



Leon van Aerts

# Risk assessment of new psychoactive substances

Congrès annuel de la Société Française de Toxicologie 2006



*rivm*

## Disclaimer

The views expressed in this presentation are those of the author and do not necessarily represent the views of the Institute (RIVM) or reflect the official Dutch policy on any of the issues discussed.

# New psychoactive substances



- Non-medical use
- Recreational drugs
- New synthetic drugs
- Designer drugs
- Ecstasy look-alikes

SET

Personality/psychological make-up

Physiology/genetic factors

EXPERIENCE

SETTING

SUBSTANCE

Environmental factors

Intrinsic properties

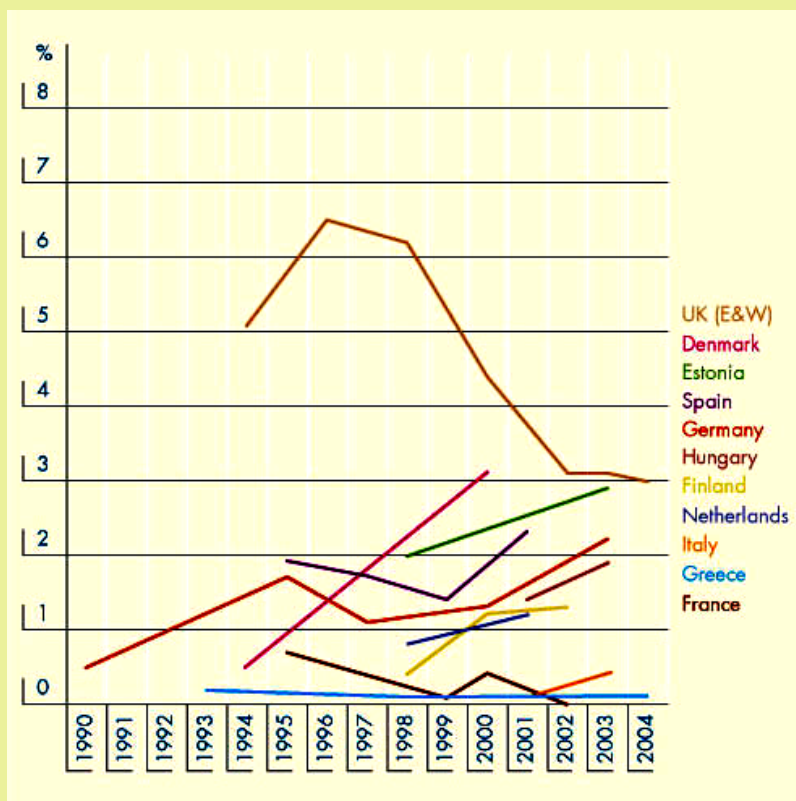
*rivm*

23 October 2006

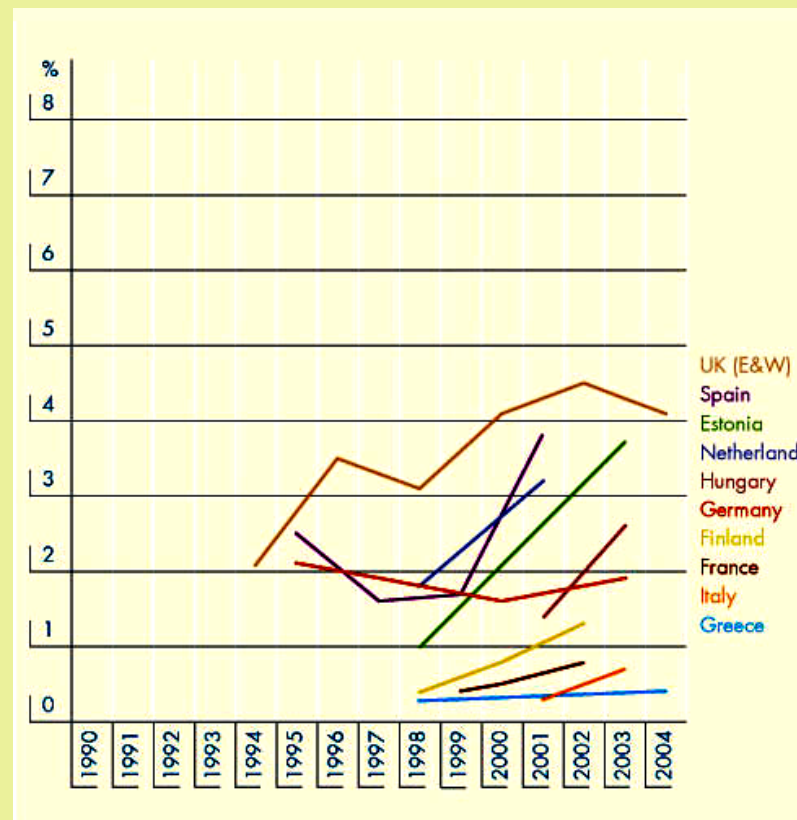
Leon van Aerts | Paris

4

## Trends in recent (last year) amphetamine + ecstasy use in young adults (15–34 years)



amphetamine



ecstasy

EMCDDA annual report 2005

## New psychoactive substances (NPS) noted in EU

Abbreviation	chemical name	reports
mCPP	1-(3-chlorophenyl)piperazine	64
GHB	gamma-hydroxybutyric acid	33
BZP	1-benzylpiperazine	24
Ketamine	2-(2-chlorophenyl)-2-(methylamino)-cyclohexanone	24
2C-I	2,5-dimethoxy-4-iodophenethylamine	19
5-MeO-DIPT	N,N-diisopropyl-5-methoxy-tryptamine	15
2C-T-2	2,5-dimethoxy-4-ethylthiophenethylamine	13
5-MeO-DMT	5-methoxy-N,N-dimethyltryptamine	12
TFMPP	1-(3-trifluoromethylphenyl)-piperazine	11
TMA-2	2,4,5-trimethoxyamphetamine	8
2C-T-7	2,5-dimethoxy-4-(n)-propylthiophenethylamine	8
2C-E	2,5-dimethoxy-4-ethylphenethylamine	7
MDHOET	3,4-methylenedioxy-N-(2-hydroxyethyl)amphetamine	6
5-MeO-AMT	5-methoxy-alpha-methyltryptamine	5
DPIA	Di-(beta-phenylisopropyl)amine	5
MBDB	N-Methyl-1-(1,3-BenzoDioxol-5-yl)-2-Butanamine	4

## New psychoactive substances (NPS) noted in EU

Abbreviation	chemical name	reports
2C-D	2,5-dimethoxy-4-methylphenethylamine	3
PCP	1-(1-Phenyl-cyclohexyl)-piperidine	3
2C-T-4	2,5-dimethoxy-4-isopropylthiophenethylamine	3
4-MTA	4-methylthioamphetamine	3
pFPP	p-Fluorophenylpiperazine	2
pMeOPP	p-Methoxyphenylpiperazine	2
2C-P	2,5-dimethoxy-4-(n)-propylphenethylamine	1
Methylone	3,4-methylenedioxyamfetamine	2
MIPT	N-Methyl-N-isopropyltryptamine	2
4-HO-DIPT	4-hydroxy-N,N-diisopropyltryptamine	2
4-AcO-DIPT	4-acetoxy-N,N-diisopropyltryptamin	2
4-HO-DET	4-hydroxy-N,N-diethyltryptamine	1
DIPT	Diisopropyltryptamine	1
DOC	2,5-dimethoxy-4-chloroamphetamine	1

## Current approach regarding NPS in EU

- Early Warning System
- Evaluation of information accumulated
- Risk assessment
- Decision on further actions
  - Control measures
  - Monitoring
  
- Legislative framework
  - 1997: Joint Action, concerning the information exchange, risk assessment and the control of new synthetic drugs
  - 2005: Council Decision on the information exchange, risk-assessment and control of new psychoactive substances

## Risk assessments under Joint Action

- MBDB (N-methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine)
- 4-MTA (4-methylthioamphetamine)
- ketamine
- GHB (gamma-hydroxybutyric acid)
- PMMA (para-methoxymethamphetamine)
- 2C-I (2,5-dimethoxy-4-iodophenethylamine)
- 2C-T-2 (2,5-dimethoxy-4-ethylthiophenethylamine)
- 2C-T-7 (2,5-dimethoxy-4-(n)- propylthiophenethylamine)
- TMA-2 (2,4,5-trimethoxyamphetamine)

## Non-clinical data in risk assessments of NPS

Substance	# sources of non-clinical data		
	Pharmacology	Toxicology	Dependence potential
MBDB	16	2	3
4-MTA	5	1	2
ketamine	9	15	7
GHB	34	1	2
PMMA	3	3	2
2C-I	2	0	0
2C-T-2	0	0	0
2C-T-7	0	0	0
TMA-2	6	2	4

## Non-clinical data in risk assessments of NPS

- Often little information available
- Mostly pharmacological data
- Primarily related to CNS pharmacology
- Few safety pharmacology data
- Little if any toxicological information
- Little information on dependence potential: mostly drug discrimination studies
- Ketamine and GHB are exceptions: active substances of medicinal products

## Non-clinical safety data in development of medicinal products

- Assess safety margin
- Detect target organs
- Investigate reversibility of toxicity
- Identify monitoring parameters
- Assess toxicity not readily detected clinically
  - Genotoxicity
  - Carcinogenicity
  - Reproductive toxicity
  - Immunotoxicity

## Minimal package for non-clinical safety data on NPS

- Safety pharmacology data
  - Cardiovascular (in vivo/in vitro)
  - Respiratory
  - CNS
- Acute and subacute toxicity
  - Safety margin
- Genotoxic potential
- Dependence potential

## Why more non-clinical data on NPS are needed

- better informed decision on actions to be taken
- precautionary attitude
- pro-active role of authorities
- facilitates interpretation of human data
- Provides information for education