline</td>
</tr>
<tr>
<td>Atenolol</td>
</tr>
<tr>
<td>Benzocaine</td>
</tr>
<tr>
<td>Benzoylcegonine</td>
</tr>
<tr>
<td>Benzydamine</td>
</tr>
<tr>
<td>Bisoprolol</td>
</tr>
<tr>
<td>Bromhexine</td>
</tr>
<tr>
<td>Buprenorphine</td>
</tr>
<tr>
<td>Buprenophine-nor</td>
</tr>
<tr>
<td>Caffeine</td>
</tr>
<tr>
<td>Camphor</td>
</tr>
<tr>
<td>Capsaicin</td>
</tr>
<tr>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Carboxy THC</td>
</tr>
<tr>
<td>Cathine</td>
</tr>
<tr>
<td>Cathinone</td>
</tr>
<tr>
<td>Celecoxib</td>
</tr>
<tr>
<td>Cetirizine</td>
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<tr>
<td>Chlorzylazine</td>
</tr>
</tbody>
</table>
Coverage vs Traditional Workplace test

Enhanced vs traditional workplace test on samples analysed to date

<table>
<thead>
<tr>
<th>Drugs detected on enhanced workplace test</th>
<th>Traditional workplace test drugs detected on enhanced screen</th>
<th>Drugs with potential for abuse</th>
<th>'Legal Highs' not covered by traditional workplace test</th>
</tr>
</thead>
<tbody>
<tr>
<td>164</td>
<td>21</td>
<td>67</td>
<td>25</td>
</tr>
</tbody>
</table>

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Population A

Specific study population – already undergoing ‘standard’ urine drug testing

1. Thousands of samples run
2. HRAM screening positive rate double the traditional type testing
3. Positives included controlled (classified) drugs not in routine testing panels – bufotenine
4. Non controlled substances which are suspected to have psychoactive outcomes not in routine testing – glaucine, 5F AKB-48.
5. Other substances (medication) available on prescription only not included in routine testing – zopiclone, gabapentin, pregabalin
Population B

Specific study population – already undergoing urine drug testing

1. Thousands of samples run
2. Current programme includes rudimentary NPS screening
3. HRAM screening positive rate over 18% on samples previously screened as negative
4. Anabolic steroid positive rate over 10%
# Synthetic Cannabinoids detected in study

<table>
<thead>
<tr>
<th>Substance</th>
<th>LGC Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>5F AB-PINACA</td>
<td>EAM-2201</td>
</tr>
<tr>
<td>5F AKB-48</td>
<td>FAM-2201</td>
</tr>
<tr>
<td>5F PB-22</td>
<td>MAM2201</td>
</tr>
<tr>
<td>5F UR-144</td>
<td>MDMB-CHMICA</td>
</tr>
<tr>
<td>AB-CHMINACAC</td>
<td>STS-135</td>
</tr>
<tr>
<td>AM-2201</td>
<td>THJ-018</td>
</tr>
<tr>
<td>AM694</td>
<td>THJ-2201</td>
</tr>
<tr>
<td>Cumyl 5F PINACA</td>
<td>UR-144</td>
</tr>
<tr>
<td>BB-22</td>
<td></td>
</tr>
</tbody>
</table>
Challenges

• Standards
  • Often not available, purchase and purify
• Metabolites
  • Often none are published, In-vitro options
• Interpretation
  • Limited peer reviewed options
• Employment Policy
  • Often limited to ‘impairment’, controlled substances, or listed drugs
• Current
  • Keeping up to date, ‘white powder’ analysis
In Vitro Metabolism

- Knowledge of breakdown in the body is required – metabolism
- Many drugs only leave detectable concentrations of metabolites and not parent drug
- Metabolite information for many NPS are not available
- Able to mimic metabolism in a test tube using the drug and enzymes from liver cells
- Information is then used in testing process
MDMB CHMICA

- Current synthetic cannabinoid in UK
- Related to deaths across Europe and USA
- No metabolism information
- No reference material for metabolite
In vitro data for MDMB-CHMICA

RT: 0.00 - 6.51

**Parent**

- m/z= 385.2456-385.2516 F: FTMS + c
- ESI Full ms [240.00-550.00] MS MDMBCHMICA

**Hydroxy metabolites**

- m/z= 401.2406-401.2465 F: FTMS + c
- ESI Full ms [240.00-550.00] MS MDMBCHMICA

**Di-hydroxy metabolites**

- m/z= 417.2351-417.2411 F: FTMS + c
- ESI Full ms [240.00-550.00] MS MDMBCHMICA

- m/z= 240.1352-240.1412 F: FTMS + c
- ESI Full ms2 395.00@hcd41.00 [95.00-500.00] MS MDMBCHMICA

- m/z= 256.1302-256.1362 F: FTMS + c
- ESI Full ms2 395.00@hcd41.00 [95.00-500.00] MS MDMBCHMICA

- m/z= 272.1246-272.1306 F: FTMS + c
- ESI Full ms2 395.00@hcd41.00 [95.00-500.00] MS MDMBCHMICA
MS/MS spectra on MDMB-CHMICA hydroxy metabolite
Major metabolite in positive urine
Questions?

• Can we use in vitro generated metabolites as reference materials where no other alternatives exist?