EMCDDA Action on new drugs: information exchange and risk assessment

Dr. R. Sedefov, Action on New Drugs
28th Scientific Committee meeting, 14-15 February 2008
EU actions on new drugs: legal base

- June 1997 – May 2005

- May 2005 – present

Council Decision 2005/387/JHA concerns NPAS:

- new psychotropic and new narcotic drugs (synthetic and natural alike) similar to those listed 1961 & 1971 UN Conventions, i.e. natural and synthetic alike (in pure form or in a preparation);

- relates to end products (excluding precursors Council Regulation (EEC) No 3677/90 & Regulation (EC) No 273/2004);

- may include medicinal products as defined in Directive 2001/82/EC and in Directive 2001/83/EC but substances of established and acknowledged medical value are excluded from control measures based on the Decision, i.e. medicinal products and API are in the scope of the info exchange only;

- stimulates exchange of information on misused psychoactive medicines and on emerging trends in new uses of existing substances;

- maintains the three steps - EWS, risk assessment, decision-making.

Information exchange/Early-warning

A new psychoactive substance is detected in the EU Member States and described in a reporting form

Reitox focal points

EMCDDA

The European Commission

Europol national units

Europol

European Medicines Agency (EMEA)

Risk assessment

The Council of the EU may request a risk assessment, based on a EMCDDA–Europol Joint report

EMCDDA extended Scientific Committee

Risk assessment report

Decision-making

At the initiative of the European Commission or a Member State based on the Risk assessment report

Council of the EU decides whether or not to submit the new psychoactive substance to control measures

Council Decision on control measures

Control measures and criminal penalties in the EU Member States

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Council Decision mechanism: info sources and response

Indicator-based

KE Indicators
- Core data
- Crime & supply
- Responses

Event-based

Evidence-based info

Reitox EWS
- Notiﬁcation new drugs
- Limited-warning
- Public-health warning

Europol

Risk assessment

Adapted from R. Kaiser at al., 2005
EWS Operating guidelines

Primary data on new psychoactive substances
- use, traffic and manufacture: chemical and physical description, names, frequency and circumstances, means and methods, organised crime, first indications of health and social risks
- technical information (analytical data and spectra)
- scientific literature

Public-health related information/health alerts
- unusual adulterants
- seizures or detections of uncommon scheduled drugs
- problems with established drugs, e.g. dosage units (tablets, etc.) containing unusually large amounts of active substance, etc

Tools
- Reporting Form
- Progress reports (longer-term monitoring)
- Joint Report
- Active monitoring

REPORTING FORM ON NEW PSYCHOACTIVE DRUGS


This section should be filled in by Europol or EMCDDA

Transmitted by Europol
Transmitted by EMCDDA

Ref. no.: Date of transmission:

The following sections should be filled by the Europol national units (ENU) or Reitox national focal points (NFP) based on the information available and their respective competences

1. Member State:       Ref. no.:       Date:  Reporting authority:       ENU
                      Reitox NFP
                      
2. Chemical name:     Other name(s):    Street name(s):
                      
3. Source of information (fill one or more as appropriate)
   Seizure(s) Specify amount (weight, number of tablets, etc.):
   Seizing 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 ingredients:
   Other ingredients:

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Joint Report: assessment criteria

- amount of the seized material
- evidence of organised crime involvement
- evidence of international trafficking
- analogy to better-studied compounds
- evidence about the potential for further (rapid) spread
- evidence about serious intoxications or death cases
Joint Report: EMEA contribution

The EMEA submits information on whether in the EU or in any Member State:

- existing/application for/suspended marketing authorisation
- where this information relates to marketing authorisations granted by Member States, they shall inform EMEA

By analogy the EMEA informs on:

- adverse reactions of a medicinal product (if the NPAS is a metabolite of an active substance)
- whether the NPAS is an intermediate in the production of an active subscales (API)
New substances notified in 2007

1. **2C-B-Fly** (8-bromo-2,3,6,7-benzo-dihydro-difuran-ethylamine) – 15 February 2007 – Finland

2. **5-MeO-Dalt** (N,N-diallyl-5-methoxytryptamine) – 15 February 2007 – Finland

3. **N-ethyl-2C-B** (N-ethyl- 4-Bromo-2,5-dimethoxybenzeneethanamine) – 22 February 2007 – Finland

4. **Vanoxerine** (1-[2-[bis(4-fluorophenyl)methoxy]ethyl]-4-(3-phenylpropyl)piperazine) – 3 May 2007 – Belgium

5. **D2PM** ((S)-(−)-α,α-Diphenyl-2-pyrrolidinylmethanol) – 11 May 2007 – United Kingdom

6. **N-Acetyl-DOB** (N-Acetyl-4-bromo-2,5-dimethoxyamphetamine) – 11 June 2007 – United Kingdom

7. **Glaucine** ((6αS)-1,2,9,10-tetramethoxyaporphine) – 2 July 2007 – United Kingdom

8. **4-MTA** (4-methylthioamphetamine) – 5 June 2007 – France
New substances notified in 2007 (cont.)

8. **Fenazepam** (7-brom-5/o-chlorophenyl/1,2-dihydro-3H-1,4-benzodiazepin-2-on) – 1st half 2007 – Finland

9. **Harmine** (7-Methoxy-1-methyl-9H-pyrido[3,4-b]indole) – 1st half 2007 – Finland

10. **Bufotenine** (3-(2-dimethylaminoethyl)-1H-indol-5-ol) – 1st half 2007 – United Kingdom

11. **Salvia Divinorum** – 1st half 2007 – United Kingdom

12. **1-PEA** (1-Phenylethylamine) – 1st half 2007 – United Kingdom

13. **Nimetazepam** (2-methyl-9-nitro-6-phenyl-2,5-diazabicyclo[5.4.0]undeca-5,8,10,12-tetraen-3-one) – 1st half 2007 – United Kingdom

14. **Gelbes** 1-(3-chlorophenyl)-4-(3-chloropropyl)piperazine – Austria

15. **NMPEA** (N methyl phenylethylamine) – 6 December 2007

16. **N-desmethlysibutramine** – reported on 14 December 2007 by Poland
**N-Arylpiperazines: Structures**

Ar—N\[\text{NH}]

- Benzylpiperazine (BZP)
- m-Chlorophenylpiperazine (mCPP)
- p-Methoxyphenylpiperazine (MeOPP)

All reported in EU as NSD/NPAS
DIMS – Trimbos institute

% XTC-pills containing mCPP

- mCPP
- mCPP + MDMA

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Deadlines 1

Launch of a Joint Report

Information collected

EMCDDA-Europol Joint Report

Risk Assessment requested

Risk Assessment Report

Subtotal

6 weeks

4 weeks

4 weeks

12 weeks

26 weeks
Deadlines 2

Risk Assessment Report → 6 weeks
Initiative to control → no deadline
Council Decision on control measures → 52 weeks
Control measures in all Member States
## Risk assessments 1998-2007

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<tr>
<th>Substance</th>
<th>Chemical Name</th>
<th>Year</th>
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<td>MBDB</td>
<td>N-methyl-1-(1,3-benzo-dioxol-5-yl)-2-butanamine (1998)</td>
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<td>4-MTA</td>
<td>4-methylthioamphetamine (1999)</td>
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<td>ketamine</td>
<td>2-(2-chlorophenyl)-2-(methylamino)-cyclohexanone (2000)</td>
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<td>GHB</td>
<td>gamma-hydroxybutyrate (2000)</td>
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<td>PMMA</td>
<td>para-methoxymethamphetamine (2001)</td>
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<td>2,5-dimethoxy-4-iodophenethylamine (2003)</td>
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<td>2,4,5-trimethoxyamphetamine (2003)</td>
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<td>BZP</td>
<td>1-benzylpiperazine (2007)</td>
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Challenges

• Internet sales

• New unanticipated chemicals, plants, medicinal products

• Reference materials (seized substances or reference substances)

• Public health related actions beyond the legal scope of the Council Decision (cannabis, cocatropine, fentanyl)

• New trends identification and monitoring (GHB, ketamine, methamphetamine, ‘herbal highs’)

• Risk assessment guidelines
Council Decision: risk assessment headings/assessment categories

- Description
  - physical and chemical
  - mechanism of action
  - medical value

- Chemical precursors

- Health risks
  - pharmacotoxicological evidence
  - psychological risk assessment
  - public health risks – epidemiological evidence

- Social risks
  - sociological evidence
  - criminological evidence

- Involvement of organised crime, seizures, manufacture

- Options for control and possible consequences (risk management)
Risk assessment guidelines: technical annexes

A. Pharmacotoxicological evidence

B. Psychological risk assessment

C. Sociological evidence

D. Public health risks: epidemiological evidence

E. Involvement of organised crime
Risk assessment: options for control & possible consequences

- The Decision does not provide for a range of options for control of new psychoactive substances to be considered. Art. 9(1): the option for control that is available at EU level is for the MS to submit BZP to control measures and criminal penalties as provided under their legislation by virtue of their obligations under the 1971 UN Convention.

Contradictory effects/consequences:

- limit the potential for expansion of the supply and use by facilitating the capacity for the detection and monitoring of illegal manufacturing of and trafficking and the international law enforcement cooperation;
- could create an illegal market with an increased risk of criminal activity, or even lead to its replacement with other psychoactive substances which may also have public health consequences.
Assessment categories: CAM

Health:

- Individual health
  - Acute toxicity
  - Chronic toxicity
  - Dependence potential

- Public health
  - Extent and frequency of use
  - Vulnerable groups
  - Quality of information
  - Availability of substance
  - Quality of substance
  - Quality of distribution system
  - Reporting of incidents
Assessment categories: CAM (cont.)

Social
- Civil order
  - Annoyance to the public
  - Violence
  - Impaired reaction (traffic)

Organised crime
- Regarding final product
- Regarding raw materials
Assessment categories: Nutt et al., 2006

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<th>Chronic</th>
<th>Intravenous harm</th>
<th>Intensity of pleasure</th>
<th>Psychological dependence</th>
<th>Physical dependence</th>
<th>Intoxication</th>
<th>Other social harms</th>
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Table 1: Assessment parameters
The process

- Committee members get details of drugs and a score sheet to complete in their own time prior to the meeting.
- Present scores at meeting.
- Each person reviews scores in the light of others’ knowledge in open discussion facilitated by chair – revision of scores is encouraged.
- Final score used for analysis.
- Some people did not score an item so number of scores for each variable may differ.
- Number of members present at each meeting also varied – usually 12-15 with wide range of expertise.
- Twenty substances examined over two years.
Mean Scores: all parameters for 20 drugs

1 Heroin
2 Cocaine
3 Barbiturates
4 Street methadone
5 Alcohol
6 Ketamine
7 Benzodiazepines
8 Amphetamine
9 Tobacco
10 Buprenorphine
11 Cannabis
12 Solvents
13 4-MTA
14 LSD
15 Methylphenidate
16 Anabolic steroids
17 GHB
18 Ecstasy
19 Alkyl nitrites
20 Khat
Issues

• Other factors – criminological, prevalence
• Social vs. Individual harms
• Parameter weightings
• ‘Non-scores’
• Fixed panels of scorers
• Process itself valuable
Delphic method

1st round: Individual scoring by experts on each criterion

2nd round: Discussion
  - Difference of opinion?
  - Reaching consensus?
  - New score if needed

Suitable for complex social and medical problems were multiple criteria are relevant
Advantages of using multiple risk scales

• Comprehensive
• Standardised
• Transparent
• Rational and scientific basis
• Facilitates drug-drug comparisons
• Can be repeated
  - as knowledge advances
  - or pattern of drug use develops
• Suitable for Delphic approach
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• Suitable for Delphic approach
Pitfalls of using numerical scores

• Extreme risks on a single criterion are not visible in average scores

• Average or total scores can be overemphasised
How to proceed with ranking system

- Delphi method to make optimal use of expert knowledge
- Define criteria and categories of risks that cover the relevant aspects of risk associated with drug use
- Do not inappropriately add up or average all values
- Consider it as a tool
Risk assessment: recommendations from previous SC (1)

Technical annexes

- Technical Annex A *Pharmacotoxicological evidence*, covers all necessary items, it is compatible with other health risk assessment approaches.

- The new SC might wish to consider ways in which the criteria in technical Annexes B, C and D could to be revised so as to reduce an unnecessary overlap.

- Technical Annex E *Involvement of organised crime* needs to be reviewed in conjunction with relevant high level experts and with an input from Europol so as to better reflect the increased emphasis on this domain within the Council Decision.
Numerical scoring system

- A numerical scoring system could be a useful working tool in the preparation of the actual risk assessment. It should not constitute a formal part of the risk assessment report. The system should be used as a trigger to focus the discussion on the relevant items.

- Individual SC members may present an opinion on two or three selected domains or subgroups within a domain which they feel represent a severe (or greater than moderate) risks, explaining their views.

- No mean values should be calculated, only items where severe or moderate risk ratings are presented by SC members should be put forward and discussed by the full Risk Assessment committee.

Risk assessment meeting

- The Risk Assessment meetings could explore the viability of utilising small working groups and rapporteurs for each domain.
Contacts

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