European Early Warning System: responding to novel recreational drugs

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Symposium: Novel recreational drugs of abuse
EAPCCT Annual Congress, Dubrovnik, 24 – 27 Mau 2011
EMCDDA member countries: 27 EU Member States, Croatia, Turkey & Norway
Early-warning system (EWS): sources and outputs

- Indicator-based
- Event-based & Internet

- EPI indicators
- Market & supply data

- Evidence base

- Reitox EWS
- Europol EWS

- Early-warning new drugs
- Risk assessment
- Public-health warnings
- New phenomena

Description state of the drugs problem in Europe

Adapted from R. Kaiser at al., 2005
European database on new drugs

The European information system and database on new drugs (EDND) is an online platform for the provision and exchange of information in the frame of the Council Decision on information exchange, risk assessment and control of new psychoactive substances. It is accessible to the main partners of the mechanism established by this Decision and offers instant access to the main reports, information on new drugs and early warning system alerts.

You may also consult the European legal database on drugs, which includes an overview of the various legal classifications of substances, and a comprehensive table of substances controlled by EU Member States.

- Latest announcements:

  11th Annual meeting of the Reitox Early-warning system and International Forum on New Drugs – Lisbon, 11-12 May

- See latest alerts on Alprazolam as cutting agent in heroin, France, 18 March 2011 and Fatality related to PMMA, Austria, 9 March 2011

- See Miscellaneous updated

- Click here to create your own report
Considerations for issuing public-health alert

• Dual definition of risk
  ─ risk: probability that some harm may occur
  ─ hazard: degree of seriousness of such a harm

• Risks of a substance, independently of its legal status

• Scientific evidence in relation to better-known substances

• Prevalence of use
  ─ evidence that the substance is being (or is likely to be) used so as to constitute a public health and social threat

• Quality of data: weighing the issues of reliability and relevance separately
Triangulation of information from different sources

- Internet, media, users
- Public
- Research, NFP, ENU
- Research, test purchase, WW analysis
- Health & care; law enforcement; forensic science
New psychoactive substances notified to the EWS

Year of notification

- Other substances
- Synthetic cannabinoids
- Cathinones
- Piperazines
- Tryptamines
- Phenethylamines

In pipeline
‘Spice’ compounds 27 reported to EWS
Diffusion patterns – speed of geographical spread

'Speed of geographical spread'

Year of first notification

Cumulative number of countries

First notification

2003 2004 2005 2006 2007 2008 2009 2010 2011

0 5 10 15 20 25 30

mCPP BZP Mephedrone Methylone BDF
What has changed?

Globalisation and advances in information technology, Internet as:
- Communication tool
- Access to information (medicinal chemistry, patent, etc)
- Market place

Cheaper organic synthesis (‘legally’ sourced often outside Europe)

Entrepreneurship and innovative marketing strategies

The role of organised crime

Dynamic (stimulants) drug market (precursors; interplay use & supply)
Cocaine use: LYP young adults in Europe, Australia, Canada & USA

[Bar chart showing the percentage of young people using cocaine in various countries.]

Locating new drugs within the EU drug market

- Stimulants increasingly important in EU
  - Problem drugs use
  - Recreational scene

- Poly-drug use norm

- Dynamic - can be competing products
  - Supply/demanded interconnected

- Where do new drugs fit in the stimulant market
  - New consumers?
  - Replacement products (displacement)?
Changing ecstasy market: UK FSS data

FSS MDMA, Piperazine and Cathinone Derivative Records: Seizure Date July 2005 - March 2010

UK Forensic Science Service
Changing ecstasy market: DIMS data, NL

Brunt T, et al. 2010
Can we anticipate the new drugs?

More derivatives of known drugs

- **stimulants** (incl. synthetic cocaine(s))
- PCP & ketamine (latest additions)
- synthetic cannabinoids
- opioids, sedatives (BDZ?, others)

‘Designer’ medicines (medical research)

Metabolites of medicines
Scope for other new families

- Cyclohexylamines (phenyl-R-amino-cyclohexanes)
  ketamine, methoxetamine, phencyclidine (PCP), 4-MeO-PCP, 4-MeO-PCE

- Arylamine derivatives
  2-aminoindoane, bromodragonfly, 2C-B-fly, methiopropamine

- Pipradol analogues (diphenyl-R-amines)
  2-DPMP, D2PM, desoxy-D2PM
Designer synthetic cocaines

**pFBT** (fluorotropacocaine, 3-pseudotropyl-4-fluorobenzoate)
- First detection: Finland (2008); identified in head shop products in IE (2010)
- Controlled in Denmark
- Tropane derivative

**dimethocaine** ((3-diethylamino-2,2-dimethylpropyl)-4-aminobenzoate)
- First detection: Ireland (2010); identified in head shop products
- \( p\text{-NH}_2\) pharmacophore
Designer medicines – ketamine and methoxetamine

• Ketamine is an anaesthetic and analgesic used in veterinary practice and in human medicine
• It was risk-assessed in 2000
• Methoxetamine is a derivative of ketamine, reported by the UK in 2010
PCP and 4-MeO-PCP

- Phencyclidine (PCP) is a synthetic dissociative anaesthetic, which is internationally controlled by the 1971 UN Convention on Psychotropic Substances.
- The 4-methoxy derivative of PCP (4-MeO-PCP) was notified by Finland in 2011.
Designer medicines – etaqualone

• Methaqualone was developed in the 1960s and marketed for the treatment of insomnia; it has sedative and hypnotic properties

• Etaqualone was first reported to the EWS by DK in Nov 2009
Metabolites of medicines – ODT

- *o*-desmethyltramadol (ODT) is a centrally acting synthetic opioid analgesic
- It is a metabolite of tramadol and a potent \( \mu \)-opioid agonist
- Reported for the first time by DE, in June 2009
Misuse of medicines – pregabalin

- Prescription medicine marketed by Pfizer (Lyrica ®)
- CNS depressive properties;
- Adverse drug reactions: euphoria, sedation, somnolence
- ‘Low abuse potential’
- Reported effects comparable to that of GHB and benzodiazepines
- Reportedly: used in combination with other substances to potentiate their effect or to alleviate opiate withdrawal effects
- Reported fatal cases involving pregabalin:
  - UK: 1 in 2006; 2 in 2007; 5 in 2008 and 1 in 2009
  - Sweden: 11 post-mortem biological samples in 2009
  - Norway: data to be confirmed
  - Finland: from 9 cases in 2005 to more than 80 cases in 2009
4-methylmethcathinone – mephedrone
Has it made the transition from ‘legal’ to illicit market?

— First detected Nov 2007
— Risk assessment July 2010
— EU wide control Dec 2010

— Ongoing monitoring: Internet surveys with clubbers
  - A 2010 Internet survey among UK clubbers LTP placed at around 40% (33% last month use)
  - 2011, a similar survey found LTP had increased to 61%, last month use had fallen to 25% (Winstock, 2011).
  - Deaths and intoxications (2010), 65 suspected mephedrone-related deaths in England, 46 cases were found to be positive for mephedrone and 14 tested negative.
Substance: Mephedrone

Created
April 2008

Updated
March 2011

Type
Psychotropic substances

Group
Cathinones

Name
Mephedrone

Nature of substance
4-Methylmethcathinone (mephedrone) is a stimulant drug. It is a synthetic compound of the cathinone family, differing only by a keto functional group at the beta carbon.

Systematic chemical name
4-methylmethcathinone

Other names
'Mephedrone' is the common (trivial) name for 4-methylmethcathinone. Other synonyms include '4-Methyl-M-Cat', Bubbles and 'Miaow', among others.

COUNCIL DECISION of 2 December 2010 on submitting 4-methylmethcathinone (mephedrone) to control measures (2010/753/EU)

Alerts
No alerts

Reports to EMCDDA

Hungary (Reporting Form): On 25 March 2011 the NFP reported a seizure of 186 green tablets seized in June 2010 by the police at Cegléd. Containing also
Toxicity: recent cases

- PMMA - para-methoxymethamphetamine
  - Found in combination with PMA
  - Fatalities (Norway, the Netherlands and Austria)
- MDPV – 3,4-methylenedioxypyrovalerone
  - 6 fatalities in 2009 and 13 in 2010 (Finland)
- 2-DPMP – desoxypipradrol
  - Adverse health effects, product ‘A3A methano’ (UK)
- D2PM – diphenylprolinol and desoxy-D2PM
  - Acute toxicity, neuropsychiatric symptoms (UK)
- Synthetic cannabinoid JWH-122
  - Adverse effects (Italy and Germany)
Enhanced toxicity with certain substitution patterns

- PMA and PMMA (4-methoxy methylamphetamine)
- 4-MTA (4-methylthioamphetamine)
- DOI (2,5-dimethoxy-4-iodoamphetamine)
EWS: (3-methyl)fentanyl (Chronicle of a death foretold)

- Large seizure in Austrian (March 2004), Estonia cluster of OD (May 2004); dangerous paper trips, the Netherlands (July 2006).

- ED Tallinn, 2-9 May 04 – app. 100 OD caused by ‘white Persian’, on average 13-15 overdoses case per day (usually ED deals with 30 overdoses case per months).

- 13 deaths related to Fentanyl in Sweden (2003), reported in 2004.

- US epidemic, June 2006 alert CSAT, SAMHSA.

- Warning included specific intervention: ‘suspected OD to be treated with Naloxone injection, 0.4-2 mg IV, SC or IM every 2 to 3 minutes which should rapidly reverse symptoms related to a narcotic overdose. If there is no response after 10 minutes, a different diagnosis should be considered. (Naloxone can also precipitate immediate narcotic withdrawal symptoms as overdose symptoms are reversed.)’
EWS: Fentanyl

Source: http://www.blotterart.net/gallery/Blotter-Art-2000-Present/05_G
Levamisole – warning and survey

• Levamisole is an adulterant of cocaine, not routinely identified and only rarely quantified

• In 2009, over 70% of cocaine seizures that were analysed in the US contained levamisole

• In 2009, the EWS issued a public health warning and a survey
  – Information sources: national toxicology, forensic science and customs services
  – Increase in the percentage of cocaine samples adulterated with levamisole: 1/3 (Belgium, France, Spain and Sweden) and 1/2 of the cocaine seizures analysed (the Netherlands, Ireland and the UK) contained levamisole
  – Increase in the concentration of levamisole in cocaine samples

• Levamisole may cause a number of adverse effects, of which agranulocytosis is the most alarming
Reports of control of new substances using different laws

B ZP, S pice, Mephedrone

- Medicinal Products (8)
- Consumer Safety (3)
- General (1)
- Doping laws (1)
- Drug laws (or equivalent)

B. Hughes, EMCDDA

www.emcdda.europa.eu
New drugs… future perspectives

• Dynamic phenomenon of which we have partial awareness
• Rapidly changing market place
• EWS: proactive monitoring, research, triangulation, build capacity to identify substances
• EWS has an important role but response models are translated differently in different countries
• Legal measures difficult to formulate
• Increasing convergence with the illicit drug market
• Little data on risks but some substances are clearly damaging to health
Wastewater analysis / sewage epidemiology

Drugs
- cocaine
- cannabis
- heroin
- amphetamines

CONSUMER
Excretes residues of the drugs with urine after the intake

TREATMENT PLANT
Residues are transported to the treatment plant with the wastewater

DRUG RESIDUES QUANTIFICATION
Wastewater is sampled and the residues of the drugs are measured

CONSUMPTION ESTIMATE
Concentrations are used to calculate residue loads (g/day)
Loads can be used to back-calculate drug consumption

Sources of uncertainty

Sources of variability

Mario Negri Institute, presented at the EMCDDA WW meeting
Challenge of rapidly changing legal highs market
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