ALICE RAP Policy Paper Series

Policy Brief 3.

Novel Psychoactive Substances – Challenges and policy responses

AR Policy Paper 3

Novel Psychoactive Substances – Challenges and policy responses

ALICE RAP (Addictions and Lifestyles in Contemporary Europe – Reframing Addictions Project) is the first major Europe wide project studying addictions as a whole and their influence on wealth, health and stealth. The aim of this five year, €10 million, co-financed EU project is to stimulate and feed scientific evidence into a comprehensive public dialogue and debate on current and alternative approaches to addictions.

The AR Policy Paper series aims to provide succinct evidence briefs for decision-makers and advocates working on key addiction-related issues. This third paper focuses on Novel Psychoactive Substances. The emergence of Novel Psychoactive Substances (NPS) over the last decade, and their shifting legal status and points of sale and distribution, poses particular challenges to policy makers. These are substances which are not controlled under United Nations Drugs Conventions, and whilst few have been recommended for control by the Council of the European Union, Member States have introduced their own legislation, leading to a broad array of policy responses.

This AR policy paper gives an introduction into the field of NPS, outlining the current situation regarding the use of these substances, the potential threat to public health and well-being that they pose and describes various policy options and legislative measures that are undertaken across Europe.

This policy paper was prepared by:
Harry Sumnall, Angelina Brotherhood, and Amanda Atkinson

Centre for Public Health, Liverpool John Moores University, UK
(Contact: h.sumnall@ljmu.ac.uk)

The following ALICE RAP scientists have commented on drafts of this paper:
Joe Barry, Fleur Braddick, Maria Moreira, Juan C. Negrete, David Nutt, Jan Ramaekers, Martine Stead.

Disclaimer: The views expressed in this paper do not necessarily reflect the views of the European Commission, the EMCDDA or of all ALICE RAP partners.

The ALICE RAP Project is co-financed by the European Commission, under the 7th Framework Programme; Contract Number: 266813; www.alicerap.eu.

AR Policy Paper 3

Novel Psychoactive Substances – Challenges and policy responses

1 Introduction

The emergence of Novel Psychoactive Substances (NPS[1]) over the last decade poses particular challenges to policy makers. These are substances which are not controlled under United Nations Drugs Conventions, and whilst few have been recommended for control by the Council of the European Union, Member States have introduced their own legislation, leading to a broad array of policy responses.

New NPS are typically identified by manufacturers through surveys of the scientific literature, or the specialised work of market orientated chemists. Production facilities are present in a number of countries, and well established (quasi) legitimate distribution networks means that products are rapidly brought to market. NPS are appealing to consumers for a number of reasons, including: ease of availability; legal status (in some countries); and the potential to produce unique subjective effects. Whilst the Internet is an important retail agent, available data suggest that most consumers still purchase NPS though friends or traditional 'dealing' networks.

There are few estimates of the prevalence of NPS use, particularly in key groups with an increased propensity to use, and there is no high quality data that allows for the comparison of use across different countries. The novelty and rapid emergence of NPS, delays in publishing scientific data, and a constantly changing market means that there is an incomplete understanding of the public health and societal impact of NPS. Although some pre-clinical toxicity research, clinical case reports, and community surveys on a small number of NPS have been published, accurate risk assessment has been hampered by an inability to predict the impact of use at the population level. Similarly, the quality of data on NPS related deaths is generally poor across the EU, and so it is not possible to determine whether the risk of mortality is greater for these products than traditional street drugs. This also has implications for NPS consumers. Even where information on potential harms is available, as NPS sales are rarely regulated and as many products are mis-sold or mislabelled, consumers are not provided with accurate information about the products they buy.

NPS policy has typically taken one of three broad forms; consumer protection; medicine laws; and amendment of illicit drug laws. A lack of scientific data means that most national

[1] Please note that this policy briefing excludes misuse of prescription medicines.

NPS policies have been drafted with an assumption of product harm. Approaches such as analogue legislation or 'zero tolerance' control on the basis of supposed NPS 'psychoactivity' are challenging for advocates of evidence based policy as evidence is rarely available to support decision making. Furthermore, to the best of our knowledge no NPS policy has been subject to impact assessment to determine whether it reduces use and associated harm. Internationally, the New Zealand Government has implemented a system of NPS licensing, whereby products assessed to be 'low risk' are allowed to be retailed, under certain market restrictions. Proposed new EC rules indicate the implementation of a graduated system whereby NPS are considered to present "low risk" will not be subject to action, whereas "moderate risk" products will be subject to consumer market restrictions, and substances posing a "high risk" to full market restrictions. The "most harmful" substances, posing "severe risks" to consumers' health, will be submitted to criminal law provisions, as in the case of illicit drugs. At the time of writing it is uncertain how risk thresholds will be defined, how risk categories compare to the harms of other consumer products such as alcohol and tobacco, and what types of evidence will be required to determine categorisation. It is also uncertain whether categorisation of a product as 'low' or 'moderate' risk will be seen as a marketing opportunity by retailers or if consumers will restrict their purchases to 'low risk' products.

Finally, it is clear that some users have developed high risk NPS behaviours such as injection, and concomitant and frequent use. It is therefore important that policy responses not only consider legislation but also the implementation of public health focused interventions and support. It is possible that existing interventions might be adapted for use with NPS users, but the nature of the NPS market means that other strategies might be more suitable.

2 Definition of Novel Psychoactive Substances

- *Novel psychoactive substances* (NPS) are defined as those emerging substances that are used for psychotropic effects and that are not subject to control under the United Nations Single Convention on Narcotic Drugs 1961 and the United Nations Convention on Psychotropic Drugs 1971 (although it is important to recognize that Nation States may act unilaterally and regulate them under their national controlled drug frameworks). The Council Decision 2005/387/JHA[2] extends this definition to clarify that these substances '*may pose a threat to public health*' comparable with drugs Scheduled under the UN Conventions (e.g. heroin, cocaine, cannabis, MDMA, LSD).
- These drugs exist for three main reasons, although others may also be relevant:
    1. to bypass current national and international laws controlling drug use so avoiding prosecution for users and sellers alike ;

[2] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32005D0387:EN:NOT

2. to provide alternative sources of experiences for people who wish to use drugs to change their mental state; and
3. as a result of new advances and discoveries in academic and industrial chemistry.

- Regarding this latter reason, synthesis of many new NPS are first described in the scientific or patent literature as a result of academic publication, or the development of psychiatric and chemical tools by industry. Although generic legislation exists (see below), a novel compound is usually classified as a NPS once evidence of human use is obtained.
- The archetypal modern NPS was 4-methylmethcathinone (mephedrone), which was first sold in European drug markets around 2006. The EU Council recommended mephedrone for control by Member States under national legislation in 2011. 5-(2-aminopropyl) indole (5-IT) was recommended for control in August 2013[3].

3 The current situation

NPS availability in the EU

- Most NPS are manufactured and imported from outside the EU; however, law enforcement agencies in Member States are increasingly reporting local production, and in some cases distribution by organised criminal groups[4].
- A January 2012 (latest data available) European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) analysis of Internet retailers identified that the most frequently available substances offered for sale were *kratom*; *Salvia Divinorum*; hallucinogenic mushrooms; MDAI; methoxetamine; and 6-APB[2].
- The EMCCDA co-ordinated Early Warning System (EWS) detects at least 50 NPS each year through intelligence including law enforcement and border agency seizures, test purchases, presentations to health services, and user submissions (to agencies that report to national EWS hubs). In total, since 2005, more than 275 NPS have been reported to the EMCDDA. The majority (~66%) of compounds have been classed as either synthetic cannabinoid receptor agonists (i.e. drugs that are used to mimic the effects of cannabis) or substituted cathinones (e.g. psychostimulant drugs similar in structure to mephedrone, used to mimic the effects of ecstasy or cocaine). However, it should be noted that few of these newly detected drugs are detected in street seizures and prevalence remains low.

Epidemiology

- There are few high quality estimates of the prevalence of use of NPS in the EU[5]. This is due to several reasons, including:

[3] EMCDDA (2013) *Annual Report 2013*. Lisbon, EMCDDA.
[4] http://www.emcdda.europa.eu/publications/implementation-reports/2011

1. Lack of development of appropriate methodologies to assess low prevalence behaviours such as NPS use;
2. Underrepresentation in sampling frames of populations with a high propensity for NPS use;
3. Lack of common definitions to describe NPS (e.g. 'legal highs'; 'research chemicals'; 'herbal highs'; 'plant food'; 'bath salts'; 'synthetic pot'; 'Spice');
4. Lack of national funding to survey behaviours that are not controlled under existing Member State drug laws;
5. Problems with misidentification of NPS – many NPS are sold under 'brand' names/generic slang terms or are mislabelled/mis-packaged, hence many users would not be able to accurately report use of individual NPS (e.g. 5-APB) unless purchased from a retailer which (accurately) sold them as such.

- The EMCDDA is currently developing a voluntary module for assessing NPS prevalence for its European Model Questionnaire (EMQ).

- The 2011 Eurobarometer survey commissioned by the EC, estimated that 5% (range <5-15%) of 16-24 year olds sampled across several Member States reported use of NPS[6]. Small sample sizes in individual countries and uncertainty about the comparability of methodology means that direct country comparisons are not possible with this data.

- Some Member States have included a limited number of named NPS in national surveys of substance use. In general, prevalence of most named NPS in such surveys is very low (e.g. <0.5%). However, there are exceptions, and some of this data is presented below:

    1. Mephedrone was reportedly used by 1.6% of 16 to 24 year old respondents to the Crime Survey of England and Wales in 2012/2013 (a fall from 3.3% in the previous year; for comparison ecstasy prevalence was 2.9%). *Salvia divinorum* (a plant hallucinogen) was reportedly used by 1.1% of respondents in the same survey in the previous year. 6% of 15-24 year olds reported use of mephedrone (and other 'legal highs') in Northern Ireland in 2010/11.

    2. Shortly after passing laws that closed all NPS retailers, a survey of Polish youth (aged 18-19) suggested that 11.4% had used any NPS at least once in their lifetime. The effects of legislation on use in this cohort have yet to be established.

[5] A summary of NPS epidemiology can be found in Sumnall et al., 2013. Epidemiology of Novel Psychoactive Drugs. In Dargan, Wood (Ed). Novel Psychoactive Substances. New York, Springer.
[6] www.ec.europa.eu/public_opinion/flash/fl_330_en.pdf

3. The 2010 national Spanish survey on drug use in 14-18 year olds reported that 3.5% of students had used NPS (including ketamine, 'Spice', piperazines, mephedrone, nexus (2C-B), methamphetamine, magic mushrooms, 'research chemicals' and 'legal highs') in their lifetime, and 2.5% in the previous year. It should be noted that this list included methamphetamine, which is not classed as a NPS. Lifetime use of 'Spice' was estimated at 1.1% and mephedrone 0.4%.

- Pan EU young people drugs surveys of schoolchildren such as ESPAD or HBSC do not currently include NPS. ESPAD has established a working group to develop methodology in this area.

- Although a number of estimates have been published, the type of methodology used in surveys of 'at-risk' populations (e.g. clubbers, school children, treatment seeking population) means that findings cannot usually be generalised beyond the studied population. The largest survey, the Internet delivered Global Drugs Survey, last reported in 2013 with a sample size of 22,000, mostly drawn from the UK and USA. Information on specific NPS reported in this survey have not yet been made publicly available, but 12% of UK respondents reported buying NPS in the previous 12 months (43% from a shop; 53% online; 18% from a friend; 9% from a 'dealer'). In the 2012 Global Drugs Survey, the most frequently reported NPS used in the previous 12 months were mephedrone (19.5%); synthetic cannabinoid receptor agonists (3.3%); *BenzoFury* (ostensibly 5/6-APB) (2.4%); and methylone (1.4%).

- Several studies of drug use patterns indicate that NPS are added to the existing substance repertoire rather than replace those (illegal) drugs that are already used.

4 Challenges

Social harms of NPS

- There is currently a paucity of evidence regarding the social harms of NPS. This includes a lack of evidence on the association between NPS use with crime, and prevalence of dependence and use disorders.

Health harms of NPS

- There is little scientific evidence on the acute and long term health harms of NPS (including psychological health). Beyond drug related mortality it is difficult to make an accurate assessment of the potential risks to public health (in accordance with the Council decision) of these substances.

- Both the EMCCDA[7] and the UK Independent Scientific Committee on Drugs[8] have published guidelines on conducting risk assessments of NPS. However, a lack of high quality scientific evidence means that it is difficult to apply such guidelines to the assessment of the majority of current NPS.
- In general, acute health harms are unlikely to be greatly different to existing illegal drugs, and emergency room staff tend to respond to presentation on a symptomatic, rather than substance-specific basis. However, the US experience with MPTP in the 1980s (onset of Parkinsonian-like symptoms) necessitates caution[9].
- Although specialist 'club drug' treatment services report clients with problematic NPS use, the number of presentations is low[10].
- There is some emerging evidence which suggests that use of synthetic cannabinoid receptor agonists is associated with acute kidney injury[11], something which is not observed with use of cannabis itself.
- Reviews of case reports suggest that use of synthetic cannabinoid receptor agonists, like cannabis, may precipitate acute psychotic episodes or psychotic symptomatology in predisposed individuals, or exacerbate symptomatology in those with a previous psychiatric history[12].
- Case reports suggest that ketamine, and probably its analogue methoxetamine can cause bladder toxicity.
- Health harms, as with other illegal drugs, are likely to be associated with polysubstance use, dose, ingestion frequency, use history, and route of administration.
- There is evidence from a number of countries, including Hungary, the UK, and the Republic of Ireland that some NPS (e.g. substituted cathinones such as mephedrone) are being injected by users; generally by existing drug injectors as a substitute for opiates during periods of low opiate availability/affordability.
- Published data on deaths associated with NPS is rare, and few Member States collect and report this in a systematic manner[13]. Although many deaths receive media attention, particularly those in young people, the number of deaths is relatively low compared with other drugs, although interpretation of these numbers is difficult because the total number of users is largely unknown. It is therefore unknown whether NPS are associated with a greater relative risk of mortality than other illegal drugs.

[7] http://www.emcdda.europa.eu/html.cfm/index100978EN.html
[8] http://www.drugscience.org.uk/external-resources/novel-drugs-concern-minimum-dataset/
[9] http://www.ncbi.nlm.nih.gov/books/NBK27974/
[10] E.g. http://www.nta.nhs.uk/uploads/clubdrugsreport2012%5B0%5D.pdf
[11] http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6206a1.htm?s_cid=mm6206a1_w
[12] Hum Psychopharmacol Clin Exp 2013; 28 :379-389
[13] See, for e.g. http://www.sgul.ac.uk/research/projects/icdp/our-work-programmes/substance-abuse-deaths/ for UK reporting

5 Governance

Policy responses

- In September 2013 the European commission announced new rules to withdraw harmful NPS more quickly from the market[14]. Whereas the current risk assessment process can take up to 2 years to lead to ban on a NPS, under the new procedure, where there is a concern that a harmful product is available, it will be withdrawn immediately from retail whilst a full risk assessment takes place. A graduated system is proposed whereby substances posing "low risk" will not be subject to action, whereas "moderate risk" products will be subject to consumer market restrictions, and substances posing a "high risk" to full market restrictions. Only the "most harmful" substances, posing severe risks to consumers' health, will be submitted to criminal law provisions, as in the case of illicit drugs.
- At the time of writing (September 2013) the EC Impact Assessment of these proposals had not been published. Although the proposal is based on Article 114 of the Treaty on the Functioning of the European Union, the precise legislative 'mechanisms of action' are currently unclear. Furthermore it is also currently unclear how rapid risk assessment (i.e. categorisation of products as low, moderate, and high risk) will be undertaken in the absence (presumed) of a substantial body of scientific evidence assessing harm. However, this is a limitation that is not unique to this process and may be applied to most NPS assessments under Member State law.
- Individual EU Member States have responded to NPS through a number of different policy types. These include[15]:
    - Consumer Protection (e.g. Italy, Ireland, Poland, Portugal, Romania, Sweden, UK) – e.g., laws closing down physical and Internet retailers; prosecutions against retailers selling incorrectly labelled products, requirement of retailer licensing.
    - Medicines laws (e.g. Finland, Netherlands, UK, Germany, Austria, Hungary, Spain, Norway) – e.g., prosecutions against retailers of products that have been demonstrated as being sold for human consumption, but are not licensed medicines.
    - Illegal Drug Laws (all EU Member States) – e.g. existing drug control legislation; 'fast track' and 'emergency' scheduling, generic control, named substance control, analogue control.

- Hughes and Winstock[15] outline a number of possible policy options, but most of these have yet to be tested for effectiveness for controlling psychoactive substances, and thus may inadvertently be associated with unanticipated outcomes:
    - Unrestricted sale
    - Legal sale with age, place of sale and advertising restrictions
    - Government monopoly sale (similar to sale of alcohol in Sweden, Norway and Finland)

[14] http://europa.eu/rapid/press-release_IP-13-837_en.htm
[15] Addiction 2012 107: 1894-1899; visualised at http://www.emcdda.europa.eu/topics/pods/controlling-new-psychoactive-substances

- Pharmacy only sale (over-the-counter pharmacist sales)
- Prescription only access
- Restricted sale without medical supervision
- Restricted sale with medical supervision
- Prohibition with civil penalties (i.e. fines)
- Prohibition with diversion and education options
- Prohibition with criminal penalties

- The New Zealand Government introduced the Psychoactive Substances Bill in July 2013[16]. The Bill is designed to replace emergency scheduling systems that expired in August 2013 (Temporary Class Drug Notice, a similar system operates in the UK). The Bill sets up a legal framework for the testing, manufacture, sale and regulation of psychoactive drugs (excluding alcohol, tobacco, and already controlled drugs). The bill proposes that NPS are licensed for sale if pre-clinical and human clinical testing demonstrate 'low-risk' to health (the types of data required, and an acceptable 'risk threshold' have not yet been established). These tests will be paid for by the applicant. Other proposed restrictions on sale include requirements for record keeping, and marketing restrictions. It is also proposed that it would be an offence to sell or supply an approved product to a person aged under 18, or for an individual to buy an approved product under the age of 18. Since the introduction of the Bill a number of retailers, manufacturers, importers, wholesalers, and researchers have received interim licenses to operate. A number of existing products introduced into the market prior to the Bill have received interim product approval[17] . This allows the product to be sold for three months. After expiration, data on product safety must be submitted for review by the Ministry of Health. If the product is not licensed then the license is revoked and the product becomes a controlled substance.

Effects of legal control on use of NPS

- It is currently unknown how effective policy interventions have been at reducing the use of, or health and social harms of, NPS as none have undergone formal assessment. However in the UK, a number of indicators (including general population prevalence estimates, field studies, A&E presentations, mortality data, and enquiries to national poisons helplines) suggest that fewer people are using mephedrone or are suffering harms since it was controlled in 2010. It is unknown whether this was a direct result of legal control, or an effect of informal user or marketplace regulation (e.g. change in drug preference, user driven harm reduction).

[16] http://www.parliament.nz/en-nz/pb/legislation/bills/00DBHOH_BILL12021_1/psychoactive-substances-bill. A full critique of the Bill can be found in J Psychopharmacology 2013; 27:584-589.
[17] http://www.health.govt.nz/our-work/regulation-health-and-disability-system/psychoactive-substances/interim-product-approvals

Prevention and treatment responses

- Although many Member States have encouraged the development of NPS-specific prevention responses, and several research projects have been funded by the European Commission[18], at the time of writing, none have undergone formal evaluation and therefore the effectiveness of such approaches at reducing use and associated harm is unknown.
- As NPS use is a low prevalence behaviour, universal approaches to prevention (i.e. interventions targeting all members of the population, regardless of levels of risk) are unlikely to be cost-effective. Reduction of the potential harmful effects of NPS may be achieved by targeted prevention approaches that include classic harm reduction components[19]; that aim to reduce frequency of use; and that encourage switching from NPS (which have uncertain risk profiles) to 'classic' illegal drugs (which are potentially harmful, but scientific knowledge, treatment service and preventative responses are better established (but for which the harms from punishment for being caught in possession may be serious).
- Local and regional monitoring systems that collect intelligence on the emergence of new, and potentially harmful drugs are important components of formal responses to NPS. However, even well established European monitoring systems have not yet been rigorously evaluated with regards to impact upon user behaviour (e.g. do alerts about potentially harmful drugs dissuade use?). In addition, problems with identification and mis-selling/packaging of NPS mean that the impact of substance specific warnings may be minimal.

6 NPS in ALICE-RAP

- Two WorkPackages in ALICE-RAP investigate NPS:
    - Researchers at the Institute of Psychiatry (UK) are carrying out a semi-systematic review of the Internet marketing of illicit drugs and 'legal highs' and analyzing trends over 5 years. The work, aims to identify 100+ websites and analyse their marketing practices.
    - As part of a broader work, researchers from Liverpool Moores University (UK) have investigated the evidence base of policies designed to respond to young people's participation in 'addictive behaviours' (including use of NPS).

[18] (e.g. DPIP programme funded projects #4000003597 / UNIVERSITÄTSKLINIKUM FREIBURG/ UNIVERSITÄTSKLINIKUM FREIBURG / SPICE II Plus: New synthetic cannabinoids and stimulants – evaluating risk behaviour, problematic use and toxicity for developing specific approaches in primary and secondary prevention / DE; #4000003600 / STICHTING NOVADIC-KENTRON / A LOCAL approach towards the reduction of PsychoActive Substance uSe (LOCAL-PASS) / NL)

[19] E.g. Neurosci Biobehav Rev. 2011; 35:1186-202.