Workstream 5

NPS Top lists and national technical folders

Final report

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Overview of this report

The aim of this document is to outline the work stream 5 methodology and the main tasks completed within the work stream.

Aims and objectives of work stream 5

Objective

The main objective of work stream 5 was to design the methodology for the selection of NPS that would be focused upon by each partner throughout the I-TREND project.

The NPS selection methodology resulted in each partner creating an NPS Top List which included compounds that would be the main focus of monitoring and analysis within other work streams. Data collected on these compounds from work streams 1-4 would then be triangulated to create substance profiles in the form of national and aggregated European technical folders. Within work stream 5 the NTF and ITF content template was designed and implemented.

Post note:

During the project, it happened that this methodology allows partners to select NPS which could been considered as to be used the most frequently in their country – taking account the limits indicated at the end of the document.

However for the pragmatical needs of the project and notably for the purchase of samples online, it was necessary to work with a Top List with two levels :

- One level for attempting to assess which NPS was spreading the most - the list obtained from the cross-checking of data sources.
- Another level more “operational”, representing the NPS on which it was possible to conduct a full monitoring.

This decision had been took considering that:

- It was most difficult to purchase online scheduled substances, either the substance was no more available or it was sold on online web shops which do not accepted the pre-paid payment (using by several partners).
- The researchers did not have legal framework for purchasing controlled substances.

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Aims

In order to meet the objective of the project, a number of specific aims were set. Work stream 5 aimed to:

1) Establish a common working definition of NPS to be applied throughout the project through consultation with project partners and consideration of existing definitions.
2) Design a methodology for selecting a NPS ‘Top List’ containing substances that would be the main focus of monitoring and analysis by partners within work streams 1-4.
3) Monitor NPS identified in European markets during 2013 and 2014 at both the national and aggregated level.
4) To develop technical folders for the chemical compounds selected for monitoring and analysis within the I-TREND project at both national and aggregated European level.

1. Establish a common working definition of NPS

Through consultations with partners and a review of the literature, an I-TREND specific working definition of NPS was agreed. The aim was to move away from the application of solely legal definitions when researching the phenomena of NPS. However, a number of issues arose when formulating an appropriate definition that could be easily applied to each country's cultural context and NPS situation. This included debate around whether to include or exclude natural products within the definition. There was also discussion around whether branded products should be included within the definition. Due to such issues and differences in the NPS situation in each country, it was agreed that the definition would be broad in that it did not rely on legal definitions (i.e. a country could include an illegal substances if there was evidence of use and harm) and recognised the existence of natural and branded products. However, it was acknowledged that the inclusion of illegal substances had implications for work stream 4, in which substances were to be test purchased from national web shops. As such, it was agreed that the inclusion of legal substances that were available on the internet for purchase was preferred.

Although there was much debate at the beginning of the project as to whether NPS should be defined along legal terms and whether countries would include natural and branded products in their monitoring, as the project proceeded the majority of countries did not include illegal substances[1] despite these NPS being prevalent within seizure data. The main reason for excluding controlled substances was that they would not be available for purchase on web shops and as such would have impacted on the objectives and aims of work stream 4. Moreover, all partners decided to focus on synthetic products rather than natural products. Branded products were not selected for monitoring and analysis. However, where possible, data was included which indicated which branded products contained each chemical compound on the NPS Top Lists at national level.

Extended definition, the European definition

The most common definition of NPS refers to emerging substances that are used for psychotropic effects (WHO, 1994) in pure form or in preparation, that are not controlled by the 1961 United Nations Single Convention on Narcotic Drugs or the 1971 United Nations Convention on Psychotropic Substances, but which may pose a public health threat comparable to that posed by substances listed in these conventions (European Council Decision 2005/387/JHA). The European Council Decision definition of NPS includes both newer and older ('novel') synthetic, natural and medicinal products, as long as there is evidence of recreational use and misuse. The EMCDDA categorises NPS into the following groups: Phenethylamines, Indolalkylamines (f.e. tryptamines), Piperazine derivates, Cathinones, Cannabinoids, Narcotic analgesics and 'Others'. It is under this very broad, category, that some substances such as 6-APB or Methoxetamine have been listed.

[1] France included a number of controlled substances. The UK and Poland initially include controlled substances based on data, but these were not maintained and replaced by legal NPS to keep in line with the project aims.

To date, few have been recommended for control by the Council of the European Union. However, Member States have introduced their own legislation which has led to an array of policy responses. The law is thus complicated in that a substance can be controlled at national level in one EU country, but not in another, and vice-versa. Moreover, a substance may actually be controlled at national and/or international level even before its production or prior to evidence of use.

Shortened definition

The focus of the I-TREND project is New/ Novel Psychoactive Substances (NPS), or 'New Synthetic Drugs'. These substances are often and popularly referred to as 'legal highs' or 'designer drugs'.

They are also commonly sold as "research chemicals" (RC) or under a diverse range of fanciful marketing names (e.g. NRG-3, Benzofury, Funky, Cocolino etc.). In order to circumvent the law, retailers sell NPS under a disguise of misleading purposes such as "bath salts", "incense", or "goods not intended for human consumption (collector goods)". Such labels allow retailers to market NPS to a wide audience, without directly referring to them as substances for recreational consumption.

NPS imitate the effects of existing illegal drugs such as cocaine, (meth)amphetamines, ecstasy, cannabis, ketamine or opium. Most NPS can be purchased online, but they can also be sold in head shops and smart shops or on the street within traditional drug markets. They come in different forms such as powder, pills, capsules, herb and resin.

The legality of NPS can give users the false impression that such substances are safe and authorized by the law. Moreover, it is somewhat a myth that all 'legal highs' are in fact legal, as many are forbidden by national legislation even before their production. Some NPS may also be found to contain additional illegal substances. There is a relatively lack of research on these substances compared to traditional drugs

I-Trend definition

I-TREND employs the term *New/Novel Psychoactive substance* (NPS). However, it is important to note that the term 'new' might be misleading as many of these substances aren't new in their existence and have been around for many years. What is 'novel' about some of these substances isn't there actually existence, but a new pattern of use (i.e. newly 'consumed' substances). NPS are popularly referred to as 'Research Chemicals', 'Designer Drugs', or 'Legal highs'.

To some extent, employing a legal definition such as the above may be restrictive as it suggests that once a substance has been controlled, it is no longer an NPS. Thus a legal definition creates the situation where a substance may initially be seen as an NPS due to a lack of control, but may later be excluded from the list of NPS once the legal status of the substance changes. However, the unique *history* of the substance is important and may provide justification for the substance continuing to be labelled an NPS.

Thus, the I-TREND project highlights the following characteristics as key to defining NPS:

- NPS are substances that have psychoactive effects and mimic the effects of traditional drugs.

- NPS are often synthesised in order to circumvent and bypass national and international laws controlling drug use, in turn avoiding prosecution for users and retailers.

- The ever expanding manufacturing of NPS is a result of new advances in academia and chemistry, as well as the rise of the Internet age.

- Research shows that NPS are appealing to consumers for a number of reasons: ease of availability (particularly through the internet), legal status in some countries, the perception that legal presumes safe, and also the potential to produce unique subjective effects.

- NPS can include substances that have existed for some time ('novel') and substances that have recently been synthesised ('new') with the sole purpose of being sold and used as a psychoactive substance.

- The Internet is an important factor in the NPS market, making NPS widely available to a large number of people. NPS are also be sold in 'head shops' and 'smart shops' in some countries and also available through traditional dealing networks.

- On the whole, NPS are manufactured and imported from outside the EU (e.g. China).

- There has been increased interest and concern around NPS and a significant increase in the number of NPS being manufactured since the emergence of 4-methylmethcathinone (mephedrone) in 2006.

- There is a relatively lack of research on NPS compared to traditional drugs. In particular, there is a lack of data on prevalence and harm, and a dearth of research allowing for the comparison of use across countries.

- NPS compounds can be distinguished from 'classical drugs of misuse' (e.g. amphetamine, cocaine, heroin, cannabis) because NPS have had little or no history of medicinal use[2] (King and Kickman, 2011).

I-TREND employs a broad and dynamic definition of NPS that can be adapted to each participating countries cultural context without losing the comparative nature of the research. In addition to synthetic products the EMCDDA and the European Council decision definitions considers, natural and vegetal products, as well medicinal products (or API, active pharmaceutical ingredient) being used recreationally, as NPS. For example, EMCDDA

[2] Medicinal products used for recreational purposes may also be considered NPS (European Council Decision 2005/387/JHA). However, medicinal products are not a focus in the I-TREND project.

research[3] shows that both natural and synthetic substances are among the most commonly retailed NPS on the internet (e.g. Salvia Divinorum; hallucinogenic mushrooms; MDAI; methoxetamine; and 6-APB2). Vegetal and natural products include products sold as salvia, kratom and peyote. Synthetic substances refer to two types of products. Firstly, those presented in powder, liquid or pills with a commercial or chemical name. Secondly, products presented as a kind of cannabis, with a plant-based form and essentially sold with a branded name. Despite their plant-based form, they are not actually vegetal product, because synthetic substances have been vaporised on them.

Although I-TREND acknowledges that vegetal/ natural products *can* be considered as NPS, some countries wish to focus solely on *synthetic* substances only. If this review of NPS online availability shows natural, medicinal and synthetic substances, those most often reported by the EMCDDA Early Warning System (EWS) are synthetic cannabinoids and cathinones. This focus on synthetics may also be justified by national and international seizure data which shows a rapid expansion in the production of synthetic products and a higher frequency of police seizures of synthetic products. Moreover, a lack of scientific data on these products increases the need to more learn about them.

Examples of NPS currently appearing in project partner countries:

5-IT, MXE, 4-HO-MET, MDAI, 4FA, 3 MMC, N-ethylbuphedrone, some branded products such as “Spice”, Benzo Fury, Dove, Funky, Cocolino.....

Examples of substances provided by partners that would be excluded:

Modafinil and DXM as they are sold over the counter and have national marketing autorisation.

GHB and Ketamine because they are considered traditional products in that sense that they have a longer history of recreational use. Their toxicity and effects are also wide described in the scientific publication.

Examples given about the different type of substances – could be inserted in the text, visible when the reader pass the mouse on the terms

1. New/Novel Synthetic Substances

These are synthetic substances with stimulatory, hallucinogenic or sedative effects sold under various names, such as El Padrino, Ex, K2, Diablo, Funky, Cocolino etc. or under their chemical name directly, as for example GBL, mephedrone, penthedrone, methoxetamine, MDPV, 6-APB, bk-MDMA, 3,4-DMMC etc. Their effects are often compared to effects of known drugs like marijuana, pervitine, ecstasy, cocaine etc. ***This is not a question on new herbal drugs or herbal mixtures (see below).***

[3] 2012, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32005D0387:EN:NOT)

2. Synthetic Cannabinoids

For example products "spice", "Euprohia", "Utrecht", "Rotterdam" and other; these are herbal mixtures with added synthetic cannabinoids sold "as cannabis".

3. Herbal Substances

These are herbal substances with hallucinogenic, stimulatory or sedative effects in the form of extract, crushed material, dry material or mixture, as for example , kratom (Mitragyna speciosa), Salvia divinorum (not the usual one used for cooking or as a medicinal herb), damiana (Turnera diffusa) etc. None of the herbal drugs are new or recently discovered, they just appear or are on offer as "new" on the internet, and also offered under new forms (extracts, mixtures) or together with other (synthetic) drugs.

2. Selecting the NPS 'Top Lists'

2.1 Overview of the methodology employed

In order to select NPS for monitoring and analysis within the I-TREND project work streams, a suitable methodology for selecting substances was designed by LJMU and implemented by partners.

Two rounds of NPS selection were conducted.

NPS Top List selection 1

The first selection of NPS was carried out between June and July 2013. The first NPS Top List selected substances that would be the main focus of monitoring and analysis in other work streams (1-4).

Ideally data on both prevalence (e.g. seizure and survey data) and harms (e.g. fatal and non-fatal intoxication data) would be considered in the decision making process, as would the current availability of NPS online (e.g. consulting national web shops, web shops data). Compounds that appeared across a number of data sources were chosen. Following consultations with Key Informants/Experts (KIs) at national level, NPS would then be selected, again considering prevalence, harms and online availability. See section 2.2. for an overview of the data suggested as sources to consult in the selection of NPS. It was decided that around 10 substances should be included in the Top List. However, more, or less, could be included at the discretion of each partner depending on the available evidence. Note that the Top Lists do not list NPS in a hierarchical list (e.g. substance 1 in the list is not necessarily regarded as more problematic or more worthy of attention than substance 10). The aim was to create National Technical Folders (NTF) for each substance on the national Top Lists. Each national Top List was then merged to produce an aggregated European Top List. This was created by including any substances that had been chosen by two or more partners. Aggregated

European Technical Folders were then to be produced for compounds included on the aggregated Top Lists, merging data on each compound from a number of countries.

NPS Top List selection 2

The second selection of NPS was conducted between April and August 2014. This second round of NPS selection allowed us to indicate whether there had been any change in the NSP market at national and European over a 24 months period (2013 and 2014). Along with consulting the data sources outlined in 2.2, it was intended that findings from other work packages, particularly WS1, WS2 and WS3 (forum analysis, online shop analysis and survey results), would be consulted to validate each NPS continued inclusion or exclusion in the Top List. Compounds that appeared across a number of data sources were chosen. As in the first selection, around 10 substances were included in the 'Top List'. However, more, or less, could be included at the discretion of each partner based on the available evidence.

Contingent with the evidence, at this stage substances could be excluded from the Top List and replaced by others. This occurred in three countries; France, Czech Republic and Poland. Despite those changes, Top List remained mostly stable. It was originally intended that additional NTF would be created for any substances added to the Top List following the second NPS selection process by monitoring and analysing these compounds within other work streams. However, due to capacity issues and delays within other work streams, this aim was not completed. Moreover, in some countries (UK and The Netherlands) the Top Lists did not change over the 24 months period and as such no additional NTF were created. As in the first selection, each national Top List was then merged to produce an aggregated European Top List. This was created by including substances that had been chosen by two or more partners.

At the time of writing, both the Czech Republic and Poland confirmed that they would conduct a third NSP selection to assess whether there had been more recent changes in their NPS Top List. However, data was not available at the time of writing.

2.2. Data used in the Top List selection process

Guidance on what data sources should be consulted (if available) in the selection of NPS was provided. As stated, selecting the Top List of NPS aimed to consider prevalence and availability of NPS, as well as harms. Each data source is described below. Triangulating a number of data sources was advised, with compounds that appeared across a number of data sources being chosen if possible. However, all data sources were not available to all partners.

National seizures

Access to national NPS law enforcement seizure data was available through the EMCDDA's Reitox National Focal Point's Early Warning Systems on NPS and the EMCDDA's EDND. This data allowed each partner to quantify the most seized NPS at two points in time (2013 and 2014), taking into consideration the number of seizures and the amount of substance seized (if possible). It was acknowledged that controlled NPS are more likely to be seized by law enforcement agencies and as such some newly available un-controlled substances may not

show up in such data. Therefore, the use of various other data sources in the selection was required to complement seizure data.

Fatal and non-fatal intoxication data

Toxicology/laboratory data on fatal and non-fatal intoxications was available from EMCDDA's Reitox National Focal Point's Early Warning Systems on NPS and the EMCDDA's EDND. Such data is a useful measure of NSP-related harms. Specialized drug-death agencies also existed in some countries (e.g. the National Programme on Substance Abuse Deaths & Volatile Substance Abuse (NPSAD) mortality register provides data on NPS-related deaths in with UK). These agencies provided valuable data on drug fatalities that could be cross referenced with the EMDDDA's data

Other National NPS Warning Systems

Complimentary data was also available by national government Warning Systems on NPS within some countries. For example, in the UK Forensic Early Warning System (FEWS) is the main agency monitoring NPS seizures. FEWS also collect samples of NPS seized at events such as music's venues and festivals.

National Drug surveys

Some countries conduct national drug surveys which report the prevalence NPS use. Moreover, self-report surveys conducted by academics/researchers within each country report findings on use of specific NPS. Where available and relevant, findings of these surveys were consulted and considered when selecting the NPS Top List.

Health information seeking data

In some countries, tools developed for providing both users and practitioners with information on NPS generate data on the number of requests for information on specific substances. In the UK for example, data information requests to the Government's main advice and information service on drugs, 'Talk to Frank', was available and provided a picture of what NPS the public seek information on via both telephone and service's website. In addition, the National Poisons Unit in the UK provides a telephone and online substance information service to practitioners (e.g. nurses, Doctors). Where available, such data provided information on what NPS users are interested in and what NPS are of concern to practitioners.

Government NPS 'Watch Lists'

In some countries, Government agencies had their own Top Lists of NPS that were the focus of legislative attention. For example, in the UK the Home Office and the Advisory Council on the Misuse of Drugs (ACMD) have produced NPS 'Watch Lists' documenting substances of concern and substances for possible future control. Where possible, the NPS selected for ITREND national Top Lists could be cross referenced with these Government NPS lists.

National drug monitoring system data

Data collected from national data monitoring sources provides information on prevalence of use. In the UK data from the National Drug Treatment Monitoring System (NDTMS) provided information on the numbers of individuals receiving treatment for NPS use. Other examples include DIMS in The Netherlands and SINTES in France.

Substance currently available on UK web shops

As the main aim of I-TREND was to monitor the availability of NPS on the internet and to test purchase such substances for laboratory analysis, it was important to consider what substances were being sold at the national level on web shops. In some instances (UK), web shops were selling and promoting newly synthesized compounds as replacements for controlled substances that had high seizure levels and substances that had been implicated in a number of fatal intoxications. Although such substances were too new to be found within seizure data, they were included in the Top List to acknowledge this issue of the impact of legislation on the NPS market. Moreover, these newly available substances had little published research and guidance on dosage and effects and as such it was felt important to include them in the Top List and address this gap in knowledge. For example, both 5 and 6 APB were to be initially included in the UK Top List based on seizure and harms data. However, due to their control they were not availability for purchase on UK web shops. At the time, the recently synthesized 5-EAPB was being sold and promoted on UK web shops as a 5 and 6 APB replacement and was thus included in the Top List.

2.3. Consultation with Key Informants /Experts

Once the initial national Top Lists had been decided, where feasible, a consultation with Key Informants (KIs) (e.g. experts in the NPS field) from a range of backgrounds (e.g. laboratories, policy makers, academics, law enforcement) was carried out. KIs were asked if they agreed with the substances included in the Top List and if they felt any NPS had been overlooked. Consultations were carried out in person, via telephone and via email.

Examples of KIs included:

- Criminal Justice, law enforcement and government monitoring systems.
- Health (e.g. Government health departments).
- Laboratories/toxicology and pathology.
- Focal point/ EMCDDA representatives.
- Academics (e.g. leading academics in the field of NPS)

The national KIs were provided with a summary of the I-TREND project and sent a copy of the draft Top List. They were asked their general opinion on the Top List, if they felt each substances should be included in the list, and if not, why. They were also asked if there are any substances which they think should be added to the Top list and if so, why. Any suggestions of adding additional NPS to the Top List were supported by evidence. Following consultation, each partner then made a decision as to whether there was sufficient evidence to amend the Top List (e.g. add substances based on the consultation and evidence presented).

2.4. Data used when selecting the NPS ‘Top List’

Tables 1-5 below provide an overview of the data used in selecting substances for analysis in the first and second NPS selection. Most countries used a combination of both prevalence and harms data. However, prevalence data tended to be more available than data on harms, with a lack of availability to harms data in some countries (i.e. France, Poland). As such, law enforcement data tended to be relied on, and then backed up with the additional sources.

Table 1: Data sources used in the France Top List Selection process

Type of Data	Source	Toxicological analysis	Round 1	Round 2
Toxicovigilance	National Agency for Medicines and health products safety (ANSM)	Y	Y	Y
Seizures	Scientific Police	Y	Y	Y
	Custom services	Y	Y	Y
Data on adverse events involving NPS	Unknown	Y	N	Y
Substances collected from users	French EWS, SINTES	Y	Y	Y
Substances online popularity	Forums monitoring	N	Y	Y
Users answers	Online surveys last used NPS in 12 month users	N	N	Y
Key Informant/Expert Consultations	Law enforcement laboratories customs, police, French CDC, University hospital laboratory)	N	Y	N

Table 2: Data sources used in the UK Top List Selection process

Type of Data	Source	Toxicological analysis	Round 1	Round 2
Fatal and non-fatal intoxications	NPSAD, EMCDDA	Y	Y	Y
Seizures	EMCDDA, FEWS	Y	Y	Y
NPS notifications reported to the EMCDDA in 2013 and 2015 at national level	EMCDDA	Y	Y	Y
Other National NPS Warning Systems	FEWS	Y	Y	Y
Health information seeking data	UK Government 'Talk to Frank', National Poisons Information Unit	N	Y	N
National Drug Monitoring System data	NDTMS	N	Y	Y
Government NPS 'watch lists'	Home Office	N	Y	Y
Substance currently available on UK web shops	Web shops from WS 2	N	Y	N
Surveys	General population surveys, surveys of NPS users	N	Y	Y
Key Informant/Expert Consultations	FEWS, academics	Y	Y	Y

Table 3: Data sources used in The Netherlands Top List Selection process

Type of Data	Source	Toxicological analysis	Round 1	Round 2
Seizures	Forensic Institute	Y	Y	Y
	Custom services	Y	Y	Y
Substances collected from users	DIIMS	Y	Y	Y

Table 4: Data sources used in the Czech Republic Top List Selection process

Type of Data	Source	Toxicological analysis	Round 1	Round 2
Toxicovigilance	Data from toxicology labs	Y	Y	Y
Seizures	Unknown	Y	Y	Y
Web shop monitoring	Czech interface WS 2	Y	Y	Y
Substances online popularity	WS1 Forums monitoring	N	Y	Y
Surveys	WS3 Survey on internet users. General population surveys	N	Y	Y
Fatal and non-fatal intoxication monitoring	Unknown	Y	Y	Y

Table 5: Data sources used in Poland Top List Selection process

Type of Data	Source	Toxicological analysis	Round 1	Round 2
Seizures	EMCDDA	Y	Y	Y
Substance Analysis	National Institute of Medicines	Y	Y	Y
Substances online popularity	WS1 Forums monitoring	N	Y	Y
Surveys	WS3 Survey on internet users.	N	Y	Y

3. National and aggregated European Technical Folders

Based on existing data provided by the EMCDDA's EDND and reviews of the literature, as well as data collected from other work streams (1-4[4]), substance profiles (National Technical Folders (NTF)) aimed at practitioners, service providers and policy makers (i.e. non-academics) were produced for each chemical compound selected for monitoring and analysis at national level. It was also intended that International Technical Folders (ITF) for each substance on the aggregated European Top lists would be produced. Following consultation and discussion with partners, a folder template was produced and used as a guide for each partner when writing substance profiles.

Due to capacity issues and a lack of data on all substances, not all partners created NTF for all substances on their Top Lists. The UK produced NTF for 10 of the 11 substances on the Top List. A NTF for AKB48 was not created as a folder had been produced for the derivative 5F-AKB48 which more data was available for. NTF were created for seven of the 10 substances listed on the Dutch Top Lists. Poland has produced folders for 9 of the 10 substances of their Top List. A folder on MDPBP was not created due to a lack of data on the compound. Due to a lack of data and capacity issues, at the time of writing 'two or three' NTF will be created for substances on the French Top Lists. At the time of writing, the Czech Republic have planned on producing NTF for all substance son their first Top List. Due to delays in other work streams and delays in partners providing drafts copies of their NTF to LJMU, only one ITF has been produced at the time of writing combining UK and Dutch data on the psychedelic 5-MeO-DALT.

See Appendix 1 for the NTF/ITF template.

4. National and aggregated European Top Lists

National 'Top Lists'

Each country selected between 10 and 11 NPS within their Top Lists. Table 6-10 below provide an overview of the NPS selected by each country in the first and second NPS selection. The substances highlighted in yellow show the compounds controlled before the Top List Selection process. The substances highlighted in orange show those compounds controlled during the project. In the UK, four substances were controlled during the project. France included five controlled substances, which were therefore not available for test purchase on web shops. One additional substance was controlled in France during the project. During the project 4 substances on the Czech Republic Top Lists were controlled. None of the substances were controlled in the Netherlands. In the UK and The Netherlands, the NPS Top Lists remained stable between the first and second NPS selection. A number of substances were excluded in the second selection process and replaced by others in France, Poland and the Czech Republic. At the time of writing, both the Czech Republic and Poland confirmed that they would also conduct a further NSP selection. However, data was not available at the time of writing.

[4] Result of web shop marketing analysis, forum analysis data, survey results and test purchasing

Table 6: UK NPS Top lists

NPS selection 1- 2013		NPS selection 2- 2014
Cannabinoids		
1	5F-AKB48	5F-AKB48
2	AKB48	AKB48
Stimulant (Arylalkylamine)		
2	MPA	MPA
4	5-EAPB	5-EAPB
Stimulant (Piperidines and Pyrrolidines)		
5	Ethylphenidate	Ethylphenidate
Psychedelics (Indolalkylamine)		
6	AMT	AMT
7	5-Meo-Dalt	5-Meo-Dalt
Benzodiazepine		
8	Etizolam	Etizolam
Stimulant (Aminoindane)		
9	2-AI	2-AI
10	N-Methyl-2-AI	N-Methyl-2-AI
Other		
11	Methoxphendine	Methoxphendine

Table 7: The Netherlands NPS Top Lists

NPS selection 1- 2013		NPS Selection 2- 2014
Stimulants (Cathinones)		
1	MDPV	MDPV
2	4-MEC	4-MEC
Stimulants (Phenethylamine)		
3	4-Fluoroamphetamine (4-FA)	4-Fluoroamphetamine (4-FA)
Stimulants (Arylalkylamine)		
4	5-(2-Aminopropyl)indole (5-IT)	5-(2-Aminopropyl)indole (5-IT)
5	6-APB	6-APB
6	5-APB	5-APB
Psychedelics (Phenethylamine)		
7	25-I NBOME	25-I NBOME
8	5-Meo-DALT	5-Meo-DALT
Psychedelics (Indolalkylamine)		
9	AMT	AMT
Disassociatives (Arylcyclohexylamines)		
10	Methoxetamine	Methoxetamine

Table 8: Poland NPS Top lists

NPS selection 1- 2013		NPS selection 2- 2014	
Cannabinoids			
1	UR-144	1	UR-144
2	AM-2201	2	AM-2201
Stimulant (Cathinones)			
3	Pentedrone	3	Pentedrone
4	3-MMC	4	3-MMC
5	Ethcathinone	5	Ethcathinone
6	a-PVP	6	a-PVP
7	3,4-DMMC	-	-
8	Brephedrone	-	-
9	MPPP	-	-
10	MDPBP	-	-
11	Mephedrone	-	-
Stimulant (Piperidines and Pyrrolidines)			
-	-	7	Ethylphenidate (EP)
Psychedelics (Phenethylamine)			
-	-	8	25I-NBOMe4
		9	4-HO-MET
Disassociatives (Arylcyclohexylamines)			
-		10	Methoxetamine (MXE)

Table 9: Czech Republic NPS Top Lists

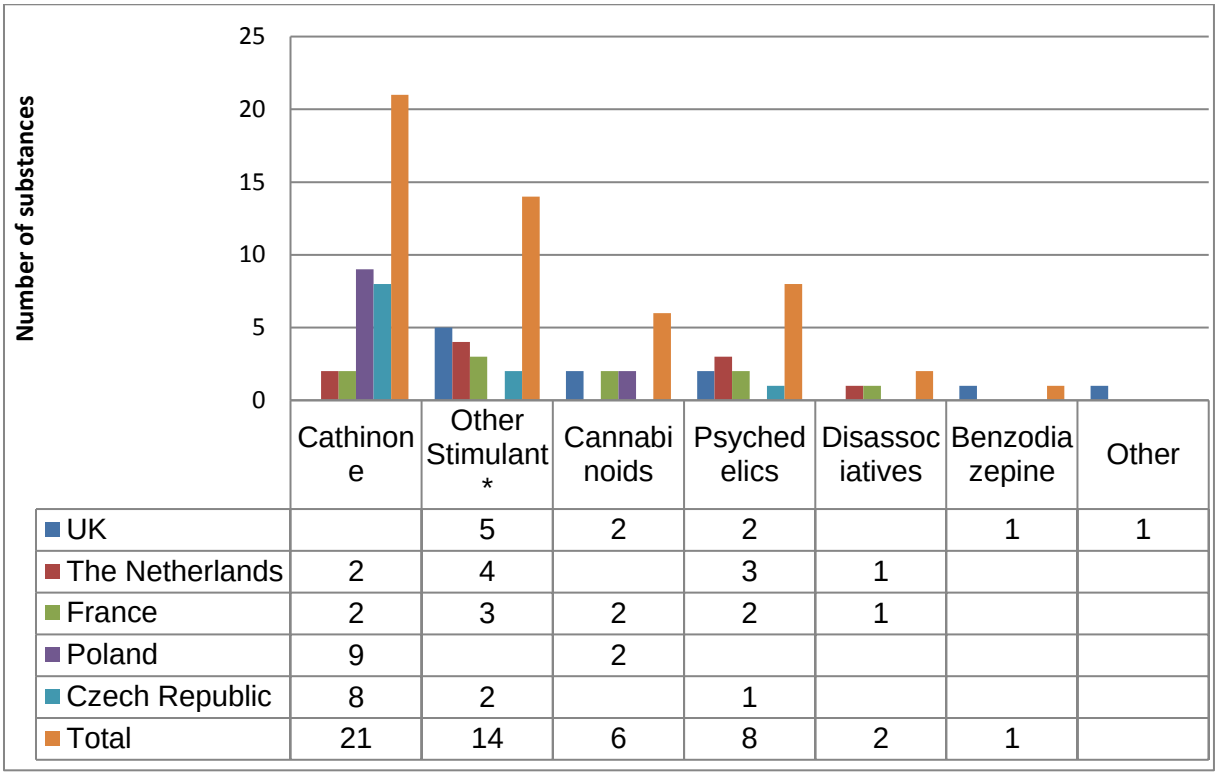
NPS selection 1- 2013		NPS selection 2- 2014	
Cannabinoids			
		1	5F-PB22
Stimulants (Cathinones)			
1	3-MMC	2	3-MMC
2	4-MEC	3	4-MEC
3	Ethcathinone	-	-
4	Pentedrone	4	Pentedrone
5	MDPBP	-	-
6	MPPP	-	-
7	alpha-PVP	5	alpha-PVP
8	bk-MDMA (Metylone)	-	-
Stimulants (Phenethylamine)			
9	4-FA (4-Fluoroamphetamine)	6	4-FA (4-Fluoroamphetamine)
-	-	7	2-FMA
Stimulants (Arylalkylamine)			
10	6-APB	-	-
	-	8	MPA
Stimulant (Piperidines and pyrrolidines)			
	-	9	Ethylphenidate
Psychedelics (Indolalkylamine)			
11	AMT	10	AMT
Arylcyclohexylamines			
	Methoxetamine (MXE)	11	Methoxetamine (MXE)

Table 10: France NPS Top Lists

NPS selection 1- 2013		NPS selection 2- 2014	
Cannabinoids			
1	AM-2201	-	-
2	UR-144	-	-
		1	5F-AKB48
Stimulant (Piperidines and pyrrolidines)			
3	Ethylphenidate	2	Ethylphenidate
Stimulants (Cathinones)			
4	MDPV	3	MDPV
5	4-MEC	4	4-MEC
-		5	ALPHA-PVP
		6	3-MMC
	-	7	Methylone
Psychedelics (Phenethylamine)			
6	25-I NBOME	8	25C-NBOMe
7	5-MEO-DALT	-	-
Arylcyclohexylamines			
8	Methoxetamine	9	Methoxetamine
Psychedelics (Phenethylamine)			
-		10	2C-E
Stimulant (Arylalkylamine)			
-		11	MPA
9	6-APB	-	
10	5-APB	-	

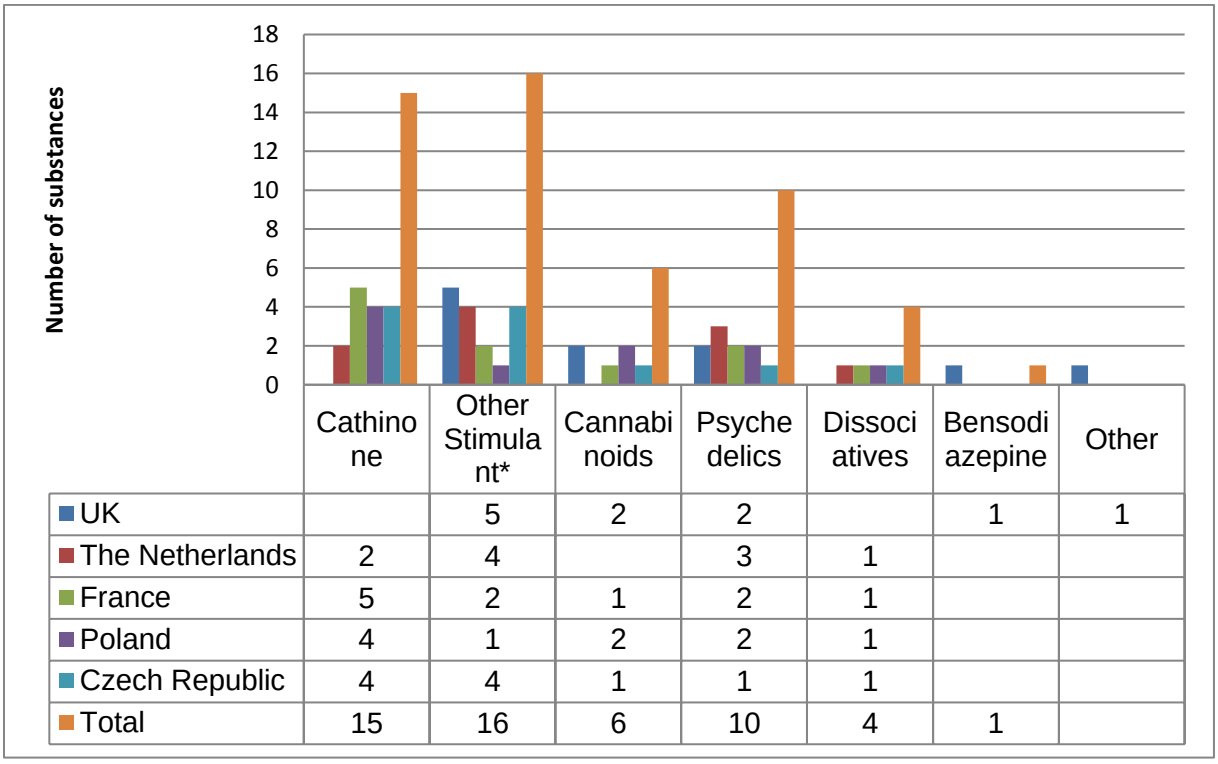
Graph 1 and 2 display the substances selected by substance group in both the first and second NPS selection. As the graphs show, there was much variety in the types of substance classification selected for analysis by each partner, highlighting the differences in the NPS situation between countries. Most NPS tended to fall within the cathinone and stimulant category in both the first and second selection.

Graph 1: Substances selected in NPS selection 1 by substance group



	Cathinone	Other Stimulant *	Cannabinoids	Psychedelics	Disassociatives	Benzodiazepine	Other
UK		5	2	2		1	1
The Netherlands	2	4		3	1		
France	2	3	2	2	1		
Poland	9		2				
Czech Republic	8	2		1			
Total	21	14	6	8	2	1	

Graph 2: Substances selected in NPS selection 2 by substance group



	Cathinone	Other Stimulant*	Cannabinoids	Psychedelics	Dissociatives	Bensodiazepine	Other
UK		5	2	2		1	1
The Netherlands	2	4		3	1		
France	5	2	1	2	1		
Poland	4	1	2	2	1		
Czech Republic	4	4	1	1	1		
Total	15	16	6	10	4	1	

Aggregated Top Lists

In the first NPS selection a total of 31 unique substances were selected across the 5 countries, 16 of which were selected by two or more countries and as such were included in the aggregated European Top List. The substances highlighted in green in Table 11 were excluded from the aggregated list following the second selection process. In the second selection a total of 31 unique substances were selected across the 5 countries, 13 of which were selected by two or more countries and as such were included in the aggregated European Top List. The substances highlighted in red in Table 12 were added to the aggregated list following the second selection process.

Table 11: Aggregated NPS Top List: NPS selection 1

Substance		Substance Classification	Number of countries selecting the substance
1	25-I NBOME	**Psychedelics (Phenethylamine**	2
2	5-MeO-DALT		3
3	AMT	**Psychedelics (Indolalkylamine)**	3
4	3-MMC	**Stimulant (Cathinones)**	2
5	Ethcathinone (ETH-CAT)		2
6	MDPBP		2
7	MDPV		2
8	MPPP		2
9	4-MEC		3
10	4-Fluoroamphetamine	**Stimulants (Phenethylamine)**	2
11	6-APB	**Stimulants (Arylalkylamine)**	3
12	5-APB		2
13	Ethylphenidate	**Stimulant (Piperidines and Pyrrolidines)**	2
14	UR-144	**Cannabinoids**	2
15	AM-2201		2
16	Methoxetamine (MXE)	**Arylcyclohexylamines/Other**	3

Table 12: Aggregated NPS Top List: round 2

Substance		Substance Classification	Number of countries selecting the substance
1	25I-NBOMe	**Psychedelics (Phenethylamine**	2
2	5-MeO-DALT		2
3	AMT	**Psychedelics (Indolalkylamine)**	3
4	MDPV	**Stimulant (Cathinones)**	2
5	3-MMC		3
6	Pentedrone		2
7	4-MEC		3
8	a-PVP	**Stimulant (Piperidines and pyrrolidines**	3
9	Ethylphenidate		4
10	MPA	**Stimulants (Arylalkylamine)**	3
11	4-Fluoroamphetamine	**Stimulants (Phenethylamine)**	2
12	5F-AKB-48	**Cannabinoids**	2
13	Methoxetamine (MXE)	**Arylcyclohexylamines/Other**	4

Table 13: Aggregated NPS Top List – comparison

Substance Top List Round 1	Number of countries selecting the substance	Substance Top List Round 2	Number of countries selecting the substance
25-I NBOME	2	25I-NBOMe	2
5-MeO-DALT	3	5-MeO-DALT	2
AMT	3	AMT	3
3-MMC	2	3-MMC	3
MDPV	2	MDPV	3
4-MEC	3	4-MEC	4
Ethylphenidate	2	Ethylphenidate	4
Methoxetamine (MXE)	3	Methoxetamine (MXE)	4
4-Fluoroamphetamine	2	4-Fluoroamphetamine	3
MDPBP	2	Pentedrone	2
MPPP	2	a-PVP	3
6-APB	3	MPA	2
5-APB	2	5F-AKB-48	2
UR-144	2		
AM-2201	2		

Limitations and difficulties encountered

It is important to draw attention to a number of limitations and difficulties encountered in work stream 5:

Adding note : In the I-TREND project The Top Lists build in the frame of the WS5 have for purpose to assess the containing substances that would be the main focus of monitoring and analysis by partners within work streams 1-4.

- The methodology was presented as an 'ideal type' for partners to use as a guide when selecting NPS for inclusion in the study. The methodology was based on data available in the UK, a country which had access to a wider range of data than other partners. As such, the suggested data presented within the methodology was not available to all partners, resulting in differences in the implementation of the methodology designed. In particular, in some countries there was a lack of availability of NPS-harms data and a general lack of available of sources. This meant it was not possible to triangulate law enforcement prevalence data with different kinds of sources.

- An additional weakness of the methodology was difficulties in deciding if and how to weight the relative importance of one type of data over another. Due to greater availability law enforcement data tended to be relied on, and backed up with other sources.

- It must also be noted that the majority of the data used in the selection process did not represent NPS 'use', but acted as proxies for use. For example, seizures, sale data and fatal and non-fatal intoxication data.

- With the acceptance of the Czech Republic and Poland, who will select NPS over 3 time periods, NPS selection was conducted over two periods of time. Several selection processes are required to identify real change in the NPS market over time.

- Overall, more consistency and unification in the implementation of methodology across different countries and across both selection procedures would have been beneficial. It was difficult to assess the comparability of the Top Lists across countries due to differing implementation. It was also difficult to assess whether the Top List selection process reflected real change in the NPS market, or whether changes were a result of differences in the sources used in the 2 selection procedures.

- The project focussed on chemical compounds as opposed to branded products, despite the use of brands being common within each country (supported by WS1 data). Producing folders on brands would have been beneficial to users. However, due to inconsistencies and variation in compounds found within branded products, producing folders on brands that captured the variety of compounds found within brands would have proven difficult. In order to address this brand issue, where available, data indicating what brands included each substance on the Top Lists were included in the NTF.

- As work stream 5 was dependent on the outputs of other work streams (work streams 1-4), delays in other work streams impacted on the production of NTFs. Moreover, due to capacity issues and a lack of data on all substances in some countries, not all partners created NTF for all substances on their Top Lists. It was also intended that International Technical Folders (ITF) for each substance on the aggregated European Top lists would be produced. Due to delays in partners providing their data to LJMU, only 1 folder has been produced at present.

- The second selection process was initially meant to impact on the monitoring of substances in other work streams, with any substances being added to the list following the second selection being subsequently monitored in work streams 1-4. NTF would then be produced for these compounds. However, due to capacity issues and delays within other work streams, this aim was not completed. However, in some countries (UK and The Netherlands) the Top Lists did not change over the 24 months period and as such no additional NTF were created.

Appendix 1: NTF/ITF template

I-TREND Substance briefing:

1. Substance name(s)

Chemical name:

Other names (e.g. popular/street/slang name(s):

Branded products:

2. Classification and effect

EMCDDA substance group classification:

Substance analysis results:

UK drug forum monitoring:

UK web shops marketing:

3. Legal status and identification of the substance

Legal status/acts/laws in the UK:

EMCDDA Notifications

Country	Dates

4. Photographs of the substance

Images used in the marketing of the product on the web shops the compound was purchased:

Images of the substance purchased from UK web shop for laboratory analysis:

5. Chemistry

Chemical Abstracts Service (CAS) registry number:

Chemical information: other chemical names or variants:

Structure (picture of structural formula):

Molecular formula:

Molecular Weight:

Structural comparison with a related substance:

6. Analytical composition: results of substance analysis carried out on samples purchased online (UK IP address web shops)

Details of laboratory analysis technique used:

Web shop	Date of purchase	Form	Substance named on package/web shop	Confirmed substances (%)

7. Price and marketing strategies on UK web shops selling the substance

Compound Prices: Powder

	British Pounds/Euros	Quantity
Minimum price		
Maximum price		

Description of availability and marketing strategies on UK web shops selling the substance

Number of UK based web shops selling the substance

Type of (insert country name) websites selling the substance

	Number of shops (date)	Number of shops (date)
Research Chemical shops		
Commercial shops		
Other (e.g.)		

8. Law enforcement and health data

Number of law enforcement seizures in the UK in 2013/2014:

EMCDDA health alerts in the UK/ fatal and non-fatal intoxication cases reported in the UK:

9. User experiences of the substance: results from an analysis of discussions in online Drug Forums

Dosage specified by drug forum users (n = x posts, n = x users)

Initial Dosing (n= x users):
Boosting (n= x users):
***Threshold* (n= x users):**
Light (n= x users):
Strong (n= x users):

Duration (n = x posts, n= x users)

***Onset* (n= x users):**
Coming up (n= x users):
Plateau (n= x users):
Coming down (n= x users):
After effects (n= x users):
Hangover/Day after (n= x users):

Effects of the substance reported by forum users (n= x posts, n = x users)

Physical effects (n= x users)
Psychological effect (n= x users)
***Sought/expected (n= x users)*:**
***Positive desired effects* (n= x users):**
***Undesired (n= x users)*:**
Tolerance (n= x users)

Route of administration (ROA) (n= x posts n= x users)

***Ingestion* (n= x users):**
Rectal (n= x users):
Smoked (n= x users):
Injection (n= x users):

Other substances referred to when discussing the substance (n= x posts, n= x users)

***Referred to as comparing the effects* (n= x users):**
***Referred to as increasing the effects (n= 3 users**):*
***Referred to managing come down* (n= 3 users**):
***Other substances discussed in the same episode/combo* (n= x users):**
Antagonist/agonist (n= x users):

Appearance and preparation (n= x posts n= x users)

Patterns/Frequency of use (n= x posts n= x users):

Context of consumption use (n= x posts n= x users):

User's views and experiences of the online market use (n= x posts n= x users):

Warnings and harm reduction advice provided by forum users (n= x posts n= x users)

References

Indicative literature

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