The EU Early Warning System: 20 years of monitoring New Psychoactive Substances in Europe

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NDEWS webinar: Examining Global Drug Early Warning Systems, Part 4: Monitoring Drug Trends in Europe

29 November 2017
20 years of monitoring NPS

+660 NPS monitored
~150 public health alerts
30 risk assessments

~300 NPS newly detected
+50 public health alerts
17 risk assessments

holistic approach
variety of information sources
triangulation of information

---since 2014---

Europol and EMA

EMCDDA

signal management
risk communication
early warning
risk assessment

police
customs
medicine regulators
public health
treatment providers
chemists
pathologists
toxicologists
policy makers
poison centres
researchers
data management
analysis

open source information

30
national early warning systems

Europol and EMA

police/customs seizures
serious adverse events
epidemiology

EMCDDA

signal management
risk communication
early warning
risk assessment
The EU EWS: who we are

1997: “New” drugs monitored under Joint Action 97/396/JHA
Until 2005: EMCDDA mainly collects data on a small number of drugs most of which controlled by the UN drug conventions


I. Information exchange
   Early-warning system (EWS) ➔ risk communication
   EMCDDA–Europol Joint Reports

II. Risk assessment ➔ EMCDDA Risk Assessments

III. Decision-making ➔ Council Decisions on control

formal notification
alerts
advisories
briefings

Future: new legislation – shorter deadlines
What we monitor......

2 types of drugs...
The EU EWS: definition and scope

‘New narcotic or psychotropic drug, in pure form or in preparation, that is not controlled by the 1961 or the 1971 UN Conventions, but which may pose a public health threat comparable to that posed by substances listed in Schedule I or II or IV of the former and in Schedule I or II or III or IV of the latter convention’ (CD 2005/387/JHA)

New psychoactive substances i.e. ‘New’ to the drug market or newly misused

Scope of the EU-EWS:

- Changes in purity of established (controlled) drugs
- Established (controlled) drugs adulterated with unusual and/or harmful cutting agents
- Substances sold as others e.g. heroin sold as cocaine
- New patterns (forms) of use e.g. injection of cathinones
- Fatal and non-fatal intoxications
- Large seizures, seizures that show evidence of international trafficking and/or involvement of organised crime
What should be reported?

Substances which are:

- Potentially psychoactive
- New (not listed in the UN conventions)

• But also:
  - Precursors
  - Medicines

In case of doubt, please report!!!
What should be reported?

First detection in Europe → formal notification
- EMCDDA-Europol Reporting Form
- Complete analytical report

First detection in the country → event-based data
- EMCDDA-Europol Reporting Form

Subsequent detections → aggregated data
- EWS Progress Reports (January – June)
- EWS Final Reports (July – December)
# Event-based seizures

EMCDDA-Europol Reporting Forms (RFs)

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**Reporting Form on New Psychoactive Drugs (NPS)**


1. **Transmitted by (EUROPEPOL) □**
2. **Transmitted by EMCCDA □**
3. **Ref: □**
4. **Date of transmision: □**

The following sections should be filled in by the European National Units (ENU) or REITOX National focal Points (NFP) based on the information available and their respective responsibilities.

### 1. **Market(s):**

- **Ref:** □
- **Date:** □

**Chemical name:** □

**Other name(s):** □

**Street name(s):** □

**5. Source of information (if one or more as appropriate):**

**Seizure(s):** □
- **Specify amount (weight, number of tablets, etc.):** □

**Seizure authority:** □
- **Date:** □
- **Place:** □

**Biological sample(s):** □
- **Specify type:** □

**Identifying authority:** □
- **Date:** □
- **Place:** □

**Collected sample(s):** □
- **Specify amount (weight, number of tablets, etc.):** □

**Collecting authority:** □
- **Date:** □
- **Place:** □

**Other substances present (if more than one case, specify for which one):** □

**Psychoactive ingredient(s):** □

**Other ingredients:** □

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1. **Physical description (in case of solidification):**

<table>
<thead>
<tr>
<th>Form</th>
<th>powder □</th>
<th>tablet □</th>
<th>capsule □</th>
<th>liquid □</th>
<th>other □</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>□</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. **For dosage unit: weight:** □

3. **Circumstance(s):** □

4. **Intrading:** □

5. **Price:** □

6. **Distribution:** □

7. **Use:** □

8. **Chemical precautions:** □

9. **Pattern(s) of use:** □

10. **Other possible uses:** □

11. **Related to:**

   - **Subjective (described by users):** □

12. **Context of use:**

   - **User group(s):** □

   - **Setting(s):** □

13. **Availability at consumer level:** □

14. **Indication on possible harm:** □

   - **Health (individual):** □

   - **Public health:** □

15. **Social:** □

   - **In case of production: large-scale □ small-scale □ unknown □**

   - **Has any form of organised crime been detected:** □

   - **In case of trafficking: large scale □ small scale □ unknown □**

   - **National □ International □**

   - **Has any form of organised crime been detected:** □

16. **In case of distribution: large scale □ small scale □ unknown □**

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*Biological (human) samples e.g. body fluids (urine, blood), tissues, hair, etc.

*Actively collected by drug monitoring system for monitoring or research purposes

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*For example, for medical, industrial, ritual, scientific, etc., purposes.*
EU EARLY WARNING SYSTEM FORMAL NOTIFICATION

1. Read me first
This email provides formal notification of the analytical identification of [IUPAC Name | Common Name] for the first time in Europe. [Insert any other relevant text]

2. Data use restrictions
As with all formal notifications issued by the EU EWS, the information contained herein is intended for use by public health officials and may not be broadly distributed. [Insert any other relevant text]

3. Names of substance and other identifiers
- IUPAC name:
- Chemical name:
- Common name:
- Other names:
- CAS Registry number:

4. Substance classification
[Amphetamine OR Amphetamine-like OR Amphetamine-analogue OR Benzodiazepine OR Cathinone OR Clandop OR Other OR Psychoactive substance OR Psychoactive OR Plant or Extract OR Psilocybin or Psilocin OR Synthetic cannabinoid OR Toxic substance]

5. Detection
Type [Seizure OR Collected sample OR Biological sample OR Other]
Details [Insert details OR No information OR Other]

6. Chemistry and analysis
[Insert summary of available information, including comments on any limitations of the method of analysis or relevant to the substance in question]

7. Pharmacology and toxicology
[Insert summary of available information or no information available at the time OR Check the EDMD profile for information]

8. Further information
[Insert other relevant information]

9. Acknowledgements
[Insert relevant acknowledgements]

10. Attachments
[There are no attachments to this document OR This email contains a total of X attachments]

11. References
[Insert relevant references]

(AND any other relevant details which are required to be transmitted to the reader)
### Aggregated data

**EWS Progress/Final Reports**

<table>
<thead>
<tr>
<th>Reporting authority, agency or company</th>
<th>Type of detection</th>
<th>NPS detected</th>
<th>Other NPS / substances detected</th>
<th>Physical form</th>
<th>Information relating to Biological samples</th>
<th>Number of cases</th>
<th>Quantity</th>
<th>Units of measurement</th>
<th>Additional information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Customs</td>
<td>S</td>
<td>1-acetyl-LSD / ALD-52</td>
<td>blotter</td>
<td>For biological samples, write in whether these relate to: • death(s) • non-fatal intoxication(s) • other(s) (write in the reason why the sample was analyzed (e.g. driving under the influence, drug treatment programme)).</td>
<td>1</td>
<td>8</td>
<td>pcs</td>
<td>Write in any additional information you have, such as: drug purities, laboratory or other source of data; qualitative data.</td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>1P-LSD</td>
<td>blotter</td>
<td>21</td>
<td>197</td>
<td>pcs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>2-, 3- or 4-CMC (cleftedrone)</td>
<td>powder</td>
<td>1</td>
<td>1.3</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>2-, 3- or 4-CMC (cleftedrone)</td>
<td>crystalline powder</td>
<td>2</td>
<td>164.5</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>2-, 3- or 4-fluoroamphetamine (2-, 3- or 4-FA-/FMP)</td>
<td>powder</td>
<td>1</td>
<td>1</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>2-, 3- or 4-fluoroamphetamine (2-, 3- or 4-FA-/FMP)</td>
<td>tablet</td>
<td>4</td>
<td>1053</td>
<td>pcs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>2-, 3- or 4-FMC</td>
<td>powder</td>
<td>3</td>
<td>2.6</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>2-, 3- or 4-MeO-PCP</td>
<td>powder</td>
<td>1</td>
<td>1.2</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>2-, 5-, or 6-methoxymethylene</td>
<td>powder</td>
<td>1</td>
<td>1.2</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>2-, 3, 4-, 5, 6- or 7-EAPB</td>
<td>powder</td>
<td>1</td>
<td>1.1</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>2-, 3-, 4-, 5, 6- or 7-EAPB</td>
<td>tablet</td>
<td>1</td>
<td>2</td>
<td>pcs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>25B-NBOH</td>
<td>blotter</td>
<td>1</td>
<td>20</td>
<td>pcs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Customs</td>
<td>S</td>
<td>25B-NBOMe</td>
<td>blotter</td>
<td>15</td>
<td>304</td>
<td>pcs</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Customs</td>
<td>S</td>
<td>25C-NBOMe</td>
<td>blotter</td>
<td>8</td>
<td>73</td>
<td>pcs</td>
<td></td>
<td></td>
<td></td>
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<td>25I-NBOH</td>
<td>blotter</td>
<td>3</td>
<td>1596</td>
<td>pcs</td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>Customs</td>
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<td>25I-NBOMe</td>
<td>blotter</td>
<td>3</td>
<td>3</td>
<td>pcs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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New psychoactive substances detected during the period covered by this report.

Refer to the worksheet NPS list for the list of NPS formally notified to the EWS system by 7 July 2014.

"Detections" is an all-encompassing term and includes seizures and/or collected and/or biological samples. Seizure means a substance available (seized) through law enforcement activities (police, customs, border guards, etc.). Collected and/or biological samples are samples taken by law enforcement activities which are not available (collected and/or biological samples) through legal processes (e.g. as part of court proceedings).
First detections of NPS in Europe
First detections of NPS in Europe

Synthetic cannabinoids

Opioids
Seizures of new psychoactive substances in Europe

Number of seizures of new psychoactive substances reported to the EU Early Warning System: trends and distribution by category in 2015

Cathinones 33%
Cannabinoids 29%
Benzodiazepines 11%

- Phenethylamines 6%
- Piperazaines 6%
- Others 5%
- Arylalkylamines 4%
- Arylcyclohexylamines 2%
- Tryptamines 1%
- Piperidines and pyrrolidines 1%
- Opioids 1%
Increasing seizures of synthetic cannabinoids and cathinones

Seizures of synthetic cannabinoids and cathinones reported to the EU Early Warning System: trends in number of seizures and quantity seized

Number of seizure cases

Cannabinoids

Number of seizure cases

Cathinones

Cannabinoids (tonnes)

Cathinones (tonnes)

Plant material | Powder | All other forms

| Powder | All other forms


Responding to NPS causing concerns

- Toxicovigilance system
- Signal Management system
- Risk Communication system
- Risk Assessments
Toxicovigilance

The active process of detecting, reporting, evaluating, understanding, monitoring and responding to adverse events associated with new psychoactive substances

In the context of early warning it focuses on serious adverse events…

Prioritisation: which substances should we react to?
Signal management system

Signal management is a stepwise process covering six steps; it begins with the detection of a signal and ends with a recommendation for action that details how we should react to the signal.

1. detection
2. validation
3. analysis
4. Prioritisation – which substances should we react to?
5. assessment
6. recommendation for action
a systematic, reproducible, and transparent approach to **detect**, **validate**, **understand**, **prioritise**, and **react** to signals, according to the **type** of risk that they pose, the **seriousness** of the risk, the **urgency** of the risk

1. Detection  →  2. Validation  →  3. Analysis

4. Prioritisation  ↓  5. Assessment

6. Response/Action
Everything begins with a signal

A signal is the information arising from one or more sources which suggests either a new association or a new aspect of a known association between a substance, and an event or set of related events that is judged to be of sufficient likelihood to justify verificatory action, and, where necessary remedial action.
Recommendations for action

• Awareness
• Intensive monitoring (solicited reporting)
• Risk communication (push and pull of information)
  – Formal notifications
  – Alerts
  – Advisories
  – Briefings
• Joint Report
Substances of Concern – monitoring and responding to harms

Public health alerts issued by the EMCDDA in 2015:

- Deaths associated with the use of potent opioids
- Clusters and outbreaks of intoxications associated with cannabinoids
- Seizures of ecstasy tablets containing 4-CMA
- Deaths associated with PMMA sold as ecstasy and heroin sold as cocaine

• Public health alerts issued in 2016 included:

  - Serious adverse events associated with the use of cannabinoids
  - Deaths associated with the use of potent opioids
  - Superman logo ecstasy tablets containing PMMA

• Public health-related advisories were also issued in 2016:

  - Fatty acid amide hydrolase (FAAH) inhibitors;
  - Ocfentanil sold as heroin
  - Cocaine containing scopolamine and associated intoxications
Joint Report — the next stage of early warning

1. Evidence of intoxication or fatalities = **serious adverse events**

2. Toxicopharmacological properties of the new psychoactive substance or analogy with better-studied compounds

3. Amount of seized material

4. Evidence of the potential for further (rapid) spread

5. Evidence of international trafficking

6. Evidence of organised crime involvement

Based on the Joint Report the Council may request a risk assessment of the health and social risks
Risk assessment domains

A) Physical, chemical, pharmaceutical and pharmacological information

B) Dependence and abuse potential

D) Health risks

E) Social risks

F) Involvement of organised crime

C) Prevalence level
Risk assessments 2017

Completed in 2017:

- Acryloylfentanyl 2017
- Furanylfentanyl (May) 2017
- AB-CHMINACA
- ADB-CHMINACA
- 5F-MDMB-PINACA
- CUMYL-4CN-BINACA
- 4-Fluoro-isobutyrylfentanyl (4F-IBF)
- Tetrohydrofuranylfentanyl (THF-F)
- Carfentanil
Synthetic Cannabinoids

Replacement

<table>
<thead>
<tr>
<th>Compound</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>JWH-018</td>
<td>2008</td>
</tr>
<tr>
<td>JWH-018 adamantyl derivative</td>
<td>2011</td>
</tr>
<tr>
<td>JWH 018 adamantyl carboxamide (Apica)</td>
<td>2012</td>
</tr>
<tr>
<td>AKB48 (Apinaca)</td>
<td>2012</td>
</tr>
<tr>
<td>5F-AKB48</td>
<td>2012</td>
</tr>
</tbody>
</table>

Forms

- Synthetic cannabinoids seized in powder form (2014)
- Herbal material (Marshmallow), SE
- Resin (JWH-206, Fi)
- Powders, SE

Manufacturing?

- Low solubility of cannabinoids (and poor practices) might lead to “hot pockets”
- “small lumps (usually 4-6 mg, but up to 120 mg) of almost pure substance”
"What's in a name? That which we call a rose
By any other name would smell as sweet….."

- Synthetic cannabinoids are structurally very diverse
- Some maintain names from original patents
- Unequivocal naming is vital for good monitoring

**Linked Group-Tail-Core-Linker**

**Linked Group:** methyl dimethyl butanoate (MDMB)

**Tail:** cyclohexylmethyl (CHM)

**Core:** indole (I)

**Linker:** carboxamide (CA)

When a tail substituent is present i.e. 5F, this would be displayed at the front of the name: 5F-LinkedGroup - TailCoreLinker).
Synthetic cannabinoid Apinaca

A synthetic cannabinoid that belongs to the adamantyl indazolecarboxamide family. It takes its codename from its systematic chemical name: N-(1-adamantyl)-1-pentyl-1H-indazole-3-carboxamide. It was first reported to the EMCDDA in May 2012 in Bulgaria when it was found in a smoking mixture product called ‘White Widow’. This substance also goes by the name ‘AKB-48’, the name of a popular all-girl band from Japan.
The biggest single seizure on MDMB-CHMICA was reported in December 2014 by Luxembourg: **40 kg of white powder packed in 1 kg packages** were seized in Dec 2014 by the Customs at Luxembourg Airport (Cargo). The product was on transit: the origin of the 2 barrels was China (Shanghai) and the destination was Spain (Madrid).
Emergence of fentanyls in the EU market

- Formal notifications 2012 - 2017

- iBF- benzyl fentanyl
- iB-α-methyl fentanyl
- Carfentanil
- Ocfentanyl
- 4F-BF
- BF
- AcF
- Despropionyl 2F-F
- 4-MeO-BF
- FuF
- Valerylfentanyl
- Acryloylfentanyl
- 2F-fentanyl
- 4Cl-iBF
- 4F-iBF
- 3F-fentanyl
- MeOAcetyl fentanyl
- THF-F
- cPentyl-F
- Benzodioxole-F
- Benzoylfentanyl
- 3-phenylpropanoylfentanyl
- Tetramethylcyclopropane-fentanyl
- Cyclopropylfentanyl
- Thiophenefentanyl
- Benzylfentanyl
Fentanils: why are they important?

- Sold as ‘legal’ replacements to illicit opioids, but also...
- Sold as heroin, cocaine, fake medicines
- Highly potent
- Disposable (appear, controlled, replaced)
- ↑ availability — ↑ open manufacture, open sale
- ↑ sales on surface web, ↑ sales on darknets
- ↑ sales of ready-to-use nasal sprays and e-liquids
- Life-threatening respiratory depression
  - ↑ outbreaks of poisonings, including deaths
  - Outbreaks have potential to overwhelm emergency responders/ERs and deplete naloxone supplies
- Users have no experience with using new opioids and their effects
Availability, supply, price

Sold as drugs in their own right, but also as other substances

... on the surface web
- typically as research chemicals
- in powders but also in ‘novel’ dosage forms (nasal sprays, liquids for electronic smoking devices, blotters)

... on the illicit market
- detected in mixtures with heroin and with cutting agents typically used for opioids (caffeine, paracetamol, etc)
- detected in mixtures with cocaine

...on ‘other’ markets
- darkweb used to distribute carfentanil (UK and internationally)

Produced in China and Hong Kong (wholesale and retail amounts)
- indications that Russia may also be a source (reported by 1 country)

...and then sold and distributed in the EU
- as received or
- mixed with other drugs (including illicit drugs)
Fentanils: a group challenge

- Users typically chronic and marginalised opioid injectors (but not always)
- Life-threatening respiratory depression
- Exacerbated by:
  - Difficulty of diluting fentanils
  - Lack of experience with fentanils (lack of familiarity with administration, effects, and dose)
  - Use of other CNS depressants (opioids, benzodiazepines, gabapentanoids, ethanol)
  - Some users may have no tolerance to opioids
  - Use environment: most found dead at home
- Strengthen community overdose prevention efforts
- Ensure adequate supply of naloxone for first responders, hospitals, lab personnel
- Increase availability of take home naloxone
Naloxone works with fentanils, but...

- Clinical and community experience in treating poisonings suggests that larger than normal doses as well as repeated doses may be required

- In the past two years a number of outbreaks of poisoning caused by fentanils have been reported in the United States and Canada

- Outbreaks can overwhelm emergency departments and deplete stocks of naloxone

- Stocks and availability of the naloxone, as well as adequacy of training in how to resuscitate poisoned patients both in clinical and community settings may need to be assessed

- Availability of naloxone to users through community and take-home naloxone programmes?
Accidental exposure in others...

- Fentanyl pose a risk of poisoning to those who may come into contact with them.

- Family and friends of users, law enforcement, emergency personnel, as well as medical and forensic laboratory personnel.

- Extreme caution when handling materials suspected to contain fentanils.

- Working environments and personnel should be equipped with appropriate protective equipment.

- Antidote naloxone should be readily available to personnel in sufficient quantities; training in naloxone administration and resuscitation should also be available.

- Responses should allow delivery of appropriate treatment without delay to patients with suspected ODs.
Challenges

• Number, diversity and availability of NPS

↑ law enforcement seizures ↑ NPS data

↑ Complexity of NPS market

↑ Serious adverse events

• Outbreaks of infections and mass poisonings

• Lack of data on pharmacology, toxicology and epidemiology
Acknowledgment and thanks to the Reitox network and the national early warning system correspondents

Email: Rachel.Christie@emcdda.europa.eu

http://www.emcdda.europa.eu/activities/action-on-new-drugs

@toxicovigilance