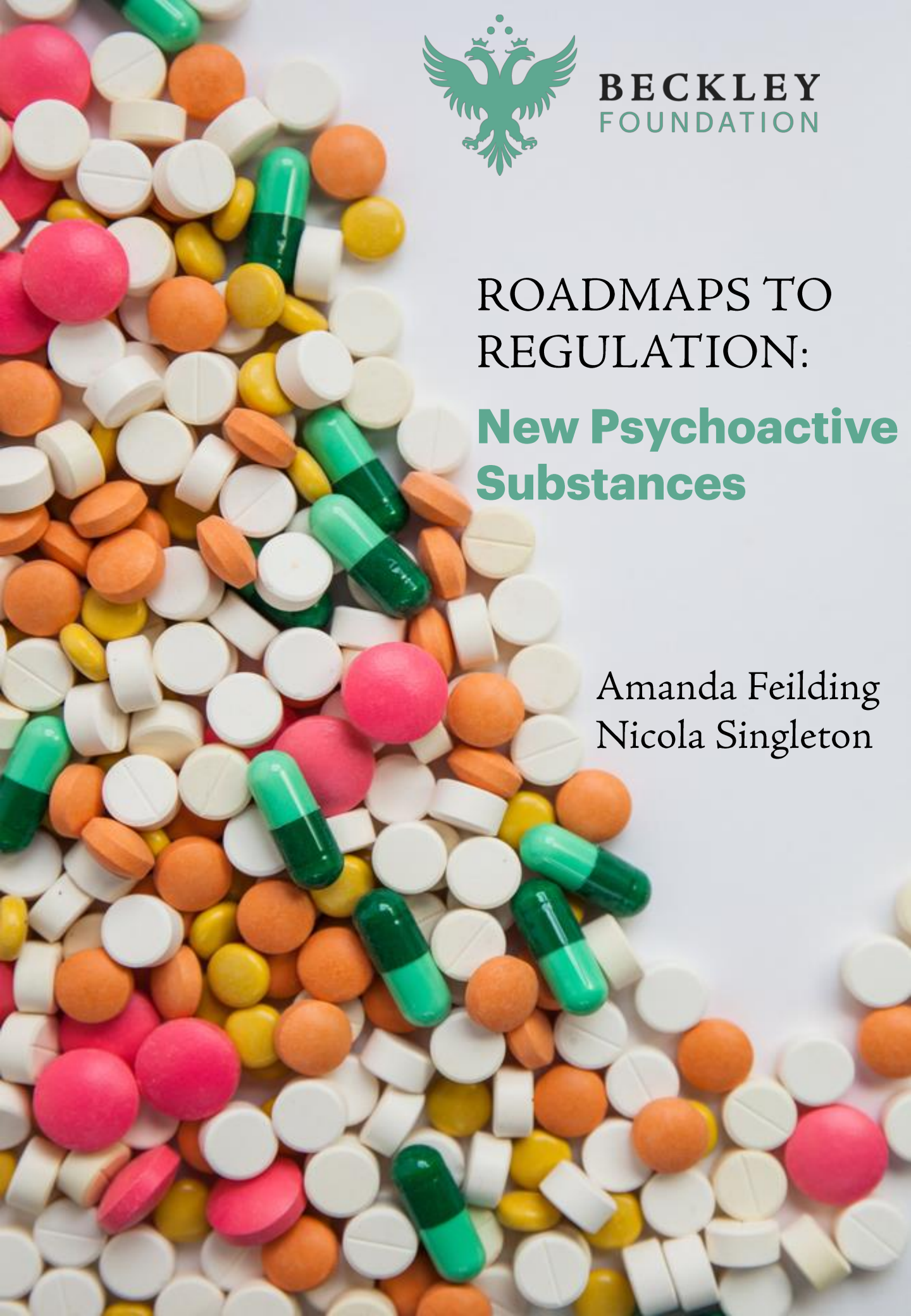

BECKLEY FOUNDATION

ROADMAPS TO REGULATION:

New Psychoactive Substances

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ROADMAPS TO REGULATION:
NEW PSYCHOACTIVE SUBSTANCES (NPS)

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THE AIM OF THE REPORT

This publication is a chapter from a four-part Report, ***Roadmaps to Regulation: Cannabis, Psychedelics, MDMA, and NPS*****, that will be published later this year. The Report was convened by Amanda Feilding, and principally funded by the** John Paul Getty Jr. Foundation with further assistance from the Open Society Foundations (OSF).

The Report aims to bring together the best available evidence on the regulation of psychoactive drugs in a rigorous, yet accessible way. In part, it is an invitation to think differently about drug policy options.

The wealth of expertise that we have gained from our work in the drug policy field strengthens our conviction that the strict legal regulation of drugs is the ultimate goal of drug policy reform. The governments of the world, duty-bound to safeguard their citizens' well-being, surely would do a better job of minimising the overall harms of drugs than the criminal organisations currently profiting from the illicit market. It is no longer acceptable to simply assume that the risks of a legal market will exceed those of prohibition, especially when there is already the beginnings of a scientific evidence-base to show that a regulated market can provide effective ways of reducing harms. In view of this, the Report was established to provide policymakers with tools to move beyond the blanket application of reactive prohibition. Our aim is to provide guidelines for considering the best available evidence, and for utilising this knowledge in supporting decisions about how to move forward with the complicated issues surrounding the regulation of different categories of psychoactive substances.

We are publishing this chapter, *The Regulation of New Psychoactive Substances (NPS)* today (26 May 2016), to coincide with the enforcement of the Home Office's *Psychoactive Substance Act 2016*, that will create a blanket-ban on the trade of "any substance intended for human consumption that is capable of producing a psychoactive effect", except for a handful of substances such as alcohol, caffeine and nicotine. The Act is an attempt to solve the problem of NPS, but flies in the face of evidence, and advice from the experts in the field. This Report highlights the problems, and offers guidelines for alternative approaches to the regulation of NPS and other psychoactive substances, such as cannabis, MDMA and magic mushrooms.

PREFACE

By Amanda Feilding

This week sees the delayed implementation of the *Psychoactive Substances Act 2016* in the UK. The *Act* is intended to finally put an end to the seemingly unstoppable proliferation of new psychoactive substances (NPS), some of which have caused serious harm and death. As this report explains, whether it can do so remains in serious doubt. Regardless of its efficacy, the introduction of the *Act* is a watershed moment in this country's legislative response to drug use.

This report describes the NPS landscape; their uses and users, their production and supply, their under-recognised diversity in pharmacology and risks. The report traces the evolution of responses to NPS that has culminated in the *Psychoactive Substances Act 2016*, a blanket ban on the production and the supply of all psychoactive drugs, known and yet to be discovered, excepting a handful, such as alcohol, tobacco and caffeine. The report then considers alternative directions we could take at this crucial crossroads - this crisis for the current drug control paradigm.

For decades, the traditional response to each emerging drug has been 'reactive prohibition'; banning the drug and criminalising its users. Whilst the evidence does not demonstrate any efficacy of this approach in deterring use and preventing harm, it has been the backbone of drug policy in the UK and internationally.

Contrary to its aims, 'reactive prohibition' seems to have promoted the proliferation of new psychoactive substances, by incentivising the creation of new substances closely resembling banned ones.

This inevitable cat-and-mouse game called forth an evolution in 'reactive prohibition', whereby a ban would apply not just to one specific substance, but could be applied 'generically' to its close analogues. Since the substitution or addition of an atom or two can completely transform a drug's effects, including its potency and toxicity, these 'generic' laws began to erode the principle that substances are banned in response to evidence of their specific risks.

With these legislative efforts spurring the exponential diversification of psychoactive substances, in recent years governments have created shortcuts to try to sustain a paradigm that is ill-equipped to cope with novel drugs appearing on a weekly basis. These legislative shortcuts, such as Temporary Class Drug Orders[1], expedite new bans at the expense of evidence-based assessment and political deliberation.

Perhaps the central futility in 'reactive prohibition' is that it does not see the wood for the trees; the market for any particular new substance such as mephedrone is not contextualised within the consistent consumer demand for mind-alteration. Drug policy should reduce drug associated harms, but even when a ban is 'successful' at curbing a particular drug's popularity, (as the mephedrone ban seems to have been), no reduction in harms will have resulted if

[1] The Home Secretary gained powers to create Temporary Class Drug Orders in 2011. These enabled a drug to be banned 'temporarily' (although in practise none of the bans have been temporary) without the typical full assessment of available evidence by the Advisory Council on the Misuse of Drugs (ACMD). The threshold criteria for a drug to qualify for a TCDO were minimal, for example if the ACMD agreed that the drug was (a) likely to be 'misused' (i.e. used), and (b) 'capable' of having harmful effects.

users simply turn to similarly risky, newer psychoactive substances, or back to established drugs. Conversely, harms may be amplified.

It is clear that the demand for untested NPS, despite their obvious risks, is largely an unintended consequence of an unmet demand for legal access to popular psychoactive substances, such as cannabis, MDMD and psychedelics. Most NPS that have emerged in recent years are synthetic cannabinoids, reflecting the demand for cannabis, which is considerably safer than the synthetic cannabinoids by every measure.

NPS account for a mere fraction of the drug market, which is dominated by long-established legal drugs such as alcohol, and 'traditional' illicit drugs from cannabis to cocaine. The growing burden of NPS-related harms in terms of damage dependence and death, and pressure on public services, remains relatively insignificant alongside the burden associated with established drugs and their mismanagement. Nonetheless, the transparent failure of the prohibition approach to address the challenges of NPS could represent an existential crisis for that paradigm. The international regime of drug-control based on reactive prohibition has been a disaster by every measure; illicit drugs are more available than ever, drug markets operate outside of any government control, criminal sanctions do not demonstrably curtail drug-use, but impose other forms of harms to users.

A commendable progressive feature of *The Psychoactive Substances Act 2016* is that it will not criminalise *simple possession*. However, the Act will operate parallel to the existing *Misuse of Drugs Act 1971*, which does impose sanctions on possession supposedly commensurate with a drug's relative harmfulness. Both sets of legislation will operate alongside laws regulating alcohol, tobacco and prescription drugs, creating a confusing situation where citizens will have no confidence in any relationship between a substance's harmfulness, accessibility and legality.

As this report describes, in the immediate-term, the regulatory model for NPS that offers the most promising substitute for the *Psychoactive Substances Act* is the one that has been passed in New Zealand. Unfortunately, the framework they constructed has been hamstrung by a variety of domestic political setbacks. Nonetheless, this report explores how the model could be instituted. Crucially, it demands that the manufacturers fully fund the assessment of the safety of the new psychoactive substances, to establish if they are low-risk, before they can be offered to consumers as a licensed and regulated product. This is in contrast to the reactive prohibition regime, which at best assesses drugs once they are already in the unregulated circulation.

There are no perfect solutions in the world of drug policy. Drug use is inherently risky and the appetite for them seems to be a natural human trait. The task then is to minimise the harms, and indeed to maximise their potential benefits. Since the drug market is an interconnected system regardless of the arbitrary territories claimed by the different UK laws in operation, this report argues that the challenge of NPS is best understood and addressed in the context of the challenge of drugs and the risks associated with their use more generally.

It would be safer for the consumer if they could satisfy their desire for a psychoactive substance with a compound which has been certified by a reputable body as being of acceptably low risk. It is time that governments accept that some of their citizens seek to alter

their consciousness in ways other than consuming alcohol or coffee, and make it possible to meet this demand in the safest possible way, with all the necessary controls to minimise harmful use. A paradigm-crisis such as that caused by NPS can set the stage for a paradigm shift. The regulated availability of a small selection of classical psychoactive products, alongside the regulation of a select few NPS that pass stringent safety testing, could satisfy virtually all that the consumer demands in their quest to alter their consciousness.

Roadmaps to Regulation: New Psychoactive Substances (NPS)

1. Introduction

Conventional supply reduction strategies used by governments around the world to stem the production, use and trade of illicit drugs, have led drug users to seek alternative, legal supplies of psychoactive substances. Governments are facing progressively complex challenges in responding to these new drug markets. The industrial scale production, distribution and use of a rapidly growing number of psychoactive substances[2] that do not fall within the remit of the UN Drug Conventions continues to test the ingenuity of law and policy makers. By altering the chemical structure of illegal substances, or designing new substances altogether, producers and suppliers exploit legal loopholes. These substances are manufactured and distributed under the guise of products 'not meant for human consumption'[3] in order to avoid regulations.

These new psychoactive substances ('NPS') are, for the most part, drugs that are similar to what may be termed "traditional drugs" and have been produced to replace them because of quality issues, cost and to circumvent drug legislation. The popular varieties have effects similar to internationally scheduled drugs such as MDMA, cocaine, cannabis or LSD. As a substance class they are, therefore, very heterogeneous and appeal to different groups of users. Their novelty does not necessarily relate to their recent discovery or synthesis, but to their entrance into new markets.

There has been a rapid emergence of 'head shops' selling a range of these drugs in some countries. They are also available through online *darknet* marketplaces, like the infamous, but now defunct, Silk Road, and its numerous copies, which have risen in prominence over recent years. The rapid globalisation of drug markets, aided by technological innovation in communication, and the emergence of new *cryptocurrencies* like Bitcoin, has allowed individuals to buy and sell substances, including NPS, in an anonymous, low-cost, low-risk market.

To date, the reaction of governments to these innovations has been to continue with the default prohibitionist approach; prohibiting new substances as they appear or putting broad blanket bans on their sales. However, these new challenges, which to a large extent have evolved in response to existing policies, might instead be viewed as providing an opportunity to adopt a new approach that considers the full range of regulatory alternatives. The obvious failure of the current strategy provides the impetus for reconsidering drug policies in their entirety.

2. What are NPS?

NPS are, for the most part, psychoactive drugs, which have been produced with the express intention of circumventing the punitive laws underlying the international drug control regime. We avoid referring to 'legal-highs' in this Report because legal structures that surround 'new'

[2] Recent figures show that from 2009 to the late 2014, the number of new psychoactive substances reported to the United Nations Office on Drugs and Crime (UNODC) rose by 134%, from 251 to 388 (1).

[3] Synthetic cathinones, for instance, were initially commercialised as 'bath salts' to avoid prosecution, which led to the popularisation of the term in the media.

drugs vary across time and space – what is a legal drug in the UK today may be illegal tomorrow, and may never be legal across the rest of Europe, or the world.

Common use of the term 'NPS', doesn't distinguish between drugs such as nitrous oxide (NOS or N_2O, laughing gas) and alkyl nitrites (poppers), that have a long history of medical and recreational use, and substances that have only recently been discovered, or that have only recently been used recreationally. Some 'legal highs' aren't 'novel' at all and have better-known risk profiles and well-established legal markets. The discussion below largely relates to dealing with truly novel psychoactive substances.

Worryingly, the UK legislation – The Psychoactive Substance Act – that will be enforced on 26 May 2016, will ban a number of substances including N_2O which have known risk profiles that suggest they are comparatively low-harm and could be better dealt with through the creation of a strictly regulated legal market.

This report is not concerned with the details of disambiguating the numerous types of novel substances, but it is worth being aware that the United Nations Office on Drugs and Crime (UNODC) (1) has identified eight main groups and a further miscellaneous group according to their chemical composition:

I. Synthetic cannabinoids

Synthetic cannabinoids are, according to the most reliable estimates available, the most widespread category of NPS[4], with over 130 synthetic cannabinoids identified and monitored by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). They are designed to act upon the same receptor in the brain as THC[5], thus mimicking the psychoactive effects of cannabis. Amongst the wide variety of these so-called mimetics[6], 5F-PB-22 and 5F-AKB48 are currently the most common substance identified in the UK (3). They are predominantly marketed as herbal blends (common brand name "Spice") that often claim to contain "natural ingredients", while in fact the main psychoactive ingredients are one or more synthetic cannabinoids. As compared to their natural counterpart, synthetic cannabinoids have at least three major drawbacks: they tend to be more potent than the THC that they mimic[7] (4); they are more addictive (5, 6); and, they do not contain any cannabidiol (CBD), which is a naturally occurring cannabinoid with potentially anti-psychotic and anxiolytic effects (7).

II. Synthetic cathinones

Synthetic cathinones are either derived from or modelled after cathinone, the psychoactive component of khat (See plant-based substances, point 8). Toxicity and dependence studies are scarce for all the substances, except for mephedrone, and most of what we know so far

4 35% is the NPS market share of the synthetic cannabinoids (2)

5 Δ9-tetrahydrocannabinol – the principal psychoactive constituent (cannabinoid) of the cannabis plant.

6 Substances that imitate the action of other drugs, without necessarily having structural similarities.

7 Apart from high potency, some cannabinoids could have particularly long half-lives potentially leading to a prolonged psychoactive effect. In addition, there could be considerable inter-and intra-batch variability in smoking mixtures, both in terms of substances present and their quantity. Thus, there is a higher potential for overdose than with cannabis.

is based on toxicity reports from individual case studies. Mephedrone[8] and methylone[9] are perhaps the most widespread and best researched substances in this chemical family. Emerging in the European market towards the mid-2000s, by 2010 they were identified as being the most common in this category, although now their popularity has declined (8).

III. Arylcyclohexylamines (e.g. ketamine)

These substances started to enter recreational drug markets back in the 1970s. They are used as recreational drugs due to their dissociative, hallucinogenic and euphoric effects. Amongst the most popular of this group of substances in the NPS market are ketamine, methoxetamine (MXE)[10] and phencyclidine (PCP). The non-medical use of ketamine has been reported since the 1980s, and expanded in the 1990s. Increased control of ketamine led to the emergence of phencyclidine-type substances in the 1990s in the USA and in 2010 in the UK (ex. methoxyeticyclidine (9)).

IV. Phenethylamines

Phenethylamines include a broad range of substances sharing a common phenylethan-2-amine structure and having stimulant, entactogenic and/or hallucinogenic effects. Some of these substances, namely amphetamine, methamphetamine, 2C-B and MDMA are under international control. In the late 2000s, the popularity of uncontrolled compounds in this family increased significantly, as demonstrated by the seizure of compounds such as those in the 2C (e.g. 2C-E, 2C-I) and D series (e.g. DOI, DOC), benzodifurans (Br-DFLY or Bromo-DragonFLY, 5-APDB or Benzo Fury) and others such as PMMA[11]. Some of these compounds were synthesised and studied as early as the 1980s and 1990s. Indeed, the extensive work of Alexander Shulgin, who documented experiences with more than 200 phenethylamines in PiHKAL (10), illustrates the proliferation of these compounds, and has contributed to an understanding of their chemistry and psychoactive effects. One of the most widespread NPS that falls into this category is 25I-NBOMe (marketed in some countries as 'N-Bomb', but reportedly also sold as LSD (11)), a potent psychedelic which was first synthesised in 2003, and soared to recreational popularity in 2010 (12). It is now prohibited in many countries. In addition to hallucinogenic 25I-NBOMe, there is a plethora of other substances in the family designed and marketed as substitutes for cocaine, or 'party-pills' and stimulants.

V. Tryptamines

Tryptamines are a class of chemical substances that are structurally similar to the amino acid tryptophan and include well-known hallucinogenic drugs such as psilocybin, DMT and LSD[12]. A large number of tryptamines have psychoactive properties, and many have been extensively documented by Alexander Shulgin in TiHKAL (13). The most well-known NPS tryptamines are AMT, 5-MeO-DALT, 1p-LSD.

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8 4-methylmethcathinone (4-MMC)

9 3,4-methylenedioxy-N-methylcathinone

10 Anecdotal evidence suggests that street dealers often sell this drug as ketamine.

11 para-Methoxy-N-methylamphetamine

12 LSD has a more complex chemical structure

VI. Piperazines

Piperazines were initially developed as antidepressants but their potential for dependence was quickly identified. The most widespread compounds in this family are meta-chlorophenylpiperazine (mCPP), which was marketed as 'ecstasy', and benzylpiperazine (BZP), which has been sold as a 'safer legal alternative' to methamphetamine' (14). The combination of another piperazine, 3- trifluoromethylphenylpiperazine (TFMPP), and BZP has been marketed as 'party pills', supposedly having similar subjective effects to MDMA ('ecstasy') (15, 16).

VII. Aminoindanes

Aminoindanes such as methylenedioxyaminoindane (MDAI) or 5-Iodo-2-aminoindane (2-AI) produce entactogenic effects[13], although they are less common than other drugs of similar effects.

VIII. Plant-based substances

Used for their psychoactive properties for hundreds (and in some cases, thousands) of years, plant-based psychoactive substances are considered to be NPS due to their novelty in certain markets[14]. Khat or qat (*Catha edulis*), recently banned in the UK, is normally chewed as leaves and acts as a mild stimulant, not dissimilar to coffee. It is particularly popular in the Horn of Africa and the Arabian Peninsula, where it is widely grown and has been used for centuries. Kratom (*Mitragyna speciosa)*, another plant-based NPS, is also consumed by chewing the leaf of the kratom tree. It is a μ-opioid receptor agonist and is popular in East and South-East Asia, especially in Malaysia, Myanmar and Thailand[15]. *Salvia divinorum*, which remains legal in most countries, can be smoked, chewed or imbibed from a tea preparation and can produce powerful 'visions' and other hallucinatory experiences. It is native to Southern Mexico.

IX. Miscellaneous substances

This is a residual category, which captures any NPS that does not fall into one of the previous eight categories. For example, 1,3-dimethylamylamine (DMAA) and other substances that are

[13] The most popular entactogenic is MDMA. Entactogen means "touching within", and is used synonymously with empathogen to refer to these classes of drugs, although some prefer the tem entactogen because of the additional effects beyond increasing empathy.

[14] Questions have been raised about the feasibility or value of including plant based substances in an NPS category. This Report includes them in order to remain categorically consistent with the main data sources (e.g., UNODC and EMCDDA), but it does so with reservation. It should be noted that many of these substances are not in any real sense 'new', and that when considering the legislation and regulation of NPS, this report is mostly concerned with synthetically produced NPS, not those that are plant based.

[15] Interestingly, kratom is increasingly being recognised as a remedy for opioid withdrawal (Boyer et al., 2008).

less common that the other specific NPS classes mentioned above but are also considered in this Report.

3. Overview of issues concerning the use of new psychoactive substances

The NPS market is a rapidly changing market in new substances with unknown risk profiles. These NPS are widely perceived to be increasingly harmful, and in some of the rare instances when sufficient information is available to form a reliable opinion, are indeed more harmful than the traditional illicit drugs, which they are trying to replace.

The varied and transient nature of NPS and the fact that they are marketed under a variety of 'brand' names, such as *Benzofury*, *Spice*, *Kronic*, which may in fact have different compositions at different times, and no list of active ingredients to compare, makes it very difficult to assess the extent of use of particular substances. Users will often not be aware of the contents of the product they are buying.

The key concerns for NPS are the unknown risk profiles of these products, the availability of these substances without controls, the lack of guidance on how to use them more safely and the difficulties faced by medical practitioners in being unable to identify the substance taken and the best options for treatment in emergencies.

4. Prevalence of use and demographical characteristics of users

NPS is a global phenomenon, however it is particularly relevant to the UK drug policies, as 23% of all the European NPS drug users are UK residents (18).

The available evidence suggests the use of NPS is not nearly as prevalent among the general population as use of the controlled substances that they tend to mimic. While nationwide statistics are limited in breadth and depth[16], the different NPS that have been featured in the Crime Survey for England and Wales have shown that the general interest for these substances is usually transient (0.9% of adults used an NPS in the last year). For instance, the survey suggests that mephedrone use peaked in 2010, among all adults (1.3%) and young adults (4.4%) and has decreased ever since, more than halving among both groups by 2014 (for more information about mephedrone and its use in the UK see the case study in the appendix) (19). Even when a more general question on NPS use was included in a different survey (Global Drug Survey, GDS) only a small proportion (8.6% of people from GDS2015) reported using them in the past year (20). There are pockets of higher use among clubbers, men who have sex with men (MSM), psychonauts, prisoners and others. Nevertheless, even in these groups, traditional illicit drugs often predominate.

[16] The CSEW survey focuses on the general population, which inevitably reduces its capacity to identify pockets of use, especially if they are as dynamic and volatile as seems to be the case with NPS. Moreover, it is a household survey, so it misses certain groups for which drug use is potentially high, e.g. students living in residence halls, the homeless and prisoners. Furthermore, the NPS surveyed are very few in number and have changed over time: mephedrone (from 2010/11); GBL/GHB, BZP and *Spice* (2009/10 - 2011/12); and Salvia (from 2012/13).

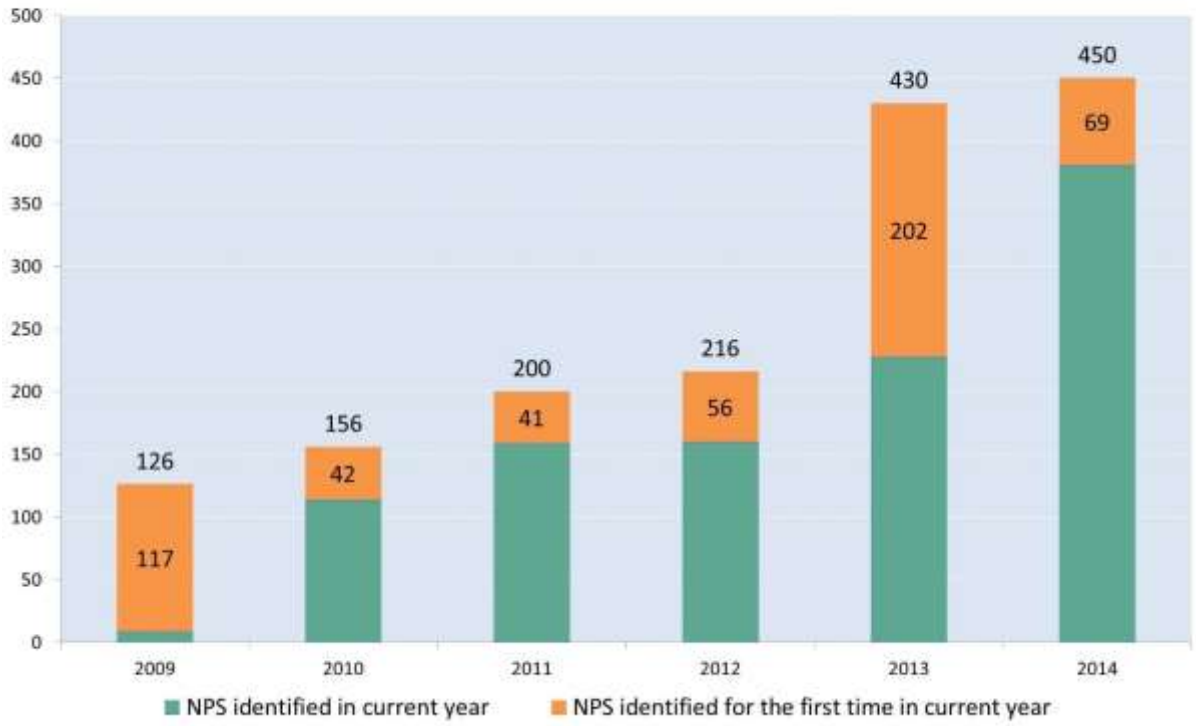

Figure 1. Rising Numbers of NPS (number of the NPS reported to UNODC in 2014)
Source: United Nations Office on Drugs and Crime (UNODC), Early Warning Advisory on new psychoactive substances 2008-14 (17)

5. Why people use NPS?

The existence of the market for new psychoactive substances can be largely put down to two factors – the unending demand for mind altering substances other than those which are culturally and legally acceptable (e.g. alcohol & caffeine), and the punitive measures underlying the control of those drugs which are internationally scheduled. Demand calls forth its own supply, and never is this truer than in the international market for psychoactive substances. Through the arbitrary prohibition of some the world's most highly demanded goods, the UN drug control conventions have all but ensured a thriving market for similar goods that are not banned.

Alongside these two major factors are myriad individual motivations underpinning NPS uptake, which tend to revolve around quality, accessibility and availability, both of the novel substances themselves and other –controlled– substances. Traditional drugs, traded on the black market, are of uncertain quality and in recent years many of them had become increasingly 'cut' with a range of, often harmful, substances. This, together with the other risks of participating in a criminal market, makes the ability to purchase similar substances from a much broader range of outlets, from *head shops* and the *clearnet* to the *darknet*, very attractive. In many cases prices and perceived risks are lower and some information may be provided on the content of the substances being purchased. These factors contribute to

making NPS attractive to many people (19,20). However, more often than not, the labelling information is misleading, especially when it's sold as "plant food", "bath salts" etc.

Another driver of use, particularly in the case of the synthetic cannabinoids, is the fact that they are not detected by the standard drug tests. For people, such as prisoners, who are subject to random testing this may make them particularly attractive (21). There is a further small niche demographic of "psychonauts", individuals who try new psychoactive substances out of curiosity and a desire to explore new altered states of consciousness. Whilst research isn't available to determine the scale of this group, it is thought to be a small section of users(22).

Also important, although less understood, is the role of public perception and the media as the drivers of NPS use. Indeed, some authors have suggested these substances are 'increasingly accepted as part of a "trendy" lifestyle', (21) while others blame sensationalistic media accounts for a spike in 'curiosity' towards the so-called 'legal highs' (23). Nevertheless, as the Global Drug Survey illustrates (20), most users would prefer to use the traditional drugs if they were available with acceptable quality levels.

6. The Evolving Market

For decades, chemists have designed and produced psychoactive substances with the aim of exploiting loopholes in national and international drugs legislation. Whilst the NPS phenomenon is not new, the form it has taken recently represents a significant break with the past. Writing in *Addiction*, Paul Griffiths et al., point to the rapid transformation of the NPS landscape -

> '*Only a few years ago the issue of the 'legal highs' market was regarded as an area of limited significance… today the question of how to respond to the challenges posed by the emergence of new drugs has become one of major international concern*' (24).

The foundations of the modern market for NPS were laid by the ground-breaking experiments of Alexander Shulgin on phenethylamines and tryptamines in the 1960s and 1970s. Shulgin synthesized and evaluated the psychedelic and entactogenic potential of hundreds of psychoactive compounds. He published many of his findings in two books, PiHKAL (1991), and TiHKAL (1997)[17](10, 13). In decades gone by, it was the 'recipes' in these two books that gave rise to many of the psychoactive substances newly appearing in international markets. In more recent years, a host of new factors have come into play, causing a shift in the type of substances emerging onto the NPS market.

In some ways, the evolution of the NPS market is unsurprising. The continuous dissolution of cultural, economic and legal boundaries means that goods, ideas and information can flow more freely than ever before, and disparities between jurisdictions can be easily exploited. Slow and cumbersome national and international drug control regimes are being outpaced by a dynamic and quick-moving industry, which has proved next to impossible to restrict.

7. How has the internet helped shape the market for NPS?

The internet has played a significant role in the evolution of the market for NPS. Indeed, the UNODC notes that of those countries that responded to the question of the importance of the

[17] The titles are acronyms standing for 'Phenethylamines/Tryptamines I Have Known And Loved'

internet in their domestic market, 88% indicated that the internet was a 'key source' for NPS (18). Furthermore, an EMCDDA study revealed that the number of online shops with NPS for sale in Europe increased considerably. In 2013 in Europe there were 651 online shops selling NPS, a three-fold increase from 170 shops in 2010 (25). It is estimated that around 250 of these were based in the UK (26).

However, it is worth noting that the 2011 Eurobarometer survey (27) indicates that only around 7% of young (16-24) NPS consumers purchased them on the internet[18] (with the majority being offered the substances by a friend, and a significant proportion either buying the substance in a club or in a specialised shop). The Crime Survey of England and Wales 2015 findings confirm this trend, where adults aged 16 to 59 typically obtained NPS from a shop (34%), a friend, neighbour or colleague (34%), or a known dealer (9%), and only 6% used the internet to source their drugs.

Far from being contradictory, these data shed light on the dynamics of the NPS market. While the proportion of end consumers that seems to be acquiring these substances on the internet is limited, the available data suggest that retailers (e.g. smart-shops) and small-scale dealers are significantly influenced by the increased availability of NPS on the internet. Indeed, the widespread availability of NPS online has lowered the costs of entering the NPS market, and has been an incentive for distributors looking to ship larger amounts of these substances. Furthermore, within the last decade or so, it has become increasingly easy for NPS designers to use the internet to search for inspiration for new NPS in the scientific literature, which contains a vast array of research chemicals and substances (29). This has been at least partially responsible for the rapid proliferation of NPS, one of the major factors explaining the NPS market's ability to outpace attempts to control it. Additionally, the internet has also been used to purchase precursor chemicals, as well as to organise the large scale manufacture of a substance once it has been designed. In short, the internet has ensured that potential producers of NPS face attractively low barriers to entry, and can remain responsive and dynamic in the face of drug control regimes.

As is the case with any manufactured goods, purchase by the end consumer comes at the end of a longer supply chain, which starts with drug design, and progresses through production, to distribution and retail. Anything that has a big influence on any part of this chain can have profound effects on the nature of the market as a whole. The Internet has ensured low barriers to entry for potential NPS entrepreneurs at the manufacturing level; it has increased the ease and appeal of setting one's self up as a small scale distributor or retailer of psychoactive substances; and it has empowered users by acting as a useful tool for consumers to exchange information about the risks, experiences and consumption methods associated with NPS (30).

[18] Eurobarometer survey 2014 has even lower numbers – 3%, although the actual figure is probably higher, as there were about 6% who did not answer this question (28).

Table 1. Moving from Key Harms to Policy Aims

Source of harms	Key harms under current regulation	Bearers of Harm	Potentiating factors	Policy aims
Production	Adulteration (toxic substances) & Contamination (by-products)	Users Families State (health services)	Illegal status Production of mimetics	Establish standards of production and quality/safety
	Physical harm from production: Fumes, burns, other accidents	Producers		
	Loss of Tax Revenue	Business (chemical precursors) Producers		
		State		
	Environmental damage: contamination	Society (dev. countries)		
Supply	Involvement with illicit suppliers	Users Neighbourhoods State (health services)		Decrease illicit sales
	Untaxed revenue	Dealers		
	Easier access to substances with unknown risks	State		
Use	Chronic and acute mental and physical damage, dependence. lack of medical information for doctors trying to treat these harms Pleasure & Enjoyment	Users Family State (health services) Society	Dose & Purity Set & Setting Interactions & poly-drug use (MAOI, other drugs, alcohol) Frequency Pre-existing co-morbidities Set & Setting	Promote safer use Discourage use by young people and vulnerable groups Ensure quality control Promote safer use Ensure quality control
	Stops Innovation of New Medicines[19]		Illegal or uncertain status	Reduce obstacles for research
Enforcement	Cost of enforcement	State Society (allocation of resources, loss of productivity, expenses)	Illegal status	Reduce criminalisation Decrease illicit production & sales

[20] The most recent report by the Home Office's Forensic Early Warning System (FEWS) suggests the majority of 'legal highs' products contain two or more new psychoactive substances (32).

8. Harms and benefits under the status quo & mediating factors

The variety of NPS means the harms and benefits associated with them are very diverse. Each group of substances, and indeed each substance within the group, will have a different risk/benefit profile so what is described below is not comprehensive, but provides some examples and recurring themes.

8.1 Associated with production and supply

Current regulations have encouraged a constant inflow of new products that seek to bypass already existing bans. In this sense, reactive prohibition of individual substances encourages the alteration of chemical structures of existing controlled substances or the creation of new substances altogether.

8.1.1 Production

New psychoactive substances and their precursors tend to be produced in Asia (mostly China and to a lesser extent India) and then shipped to Europe, where they are repackaged to sell locally or in other markets. However, some NPS are produced in clandestine laboratories in Europe. Environmental damage is always possible in loosely regulated chemical manufacturing and toxic waste products from the chemical industry often end up dumped into the rivers (31).

Many media reports refer to the risks associated with NPS being wrapped up with the "underground labs" in which they operate. Whilst it is true that it would be preferable that production took place in a fully regulated environment, due to the difficulty involved in manufacturing, these substances are largely produced by qualified specialists in professional laboratories. Although many of the products have unknown risk profiles, problems with adulterants and mis-sold products largely result from the poorly regulated supply of these substances, not their production.

Many (if not most) NPS are chemically challenging to synthesize, requiring expertise, equipment, training, discipline, patience and ingenuity. Merely obtaining the starting materials is challenging. Due to their novelty, the manufacturers of most NPS will encounter new methods and problems, and will have to find new solutions. Often, there is no-one that an NPS manufacturer can learn from, because s/he is the first in the world to manufacture a specific compound on a large scale. In this regard, the rhetoric of "underground labs" comes from the illicit drug world and is borrowed by journalists that are repeating a well-known narrative and its catch phrases. However, the two undertakings – making illicit drugs vs. making NPS – could not be more different.

With cocaine for example, the *Erythroxylum coca* plants produce ready-to-extract cocaine for its distributor. All of the complex chemistry is performed through the botanical wizardry of the coca plant itself. The clandestine labs erected in the jungles of South America are little more than extraction and packaging stations. Producing, for instance, mephedrone, is a three-step process, the first of which is bromination. Bromination requires access to bromine. Handling bromine requires trained staff and precision equipment to achieve high yields. So despite misleading rhetoric, NPS manufacturers are, more often than not, legitimate and established organic chemists. They can be manufacturers of fine chemicals, aromas, pigments or pharmaceuticals. Due to the legal nature of most NPS, the interested distributor in Europe initiates a purchase order with the manufacturer in the Far East. Standard business practices are kept for the simple reason that standard (although loosely regulated) business is being conducted.

One of the major problems with the current production paradigm is that the producers are aiming to design compounds that are legal, but they are not able to accurately (or often at all) predict the effects of the substances that are being manufactured. Organic chemistry is an exact science, so the molecular structure that is planned is invariably what is actually synthesized, down to the last proton. However, the precision of chemistry ends with the molecular structure. Predicting that a certain substance will or will not have an effect like a popular party drug lies outside the discipline of chemistry, and is currently beyond the capability of pharmacology, neuroscience, biochemistry or medicinal chemistry. It is also beyond the most advanced computer models currently employed anywhere. This problem is termed the quantitative structure-activity relationship (QSAR) paradox and it means, in this context, that we don't know until we try.

One of the harms in banning the production and import of substances is that by removing the legal market without addressing the demand, it creates an incentive for smaller scale production in less professional, higher risk environments.

8.1.2 Supply

NPS are mainly distributed through three different channels: online retailers, either through the *clearnet* (mostly non-controlled substances) or the *darknet* (preferred for controlled substances); high-street vendors, or *head shops*, and non-retail vendors, such as family members, street-level dealers and friends. The comparatively easy access to NPS through these channels has encouraged their uptake.

Due to the illicit or legal grey area (depending on the substance) in which these substances are sold, users buying NPS are often unaware of the actual contents[20], and report using an 'unidentified white powder' (33) or, they purchase a particular 'brand' of the NPS, for example 'Spice', the actual chemical composition of which changes as the substances become banned and new substances emerge. Moreover, NPS are frequently mis-sold to customers as an illicit drug. PMA and PMMA are particularly toxic and are often found in samples of drugs sold as 'ecstasy' or MDMA. For example, out of the 22 people presented to an Australian emergency department with PMA toxicity, none had taken the drug on purpose; they all thought they were taking ecstasy (34). A more recent example is the LSD samples tested by the WEDINOS scheme in Wales in 2014 that turned out to be the phenethylamine derivatives 25I-NBOMe, 25C-NBOMe and DOB (2), which makes it even more difficult to determine the potential harms and treatment options.

The policies of prohibition have also encouraged the emergence of online markets, where the lines between the legal and illegal are blurred. While research suggests these markets have the potential of empowering users and diminishing crime (by organising transactions away from street-dealing and on the basis of trust and information), they still present challenges in terms of the enforceability of agreements and the opportunity costs resulting from their informality (ex. lack of taxation). Moreover, the lack of market separation and the fact that some of the services offered are particularly malicious (e.g., guns) constitute major drawbacks.

[20] The most recent report by the Home Office's Forensic Early Warning System (FEWS) suggests the majority of 'legal highs' products contain two or more new psychoactive substances (32).

8.2 Associated with use

The volume of information available about different NPS varies enormously from substance to substance. While a lot of these drugs are newly synthesised, and virtually no research has been done or published on them, others have been known in the scientific community for decades, and extensively researched as a potential medical treatment[21]. Others were synthesised years ago, but have only recently found their way to the consumers. The lack of knowledge about many of their mechanisms of action, pharmacology, toxicology, side effects and interactions with other drugs limits the ability to treat patients effectively and makes it difficult to estimate harms reliably.

It is clear that some NPS pose a threat to some users. However, regarding psychoactive substances generally, these play a proportionally small role. Perhaps more importantly, this report shows that the harms that arise from the traditional prohibitionist response cannot be divorced from a proper analysis of aggregate harms.

Many of the harms attributable to consumption of NPS could be significantly reduced if a strictly regulated market for drugs with a known risk profile were created. In the meantime, research needs to be encouraged and funded to investigate risk profiles, treatment options and potential benefits.

8.2.1 Legal vs. medical risks

It is often mentioned that as more substances are banned and new ones created, the new substances are perceived as, and often actually are more dangerous. This opinion has been conveyed many times by the EMCDDA (36). Intuitively, the more familiar we are with something the less it is perceived to be harmful. And practically, when many people have tried a substance we learn about it from others' experience. But formally, we know very little about the vast majority of NPS, which makes them all equally risky. There is no gradual increase in harm potential of new substances as time goes on. It is our ignorance that puts us at risk above all else.

Paradoxically, a great deal of data has accumulated that relates to traditional illicit substances. There are textbooks that inform medical practitioners as to the identification and treatment of symptoms and addiction potential of known illicit drugs by virtue of the fact that they have been around for so long. So in this regard the use of illicit substances is safer than the use of unknown but legal NPS. This medical reality lies at the centre of the controversy around legal highs. The UK government, addressing the issue of legal highs, has expressed the concern that the public identifies "legal" with "safe" which is why the public flocks so eagerly to their consumption (26). However, being "legal" in the consumer's eye is being "safe" from prosecution, which is just as big a concern for most users as being safe from medical mishap.

8.2.2 Treatment

There are legitimate concerns about high rates of users seeking treatment following use of certain NPS, especially synthetic cannabinoids. However, the larger issue is associated with an intrinsic problem with treating people on the basis of very limited information: many users are unsure which substances they have taken, and even if they do know, there is generally no or very limited available information for medical practitioners regarding treatment.

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[21] For example, zopiclone, currently class C drug in the UK, used to treat sleep disorders; or lisdexamphetamine, class B drug, used as the treatment for ADHD; or remifentanil, class A drug, about 150 times more potent than morphine, that is medically used as anaesthetic.

In the UK there is data on NPS-related emergency-treatment-seeking, with the synthetic cannabinoids being more harmful compared to other drugs.[22] Moreover, the addictive potential of the synthetic cannabinoids is higher, with 60% of the regular users (used drug more than 50 times) report withdrawal symptoms on cessation (20). Acute side effects reported by the clinicians and drug services often mention psychological/neurological effects (agitation, confusion, unpredictable behaviour, temporary psychosis, hallucinations), cardiovascular effects (tachycardia, hypertension) and others, such as nausea, hyperthermia, etc. (37, 38). Furthermore, sub-acute and chronic adverse effects related to mental health and wellbeing are often mentioned by the users, reporting intense comedowns, low mood, cravings and dependence, but little is known about the long-term physical harms (21).

Treatment providers lack the necessary evidence on which to base their treatment. Paramedics are working blind so they have to make a choice between treating or not treating, - both of which could result in potentially worsening the patient's condition. Paramedics are forced to resort to 'supportive' care – i.e., addressing symptoms to improve patient comfort (e.g., administering tranquilisers or antipsychotics), rather than addressing the actual cause of the problem. This approach, although pragmatic, is sub-optimal and often insufficient, and in severe cases can prove fatal.

This problematic situation has led people in the medical profession to demand action from politicians to reduce NPS use. This places considerable pressure on politicians to be seen to take action. The outcome of this need to be perceived to be doing something has led to the regrettably poorly drafted Psychoactive Substances Act in the UK. Emergency services may get less clarity, not more, because people may be poisoned by contaminated or badly prepared psychoactive substances as labs become smaller, more clandestine, operating with lower standards. Safety trials of NPS could dramatically improve the information available to medical professionals. Research trials investigating toxicity and side effects profiles of the drugs, before they hit the market would produce a rich foundation of clinical information, that could empower doctors to make informed decisions and thus to give proper care.

London's 'Club Drug Clinic' - a free NHS service provided by the Central and North West London NHS Foundation Trust, specialises in providing services to users of 'club drugs,' including NPS, via knowledgeable, experienced, and culturally competent staff. However, this is one of very few services provided specifically to this population – and is not sufficient to cope with the demand. This type of innovative clinic would likely not be needed in the presence of a legal market for cannabis, psychedelics and MDMA.

8.2.3 Fatalities and emergency treatment presentations

NPS have been implicated in a growing number of drug-related fatalities in England and Wales (from 20 in 2010, to 67 in 2014 (39)), although experts point out that they are rarely the cause of death (major causes of death were suicides, accidents and overdose of drugs other than NPS). NPS are only mentioned in a fraction of post-mortem and criminal casework (7% of total drug-related deaths) and often there are other substances involved, most commonly alcohol (40). Acute single-dose lethal toxicity is often unknown for many NPS.

NPS can induce pronounced clinical effects that can result in the need for emergency treatments. A recent study from the Poison Information Centre in the Netherlands showed that after NPS exposure, neurological and psychological symptoms were most frequently

[22] 3.5% of people were treated in A&E last year after using synthetic cannabinoids compared to 2.2% for other NPS and only 1% for natural cannabis (20).

reported, like agitation and hallucinations. In addition, cardiovascular symptoms like hypertension and tachycardia often occurred (41).

It is not possible to determine accurately the numbers of presentations to hospital associated with NPS toxicity because current monitoring of the drug situation in Europe focuses mainly on classical drugs of abuse and the data on NPS -related emergency presentations is scarce. The European Drug Emergencies Network (Euro-DEN) is a European Commission-funded project that aims to improve the knowledge of acute drug toxicity of both classical recreational drugs and NPS (42). They report that 5.6% of the drug-related emergency treatments in multiple European clinics were related to NPS, with mephedrone (2.8%) methedrone (1.1%) and synthetic cannabinoids (0.3%) being the most common (43).

8.2.4 Anti-Social Behaviour

Local authorities have reported intoxication and 'anti-social behaviour' as a result of the pervasiveness of 'legal' NPS, with some civil servants likening the phenomenon to public drinking (44). As a result, bans on public consumption of intoxicants and measures to seize the substances from high-street NPS shops have been implemented in some parts of the UK (45). Furthermore, NPS have been related to what has been described as a 'crisis' in prisons in the UK (46).

8.2.5 Potential Benefits

There are many potential benefits of new psychoactive substances, including for possible, yet undiscovered or untested medical applications, and reducing the harms associated with the recreational use of other drugs[23].

As has been discussed, from a health perspective, an important goal of policy should be to encourage lower risk of harm and part of this is ensuring that if people do use drugs, they use them in the safest possible way. The acceleration of the discovery of NPS in recent years presents a unique opportunity to identify drugs with lower risk profiles. This is an invaluable opportunity to investigate the potential of novel drugs and shift consumption patterns, from high-risk drugs like alcohol and nicotine, to new lower risk recreational drugs, and create a net benefit in public health terms.

Displacement from the popular recreational drugs is not, however, solely a benefit. Factors such as prohibition can also shift users to more harmful substances, as has been seen with the growing market for synthetic cannabinoids as a cheaper, legal alternative to cannabis.

8.3 Associated with regulation and its enforcement

This section takes on a slightly different form to the other chapters, due to the unique ways in which regulators and enforcement agencies are adapting their responses to this growing phenomenon. We will now look at a variety of ways in which these substances can be regulated and their relative merits and harms. At the time of writing, the UK government is still responding to new substances with specific bans and temporary bans but the Psychoactive Substances Act 2016 has received Royal Assent and is due to come into effect in May 2016 (47).

[23] A good example of such displacement were cocaine users, who switched to mephedrone, discussed in detail in the case box

The unifying feature of the approaches discussed below is that they fit into the current paradigm of supply reduction, rather than demand reduction and education. It is due to the application of supply reduction methods to traditional psychoactive substances that NPS are rapidly increasing in popularity. The continued attempt to use traditional supply reduction methods is not addressing the real issues and is exacerbating the situation.

8.3.1 Identification – Issues and Impossibilities

The significant increase in the number of substances to be identified and then controlled implies that public authorities are obliged to acquire and/or develop new technologies and standards for the detection of NPS. Similar expenditures will have to be made to increase capabilities in the collection and sharing of data, which further increases the costs of prohibition-based legislation.

Even if governments were to commit to the significant spending involved in identifying new psychoactive substances, there are serious concerns that the testing facilities will still be insufficient in a number of cases. It can be very difficult to identify an NPS. Even if a lab can identify the chemical composition of the substance in question, this is not sufficient to determine its psychoactivity, as *The Advisory Council on the Misuse of Drugs* has warned the Government (48). For example, two different molecules can have identical chemical formulas but with a different chemical structure – an isomer. Isomers contain the same number of atoms of each element, but have different arrangements of their atoms. This arrangement of their atoms is crucial in that one may produce psychoactive effects in the human brain and another not. Similarly, there is no other ways of definitively determining psychoactivity in the completely novel chemicals other than trials in humans. This presents a presents a currently insurmountable evidential hurdle to enforcement agencies.

8.3.2 International Scheduling

As a relatively recent phenomenon, NPS have been outside of the scope of UN drug control. However, the recent scheduling of a few of these novel substances might challenge this defining trait. Indeed, during the 58th session of the Commission on Narcotic Drugs, in March 2015, a group of synthetic cathinones (mephedrone, MDPV, methylone), two synthetic cannabinoids (JWH-018, AM-2201) and BZP were placed under Schedule II, while three substances of the NBOMe series (25B-NBOMe, 25C-NBOMe and 25I-NBOMe) were placed under Schedule I (49).

The 1961 Single convention and the 1971 Convention on Psychotropic Drugs allow substances to be added to the list of internationally controlled drugs[24] on the advice of the Expert Committee on Drug Dependence, which is operated by the World Health Organisation. Once this committee has decided that a substance should be scheduled (i.e., brought under international control), the recommendation is presented to the Commission on Narcotic Drugs (CND). Once approved by the CND, all member states must adopt a scheduling decision at least as stringent as that suggested by the Expert Committee.

Though potentially suitable as an international tool for addressing a static set of well-defined substances, in practice this process is far too slow to be an effective tool for the control of NPS. The Expert Committee meets once every two years, for only a few days, and so can only consider a few substances. Being unable to respond effectively to the market for NPS with

[24] i.e. drugs listed in the UN Conventions of 1961 and 1971

legislation, the UN's role has been mostly restricted to information gathering and dissemination.

8.3.3 Reactive Prohibition

In a system of reactive prohibition, substances can be manufactured, sold and used until they are banned. Reactive prohibition is an ineffective but popular response. At a high level, reactive prohibition often fails to achieve what it sets out to, because it is based on a false assumption, namely that if the current supply of an illicit substance can be eliminated, then consumption will decrease. This flies in the face of the economically sound assumption that if demand for psychoactive substances remains at a similar level, despite prohibition, other players and/or substances will enter the market to meet this shortfall in supply. It is clear that this is precisely what happens after the banning of most substances.

Early responses to the emergence of NPS (including the UK up until the Psychoactive Substances Act comes into force) tended to consist of a lengthy process of adding the newly identified substance to the list of already prohibited drugs. Ketamine was a very early NPS to emerge onto the global market and so was quite easily added to many national schedules already in existence. In the United Kingdom, it was labelled a Class C drug on 1 January 2006, and moved to Class B on 12 February 2014 (50). At the time, this was seen by most people as a relatively effective method of reducing some of the harms associated with ketamine abuse.

Despite the fact that ketamine continued be a very popular drug in many of the places where it was banned, its immediate availability diminished, and its use is thought to have declined in response to the change in the law – especially in the USA[25]. In the UK, there has been a decrease since 2008-2012 in prevalence of ketamine use in England and Wales among both the adult population as a whole and among young adults (see figure 2). However, there has been an increase in the number of people seeking treatment for ketamine in the past 6 years (1, 19, 52, 53, 54).

[25] Ketamine was listed into schedule III under the United States Controlled Substances Act in 1999. Prevalence rates for 12th graders showed a 40% decline between 2000 and 2014 (from 2.5% to 1.5%) (51).

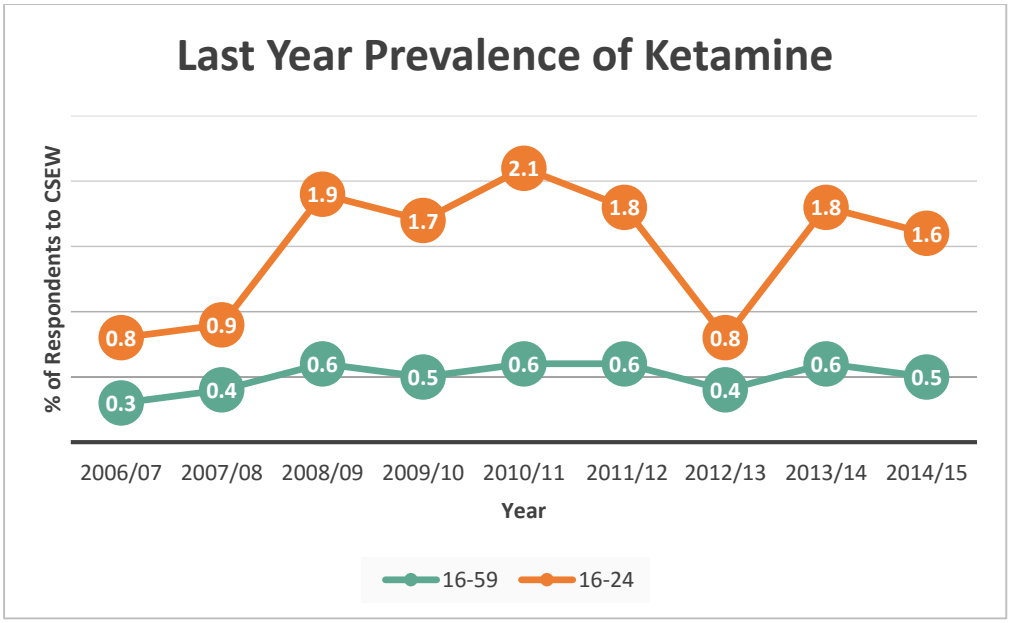

Figure 2. Last year prevalence of ketamine use.

Source: Crime Survey for England and Wales.

Since the classification of ketamine, the drug landscape has changed significantly – NPS are now emerging at a rate of two every six days, and so the market is evolving far quicker than substances can be classified in this way. Policy makers quickly realised that they needed some new legislative tools at their disposal if they were to continue to continue to react effectively to the emergence of new substances.

The reactive prohibition of newly identified compounds has been compared to a cat-and-mouse game between governments and manufactures. As soon as one substance is banned, another substance, about which even less is known, takes its place. Even when a ban of this type is successful in reducing the availability and use of a particular substance, chemists can develop, manufacture and distribute a substitute not subject to the same ban far quicker than they can be identified and prohibited by the government. Thus, reactive prohibition favours the emergence of new unknown and potentially more dangerous substances into the market. The utilisation of prohibition-based policies has meant that the number of potentially harmful NPS available on the market has increased from a few dozen around the turn of the millennium to more than 350 in 2014.

The window of *de facto* legality between the emergence of an NPS on the market and its banning, renders prohibition an ineffectual method of minimising the harms of NPS. Aside from the obvious point that the speed of prohibition – whether this is driven by cumbersome legislative processes or lack of timely data on what is available in the marketplace – renders it an ineffective policy tool, the resulting window of *de facto* legality creates a host of perverse incentives for manufacturers and undesirable behaviours in consumers that cause significant additional harms.

Manufacturers know that the substance they produce is likely to exist only for a short time in a grey area of legality, and will then be banned. This knowledge, combined with the profit incentive, can lead them to:

(i) bring new products to market as quickly as possible without conducting any safety testing;

(ii) manufacture products as cheaply as possible in unsafe facilities;

(iii) sell products in unsafe forms, like ambiguous white powders or herbal mixtures with uneven distribution of the psychoactive components, which might increase the risk of consumers overdosing; and

(iv) be secretive about the ingredients of their products, or how it is most safely consumed.[26]

The effect of the last of these responses is particularly pernicious. Intentionally misleading labels which claim a product is "not for human consumption" and give no indication as to the contents, mean that consumers are, more often than not, completely ignorant about what it is they are taking, and what dosage is likely to be appropriate.[27] Each of these behaviours has a harmful effect on the market for NPS, and importantly, on the types of NPS that are brought to market. These behaviours lead to the manufacture of substances about which almost nothing is known, where the responsibility for proving that a substance is safe falls to no-one, and where those legitimate manufactures who might have considered entering the market to produce genuinely safer alternatives to currently illicit drugs, are discouraged from doing so.

Consumers are also affected by this regime. Drug-naive individuals show a preference for purchasing and consuming legal rather than illegal drugs. However, many NPS that are currently legally available are demonstrably more harmful than the internationally scheduled substance that they aim to mimic. A proportion of consumers know that the legal substance they choose to consume is actually more harmful than its illegal counterpart (and often less enjoyable,)[28] but choose to use it nevertheless, in order to avoid the risk of a criminal conviction or being caught in workplace tests.

The reactive prohibition paradigm of control also leads to significant costs. Although there are no disaggregated data on the investment geared against NPS, the UK government has placed particular emphasis on the need to combat this new phenomenon through the concerted effort of the central government, the National Crime Agency, Border Force, Trading Standard, police forces and local authorities. Costly big-scale joint operations, such as the *NPS week of action* (2013), which concluded with 44 arrests and the seizure of 0.5kg of material, have targeted the manufacture and sale of controlled NPS in the UK (26).

One of the unintended negative consequences of reactive prohibition is that the banned substances become the subject of the legal and political barriers to research, which accompany the prohibition of substances. Potentially useful medical applications of new substances therefore go un-investigated, as do the other potential benefits of research.

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[26] The point here is not that all manufactures are by definition irresponsible – as this is clearly not the case. The point is that reactive prohibition fails entirely to encourage or incentivise 'good behaviour' – making 'bad behaviour' a default for some.

[27] This problem is compounded by branding. NPS are often sold under a particular brand that stays constant over time, even whilst the chemical composition of the substance within the packaging changes to stay in line with changes in the law, giving a false sense of product continuity.

[28] In a 2011 anonymous survey comparing patterns of use and preferences between synthetic cannabinoids and cannabis, 93% of the respondents declared preferring cannabis. Users consistently associated synthetic cannabis with more adverse effects (55).

8.3.4 Analogue and Generic Bans

At the national level, drug control policies tend to involve a system of individual listing. Extending this system, but retaining its basic prohibitionist framework, many countries have introduced analogue and generic methods of control, whereby whole groups of NPS can be prohibited with one piece of legislation. In most cases, however, adding new substances to the list of controlled drugs is a resource-intensive process, involving risk assessments and a lengthy legislative procedure.

There are obvious perceived benefits (particularly in terms of cost and efficiency) in terms of catching a number of psychoactive substances with one legislative response, but there are also a number of practical disadvantages. Not least of these, is that by defining a group of substances which are banned, legislators are implicitly defining those substances which are not banned. Armed with this knowledge, NPS manufacturers have found it surprisingly easy to design variant substances which fall outside of the defined prohibited categories.

8.3.5 Legislative Shortcuts

Recognising the rapid proliferation of NPS and the time needed to get a substance scheduled, some countries have implemented legislative shortcuts, such as *temporary class drug orders*. Since 2011, the UK's Home Secretary can make a temporary order after previous consultation with the Advisory Council on the Misuse of Drugs (ACMD), allowing certain substances to be banned without going through a full legislative process (56). In theory, these allow governments to remove specific substances from the market, which are deemed to be potentially harmful, much more rapidly than would be allowed using normal systems of control – making their appeal to law-makers obvious. In practice, temporary banning orders are problematic as a method of new substance control.

As a result of the speed with which these orders are put into place, there is generally no requirement that they are based on actual evidence of harm, turning the decision into one based on politics and moral panic rather than rationality and science. The stated aim of removing these substances from the market is rarely achieved; substances subject to these orders often remain in circulation, but manufacturers, suppliers and consumers are forced underground, thereby pushing the market further into the hands of criminal groups, impeding crucial research into the effects of the substance and increasing the likelihood that that the substance's purity and quality will decrease – thus increasing harms to the consumer.

8.3.6 Blanket Bans – The Psychoactive Substance Act 2016

The implicit premise of the prohibitionist framework is that all NPS consumption is by definition misguided,[29] that NPS are inherently dangerous and that the only effect that legislation should aim to have on the market for NPS is to diminish or eliminate it. This premise is very often enshrined in a moralistic argument, which arbitrarily defines certain psychoactive substances (such as alcohol or caffeine) as 'acceptable,' whilst others are defined as 'unacceptable,' often because of misplaced assumptions or unfamiliarity.

This is in contrast to the premise of those who suggest that because the market for NPS has the potential to breed dangerous and risky substances, it should be controlled and shaped by

[29] The UNODC for example, *defines* NPS as 'substances of abuse' (57), although EMCDDA (The European Monitoring Centre for Drugs and Drug Addiction) takes a more cautious approach: "A new psychoactive substance is defined as 'a new narcotic or psychotropic drug, in pure form or in preparation, that is not controlled by the United Nations drug conventions, but which may pose a public health threat comparable to that posed by substances listed in these conventions" (58).

governments, and that this can be best achieved through the strict testing and regulation of NPS before they are allowed to come to market.

Where blanket bans are in place on "psychoactive substances" this creates a wide ban extending to substances currently unknown to science. This creates the problem that people could be guilty of an offence relating to a substance where they neither knew, nor reasonably ought to have known that the substance in question was in fact subject to the ban.

8.3.6.1 The Psychoactive Substances Act 2016

The Psychoactive Substances Act will come into force in the UK on 26 May 2016 (59). The Act has created what has been referred to as "a blanket ban" on all substances that have any psychoactive effect. The legislation has exemptions for psychoactive substances like alcohol, tobacco, caffeine and will also include exemptions for legitimate scientific and clinical research.

The two major departures from current UK policy on drugs are:

1. No differentiation is made between substances, either in terms of harm, or in terms of 'perceived' harm – all substances covered by the Act carry the same legal sanctions and sentencing guidelines.

2. Users are not criminalised.

The bill was brought through Parliament with cross-party approval and very little political opposition despite the 2013 Report on New Psychoactive Substances, published by the All-Party Parliamentary Group for Drug Policy Reform (APPGDPR, 2013) which suggested (amongst other things): "*That the government consider adopting the key features of the New Zealand policy*" and "*that the onus should be on potential suppliers to demonstrate that a psychoactive substance has an agreed 'low risk of harm'*" (60).

8.3.6.2 Learning from Ireland

The 2016 Act is explicitly based on a similar piece of legislation enacted in the Republic of Ireland in 2010. There was, however, no formal report on the impact of the Irish legislation. The only available evidence to those drafting the UK legislation was anecdotal (61) and that anecdotal evidence showed that most of the 'head shops' (physical outlets selling NPS) had closed down. Rudi Fortson QC who consulted the House of Commons, Home Affairs Committee on this subject stated that "there has been a lamentable paucity of reliable information concerning the operation of that Act and its effectiveness or otherwise." (61). Despite numerous calls for the gathering of such information from NGOs, (62) a report gathering such information was never made. In fact, in Ireland, where a blanket ban on psychoactive substances was enacted in 2010, NPS use has increased from 16% in 2011 to 22% in 2014 according to the European Commission Report (28, see figure 3) and there have been several high profile deaths since the legislation has been enacted (63).[30]

[30] Similarly, after banning the manufacture, sale and advertising of NPS in 2010, Poland saw the number of NPS induced poisonings rise dramatically from 562 cases in 2010 to 1,600 cases in the first ten months of 2014 (64).

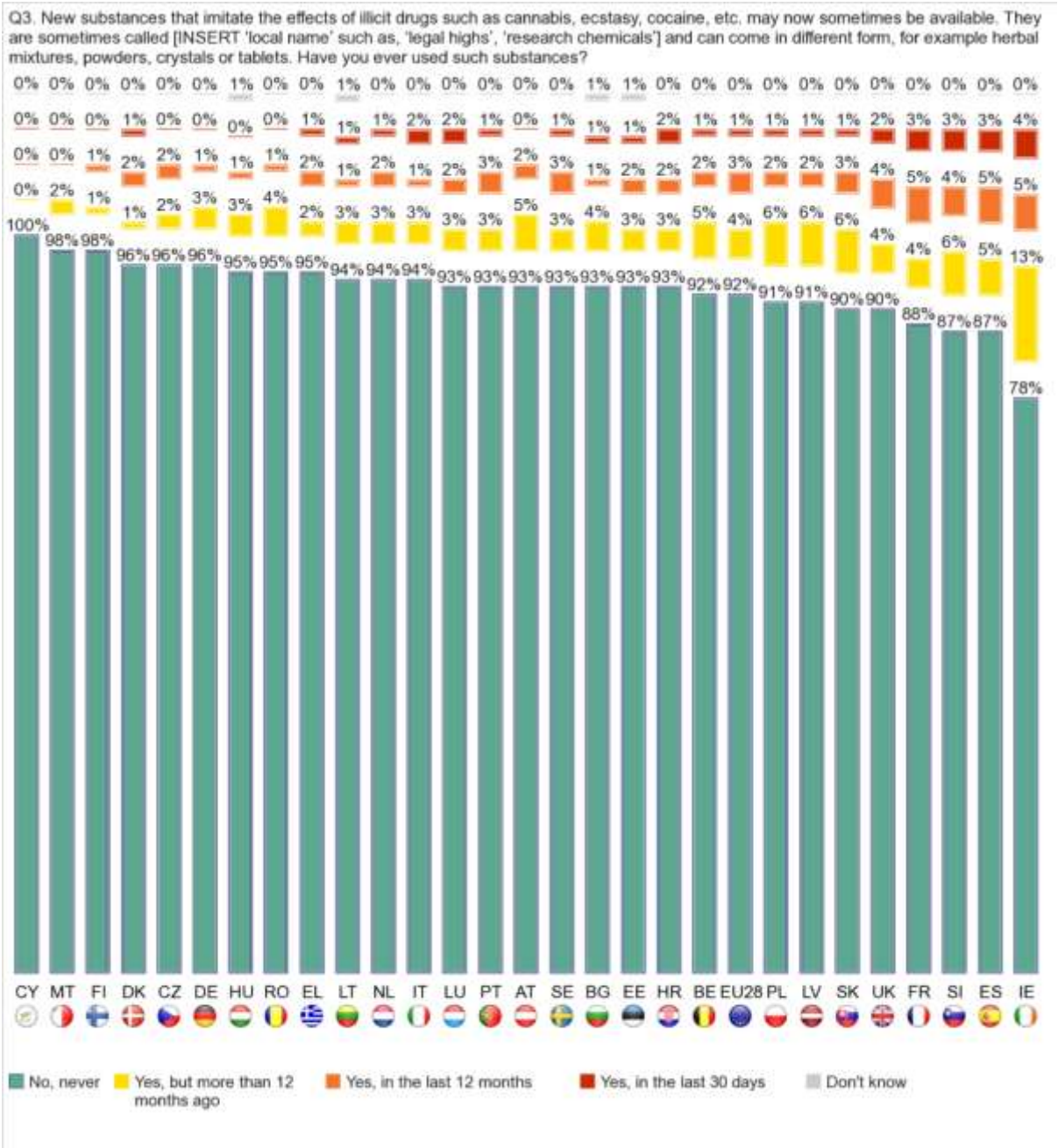

Figure 3. The prevalence of the NPS use in various European countries

Source: European Commission Report Eurobarometer 401, Young People and Drugs, 2014. The question asked was "Have you ever used any of the novel psychoactive substances (research chemicals, legal highs etc.)?"

A report ought to be commissioned on the success and failure of the Irish experiment, including but not limited to, the following issues:

- Whether NPS have become less available
- Whether NPS use rates have changed
- Whether traditional drug availability has changed
- Whether traditional drug use rates have changed
- Whether there have been successful cost-effective prosecutions

- Whether problems have been identified by law enforcement

8.3.6.3 The Definition of Psychoactive Substances

The Psychoactive Substances Act 2016 utilises a broad definition of psychoactive substances. This has a number of inherent difficulties, particularly in terms of legal certainty and the practicality of prosecutions.

The definition under the 2016 Act:

> ***Meaning of "psychoactive substance" etc***
>
> *(1) In this Act "psychoactive substance" means any substance which*
>
> *(a) is capable of producing a psychoactive effect in a person who consumes it, and*
>
> *(b) is not an exempted substance.*
>
> *(2) For the purposes of this Act a substance produces a psychoactive effect in a person if, by stimulating or depressing the person's central nervous system, it affects the person's mental functioning or emotional state; and references to a substance's psychoactive effects are to be read accordingly.*
>
> *(3) For the purposes of this Act a person consumes a substance if the person causes or allows the substance, or fumes given off by the substance, to enter the person's body in any way.*

The Chair of the Advisory Council on the Misuse of Drugs, Les Iversen, told the Home Affairs Committee that, "*we stand by our belief that the existing definition of psychoactivity in the draft Bill that we have seen is not workable*" and proposed an alternative:

"A substance produces a psychoactive effect in a person if, by stimulating or depressing the person's central nervous system, it affects the person's mental functioning or emotional state; ***as measured by the production of a pharmacological response on the central nervous system or which produces a response in in-vitro tests qualitatively identical to substances controlled under the Misuse of Drugs Act 1971****".* (48).

In response to that, the home secretary Theresa May wrote (64):

> *"The ACMD suggested narrowing the definition of a psychoactive substance to focus on substances with a pharmacologically similar response and comparable public health threat to that of controlled drugs. The term 'similar' places a burden on evidence gatherers/forensic experts to prove the similarity of a psychoactive substance to a drug controlled under the MDA 1971. There will almost certainly be discrepancies in how 'pharmacologically similar' is interpreted… Furthermore, I believe this approach would lessen the number of substances caught by the bill, limiting the number of psychoactive substances caught to those which produce pharmacologically similar responses to substances controlled by the Misuse of Drugs Act 1971".*

As the Transform and Release Joint Submission to the Public Bill Committee into the Psychoactive Substances Bill states:

> "*legally establishing that something is psychoactive is a real challenge that likely requires randomised controlled trials on humans, which would be impractical (particularly for the 100s of new substances emerging each year) and unethical. Clearly, in vitro or animal testing would not be sufficient to establish the legal test of psychoactivity, and whilst common sense may indicate that a substance is psychoactive this is not a sufficient threshold for legal proceedings*.
>
> *The reality is that attempts to clarify the definition are a legal and scientific minefield that will cause confusion and wasted resources across the criminal justice system as they are tested by experts in court. There are also a range of important outstanding questions relating to the degree of psychoactivity needed to qualify it under the 'psychoactive' definition, and how this will in turn relate to different effects on different individuals, as well as to issues of dosage and potency. The use of the terms 'it* [NPS] *affects the person's mental functioning or emotional state' will likely be subject to the De Minimis10 rule, and it appears that no discussion has been had on this matter*" (62).

An alternative to clinical trials would be to adduce the evidence of an expert to confirm that a substance was psychoactive. However, without clinical trials, the expert would still need someone to take the substance in order to confirm that it is psychoactive. There are even more serious ethical concerns in having someone take a substance with an entirely unknown risk profile without the controls that would be in place for a clinical trial.

Even if a suitable process were designed, the provision of evidence from a suitably qualified medical expert would be needed every instance a new substance was brought to trial. This would provide a substantial additional cost in bringing a prosecution to trial.

8.3.6.4 Enforcement

Commander Simon Bray, the National Police Chiefs' Council lead on psychoactive substances told the Home Affairs Committee that "*there would be a common-sense approach from law enforcement and prosecutors on what cases were pursued, that guidance would be disseminated,*" and that "*a logical and sensible approach that does not come up with silly prosecutions" would be taken* (61). This seems to implicitly acknowledge that "silly" prosecutions could possibly be pursued under the Act and that it will be left to enforcement officers to determine when and how they intend to use the act. This again raises serious issues of legal certainty, and puts people at risk of being unaware what actions are likely to result in prosecution and what are not. Any law giving great scope for how it is enforced leads to greater opportunities for it to be enforced discriminatorily.

If the legislation is to achieve its aims in reducing NPS use and availability, it must deter people from producing and supplying psychoactive substances. A major part in deterrence will be successful prosecutions. Many commentators have raised serious concerns over how the prosecution will be able to prove that a substance has psychoactive effects in the absence of human clinical trials, the use of which raises serious ethical and financial concerns. This could prove an insurmountable barrier to reaching convictions under the 2016 Act for substances, which lack pre-existing evidence from clinical trials of its psychoactivity.

Evidently, addressing this issue, in the forensic guidance released on 20th of May 2016, aimed at Forensic Service Providers (FSPs), law enforcement agencies, prosecuting agencies and

expert witnesses, the government decided to accept the scientific definition of the 'psychoactive' substance, originally proposed by ACMD (see previous section, 8.3.6.3) (65). The major implication of this is that it renders it much easier to define whether a given substance falls under the remit of the Act – namely those ones that bind to; and have similar effects on; the same receptors as the substances which are already banned under the Misuse of Drugs Act 1971.

For example, if the psychoactive component of cannabis, THC, binds to CB1 receptors, all the drugs that mimic the effects of THC by binding to the CB1 receptors would be banned. In practice, this is much easier to prove, by referring to the existing *in vitro* models, without the need for testing psychoactivity in humans.

This begs the question: Why publicly reject the recommendations of the ACMD, but then quietly incorporate them into the enforcement guidelines, but without amending the Act itself? Ian Dunt, in his article for politics.co.uk has a theory:

"... because it gives the Home Office vastly more power… Their current policing approach is tailored to addressing the original problem they encountered - those pesky chemists and their alternative versions of existing drugs. But in terms of statute, in terms of actual law, they've now got these extraordinarily expansive drug powers which ban drugs which don't even exist yet, which ban the smell of your mum's cooking if that's what ministers decide it's now going to do … you create the widest, broadest, vaguest powers possible and then when it comes to enforcement you follow a more restricted approach. But those huge powers you gave yourself, they still stay there, making all sorts of actions technically illegal. It's the state which decides when it wants to enforce them" (66).

8.3.6.5 Legal Certainty

People are, under the principle of legal certainty, entitled to know the legality of their actions at the time they take them. Every offence must be clearly and precisely defined. The House of Lords, in *R v. Rimmington and R v. Goldstein* (2005) UKHL 63 confirmed this, with Lord Bingham stating:

> "*There are two guiding principles: no one should be punished under a law unless it is sufficiently clear and certain to enable him to know what conduct is forbidden before he does it; and no one should be punished for any act which was not clearly and ascertainably punishable when the act was done*" (68).

Where a wide range of substances are banned on the basis of their effect in the brain then necessarily a producer would be guilty of producing a banned substance before it is possible to determine whether that substance produces a psychoactive effect in the brain. As the Transform and Release Joint Submission to the Public Bill Committee into the Psychoactive Substances Bill states:

> "*In its current form the Bill makes it impossible for:*
>
> - *An individual to understand whether many substances will be considered psychoactive;*
> - *The police to determine whether a substance is psychoactive and an offence has been committed;*

- *The CPS to establish whether it is appropriate to charge with an offence;*
- *A lawyer to properly advise their client on plea and potential sentence; and*
- *A Judge or jury to determine guilt or otherwise"* (62).

8.3.6.6 Production and Supply

Many psychoactive compounds can be altered to render them non-psychoactive with a relatively simple piece of home chemistry. It will legally be possible to purchase a substance that has been converted from an NPS but is not itself psychoactive. Then the user or local dealer could then reverse the conversion. The user or small-scale producer is still in contravention of the Act when he or she "produces" a psychoactive substance but the diffusion of the producers makes enforcement virtually impossible. As with all prohibition which fails to address demand reduction, the market will simply shift from retailers to the illicit market. This means there is a strong possibility that producers will simply switch the large scale production to create non-psychoactive substances which will then be activated in smaller scale production sites, increasing the risk of contamination with pre-cursor agents making purity less reliable and the related increase problems associated with potential over doses which that creates.

8.3.6.7 Harms

The explicit choice not to include any concept of harm in the 2016 Act undermines the pre-existing drugs legislation. It creates a two-tier system in which some drugs are banned despite being provably low risk, and others carry no offence of possession whilst being demonstrably more harmful than Class A substances, which carry a maximum sentence of up to 7 years imprisonment for mere possession.

The 2016 Act exempts a number of known harmful substances (alcohol and tobacco), whilst banning substances which are not harmful simply because they are psychoactive. As well as the clear moral issues that accompany this, it creates practical difficulties. When determining sentencing, a court would wish to have reference to the harm of a substance so as to determine a penalty commensurate with the offence. As noted by Rudi Fortson QC; "*in the absence of drug classification, or an expert's opinion (if accepted) as to harm, the courts will have little option but to assume that all psychoactive substances are equally harmful*" (61), an assumption which we know to false. The Home Secretary explained to the ACMD that it would give priority to policing "*those sources of supply which caused the most harm to communities in terms of crime and disorder or where connected to organised crime".* This regrettable position continues to leave enforcement down to the discretion of police and prosecuting agencies, leaving substantial scope for unequal, unprincipled and potentially discriminatory application of the law.

In addition to the serious disparity between how legal drugs such as alcohol and tobacco are regulated in comparison to controlled drugs, we now have an equally unprincipled regime for an undefined range of substances. The UK legislature has missed an opportunity to bring harm-reduction principles into regulation across the board. The stated rationale for the Misuse of Drugs Act has been to classify drugs according to harm so that sentencing for offences can be proportionate to the harms involved. This methodology has been abandoned in the 2016 Act.

8.3.6.8 Possession

The one positive to take away from the recent UK legislation is that at least users aren't criminalised for possession. The well-documented benefits of decriminalisation don't need to be explored here, although it is worth noting that the Drug Policy Alliance highlights the following:

- Reducing the number of people arrested;
- Reducing the number of people incarcerated;
- Increasing uptake into drug treatment;
- Reducing criminal justice costs and redirecting resources from criminal justice to health systems;
- Redirecting law enforcement resources to prevent serious and violent crime;
- Diminishing unjust racial disparities in drug law enforcement and sentencing, incarceration and related health characteristics and outcomes;
- Minimizing the social exclusion of people who use drugs, and creating a climate in which they are less fearful of seeking and accessing treatment, utilizing harm reduction services and receiving HIV/AIDS services;
- Improving relations between law enforcement and the community; and
- Protecting people from the wide-ranging and debilitating consequences of a criminal conviction (69).

Whilst the decision not to criminalise possession is laudable, it does create a strange inconsistency with other drug laws; police will still have to take everyone to the station to test drugs. Anyone can say that in their possession is an NPS, so everyone will need to be processed, and illicit drug users have just found an easy way to try to escape conviction for possession of a controlled substance by simply claiming that it is an NPS. The new approach is a welcome step in the right direction, but it doesn't make sense in principle or in terms of the practicalities of enforcement, until this positive change is extended to all drug use.

8.3.6.9 Drug Testing

One reason that many people use NPS is that the standard tests do not detect these substances in urine and blood samples. This makes NPS particularly attractive to populations subjected to regular drug testing, such as offshore oil-rig workers, military personnel, prison inmates, and those on parole or probation. Some drug users are moving to drugs we understand far less about in order to evade the sanctions that accompany a failed drugs test. The reality of the diversity of available drugs and the perverse incentive sometimes created by drug testing should be considered when considering drug testing as a policy.

A particular risk comes from the evolution of drug tests: although tests for NPS still pose a number of challenges to employers, courts, and treatment providers (e.g. they are not widely available, often expensive, and may not detect all current versions of a drug), the tests, like the drugs, are ever-evolving. Improvements in drug testing panels incentivise users to continuously switch to new generations of a compound or different compounds altogether, driving up the likelihood of an unintended adverse event.

8.3.6.10 Lost Research Opportunities

Finally, in terms of opportunity costs, there is a risk that blanket and analogue bans could lead to diminished research into substances that could potentially have therapeutic effects. Some of the compounds banned by the broad strokes of this policy have never been synthesised. Without any previous assessment, it is impossible to know if they could be useful in science, medicine or providing a lower risk alternative to an existing recreational or medical drug.

There is a benefit in having people commercially motivated to discover new drugs, because these may have useful applications beyond recreational use. One of the most obvious benefits is that, when creating analogues, organic chemists sometimes find substances that help in treatment. Drugs work by chemical binding to receptors in the body. Antagonists – substances which bind to the same receptors as the drug, but don't cause any effect by themselves can be used to treat overdoses by 'occupying' the receptors the original drug would bind, thus blocking its effects. For instance, Naltrexone is an opioid, but unlike heroine or morphine it is an antagonist of the opioid receptors, so it blocks or attenuates the effects of these drugs. It is widely used for the treatment of heroin dependence. It lives within the analogue space of morphine. For the research of future cures, remedies and emergency responses to drug use experimentation, the production of NPS is essential. For these reasons, experimentation with the production of NPS should be encouraged not prohibited or repressed. A blanket ban on the production of all psychoactive substances impedes this research and deprives society of its potentially helpful results.

9. Developing a new regulatory model for NPS

The aim of better drug policies should be to end the legal limbo in which these substances are produced, distributed and consumed. Thus, reasonable product quality and safety standards should be established and enforced. But perhaps more important, the policy on NPS cannot be developed in isolation from the wider legal framework on psychoactive substances with a well-established history and culture of use. As we have previously stated, the proliferation of NPS is a by-product of the global prohibition regime. Most of these substances are designed to mimic the effects of controlled drugs and would be substantially less prevalent under a system of strict regulation.

8.4 Policy goals

The NPS market is a cycle of chemical innovation, followed by legally-murky commercialisation and the seemingly inevitable prohibition of the product, which triggers further, potentially hazardous, chemical innovation. This loop leaves a trail of NPS-related acute and chronic harms that are inequitably burdensome on the users, who are trapped between the desire to avoid criminalisation and an appetite for pleasurable intoxication, and the State, which has to allocate higher amounts of resources into law enforcement and public health services. Society shares the costs of a failed system that promotes misinformation.

Consumer safety also requires that sufficient objective information about the substance's contents and effects should be available, as dose, purity and frequency of use seem to significantly condition the severity of harms related to NPS. In banning substances due consideration should also be given to the principle of legal certainty so that actors within the market can be fully aware of the legality of their actions. Furthermore, safer use should be promoted, through harm reduction strategies and targeted messaging to influence populations

particularly at risk. In parallel, measures to steer people away from high-risk substances should be implemented.

The more that is known about a drug, the easier it is to mitigate harms, so policies should be designed to encourage the use of substances known to have low risk profiles in preference to more harmful substances or ones with unknown risk profiles. These known low risk drugs could be either traditional psychoactive substances or novel substances that have undergone rigorous safety trials. Reducing the rate of appearance of new NPS and preventing substances with unknown risk profiles and no information on how to treat toxicity should be a key goal to reduce the problems associated with treating patients who have taken NPS.

Further scientific research on NPS should not be deterred, as knowledge about these substances is currently patchy at best.

Considering these aspects, alternative policies should provide:

- a mechanism for effectively regulating psychoactive substances before they reach the market;
- public confidence about the risk profile of the psychoactive products legally available for sale;
- controls on the availability of psychoactive products, including purchase age and place of sale;
- information for consumers on product contents, dose and potency;
- certainty on the status of psychoactive substances, reducing the risk that people will seek them through the black market, and giving the industry long-term financial confidence;
- an equitable process that does not disadvantage one segment of the market over another by imposing onerous requirements on either import or domestic manufacture; and establish an enduring regime to replace interim measures, analogue and restricted substances provisions.
- safer use, especially targeting at risk populations
- flexible approach and incorporate new evidence to adapt to the arising challenges
- respect for the principle of legal certainty[31]

8.5 Potential regulatory model

8.5.1 Overview

Notwithstanding the pervasive prohibitionist approach to NPS, the phenomenon has come at a particularly interesting time in the evolution of global attitudes to drug control. The taboo on discussing alternatives to prohibition is beginning to break down and the value of rational and evidence-based drug policy is beginning to be recognised. The rise in NPS provides a

[31] These objectives are substantially based on the New Zealand Ministry for Health's recommendations in their 2011 advice to the New Zealand Government about formulating NPS legislation.

fascinating opportunity to re-assess how we regulate drugs with minimising harms and maximising benefits at its core.

The proposed system is based largely on the initial concept behind New Zealand's Psychoactive Substances Act 2013, which had wide support from a broad range of stakeholders but underwent some stifling alterations in 2014. This situation is discussed below at *Section 9.2.5.5*. There have been a number of calls for the UK to implement legislation based upon the New Zealand model including the report *New Psychoactive Substances*, published by the *All-Party Parliamentary Group for Drug Policy Reform (*60).

The regulatory model is designed to ensure decisions are based on evidence. From a consumer perspective, this means consumers can have access to information about the safety of the product they are consuming. From a public health perspective, this is designed to ensure that people are more likely to consume lower risk products, and less likely to consume higher risk products.

It is envisaged that a regulatory authority ("the authority") would be established to oversee the regulation with assistance from an independent organisation who could objectively assess scientific information submitted as part of applications for regulatory approval. In order to create these bodies and provide the statutory framework, legislation would be passed ("the Act") which would allow for further regulations to be passed ("the Regulations").

There are fears that if an NPS were to be were to be declared "safe" (within certain usage limits) it could register in the public mind as safe at any dosage, and a public binge could ensue. Therefore, an inherent braking-mechanism needs to be incorporated into the system, if the failure of the BZP-experiment in New Zealand[32] is not to be repeated with the regulation of NPS in the future.

Thus we propose a method of regulation for NPS based on two principles:

1. **Testing** NPS for safety according to pharmaceutical standards.
2. **Insuring** the consumer of the NPS for each usage.

The key features of the proposed regulation are:

a) ***Precautionary prohibition of new psychoactive substances.*** A psychoactive substance that has not been approved by the Authority is prohibited, on a precautionary basis, until the Authority is satisfied that it poses no more than a low risk of harm to individuals who use it.

b) ***Low risk products are approved.*** A psychoactive product that poses no more than a low risk of harm to individuals who use the product must be approved. The Act places the responsibility on manufacturers to demonstrate that their products are low risk.

[32] Since 1999, benzylpiperazine use grew sharply in New Zealand due to an initial complete lack of regulation. The New Zealand government attempted to ban the product as of 18 December 2007, but the necessary second reading of the bill did not happen in time for the law to be passed. It was so widely used that an estimated 5 million pills were sold in New Zealand in 2007 (70).

c) ***Approval decisions are based on evidence.*** Before a psychoactive product can be approved for use by individuals, the degree of harm posed by the product to individuals who use it should be assessed by the Authority on the basis of—

i. the advice of an expert advisory committee; and

ii. evidence, including the results of preclinical and clinical trials.

d) ***Approved products are tightly regulated.*** The importation, manufacture, and sale of approved products are subject to regulation, consistent with the overarching purpose to protect health and minimise harm.

8.5.2 Definition of Psychoactive Substances

The precautionary prohibition of unapproved psychoactive substances requires a workable definition of "psychoactive substance" as does a blanket ban. The definition determines the scope of the regime i.e., which things or substances fall inside the precautionary prohibition and must be approved. This is one of the most legally contentious elements of either approach as it creates problems with legal certainty (*discussed at 8.3.6.5*). There are broadly three options available:

(a) *The "purpose" approach* - psychoactive substance is defined as something that is used for the purpose of inducing a psychoactive effect.

(b) *The "capable effect" approach* - psychoactive substance is a substance that is capable of inducing a psychoactive effect.

(c) *The "hybrid" approach* –this defines psychoactive substances using the "capable effect" definition, but for this to be mediated by an application section of the Act that provides that the Act "applies" to things used for the purpose of inducing a psychoactive effect.

The 'purpose' approach has the benefit of being better targeted (the point of the regime is to catch things which are used *for* inducing psychoactive effects, not things that *could* be psychoactive if used). However, there are concerns that it could leave open 'loopholes' where manufacturers could circumvent the regime by claiming that a substance is intended for another purpose (e.g. some synthetic cannabis products had been sold as "herbal incense").

The 'capable effect' approach avoids that loophole, but may be too broad and arguably catch things such as garden plants, strobe-lights, glue and paint. These substances can then be specifically exempted from the scope of the act, but this is far from ideal in terms of providing reliable information to people in the market as to whether their actions are legal. The UK Psychoactive Substances Bill opted for the capable approach, which received widespread condemnation for being too broad in its effect.

Our recommendation is the 'purpose approach 'as it is a question of fact whether a product was being presented as having one purpose but being used for another. Products containing synthetic cannabinoid substance(s) and sold as "herbal incense" are unlikely to escape the coverage of the proposed act. There is really no conceivable reason why synthetic cannabinoids would be incorporated into herbal incense unless it was intended to be inhaled for a psychoactive response. If a substance is contained in a product with no provable reason other than its psychoactive potential, that product could readily be deemed to be sold for the purpose of inducing a psychoactive effect. In the case of substances like glue, there are obviously rational reasons for incorporating psychoactive substances.

9.2.3. Approval of Products

The proposed legislation would provide a mechanism by which a psychoactive substance formulated into a particular product can be approved for sale to the general public. The Authority *must* grant approval to any product application which includes all of the required information, and where the Authority is satisfied that the product for which approval is sought poses no more than a low risk of harm to consumers of the product.

Low risk is a shifting concept including value judgments that change over time, so flexibility would be needed to interpret this concept. There are some mandatory criteria, which can be imposed to assist in this process. The decision must be based on clinical evidence evaluated by experts with expertise in (at least) pharmacology, toxicology, neuroscience and medicine. An independent organisation would need to evaluate all trial results and make recommendation to the regulatory authority. The independent organisation would have regard to:

(a) the specific effects of the product, including pharmacological, psychoactive, and toxicological effects;

(b) the risks, if any, to public health;

(c) the potential for use of the product to cause death;

(d) the potential for the product to create physical or psychological dependence;

(e) the likelihood of misuse of the product;

(f) the potential appeal of the product to vulnerable populations; and

(g) any other matters that the Authority considers relevant.

The precise details of what information must be included in each application would need to be capable of evolving to keep up with best scientific practice. However, it is at least clear that applicants would need to be required to provide information on:

(d) Toxicity, pharmacology and related clinical effects of a substance;

(e) The behavioural effects of the substances;

(f) Addictive potential;

(g) Proposed directions for use; and

(h) Previous use, including use in clinical trials and in the wider population.

The regulatory authority would be needed to oversee the approval of products. In assessing whether a product or substance should be approved the regulatory body would have regard to:

(a) The nature of the harms and benefits of the product;

(b) Whether the harms can be effectively managed through regulation;

(c) Likely consequences of regulation compared to prohibition; and

(d) Potential displacement issues.

9.2.3.1 How do you prove that a recreational drug is low-risk?

Traditionally, substances are deemed safe for human consumption if they pass a series of tests – both clinical (in humans) and preclinical (before humans, i.e. in animals). Preclinical trials assess the pharmacological, toxicological, and behavioural profile of a drug, and allow for close examination of vital organs and tissues following exposure to the drug. Naturally, any substance shown to damage certain organs or systems in animal trials would not be allowed to progress to human trials.

Once a drug is approved for human testing, it proceeds through multiple 'phases' of clinical trials, progressing from small 'safety and feasibility' studies in healthy subjects to large-scale multi-site trials in patient populations. The resulting evidence gives a picture of the relative risks and benefits of the drug, and if this ratio is favourable, the drug can move on to be marketed.

Although this 'development pipeline' is standard for therapeutic drugs, it is not how any government currently approaches NPS or any other recreational drugs. There is, however, no reason that the same systematic and rigorous procedures could not be used to assess NPS as well. This may even include jurisdictions that disallow preclinical trials (e.g., New Zealand), since many of the measures gathered in animal studies can now be gathered in humans with the help of imaging, medical/neurological tools, and minimally invasive blood and tissue tests. People are already self-administering NPS, providing ample opportunity to monitor these safety dimensions.

9.2.4 Offences

The proposed main offences would be:

(a) *An offence dealing with unapproved substances* – knowingly or recklessly manufacturing, importing, or supplying any unapproved psychoactive substance. There would be an exception created for persons who hold licenses to research or manufacture unapproved substances.

(b) *An offence dealing with approved substances* - manufacturing, importing, or supplying any psychoactive substance in breach of the generic or specific terms and conditions of an approval.

9.2.5 Regulation

The regulatory framework would be designed to create a tightly regulated market in approved products. To this end a range of regulatory mechanisms would be used, which can be summarised under the following headings:

(i) Licensing regulated by the Authority.

(j) Restrictions imposed directly by the Act.

(k) Regulations promulgated by the Government.

(l) Local Approved Product Policies (**"LAPP"**) created by local authorities.

9.2.5.1 Licensing

Licensing is a primary mechanism for regulating approved psychoactive products. There would be a requirement to hold a license issued by the Authority in order to import, manufacture, sell or supply psychoactive substances. The Authority may place conditions on licenses and revoke licenses.

A person may apply to the Authority for a licence to do one or more of the following:

(a) import psychoactive substances;

(b) manufacture psychoactive substances;

(c) research psychoactive substances (which might be necessary to establish an evidence base for a substance that goes into a product for which approval is later sought);

(d) sell psychoactive substances that are not approved products (the Act sets out that such substances can only be sold to researchers or wholesalers who are licensed under the Act);

(e) sell approved products by retail

(f) sell approved products by wholesale.

The Authority must grant a licence where the application is filled-in correctly, and the applicant is a "fit and proper person" (or in the case of a body corporate, is "of good repute").

9.2.5.2 Restrictions imposed directly by the Act

The Act imposes a number of restrictions directly. These include:

(m) ***Place of sale restrictions.*** For example, approved products cannot be sold in convenience stores, supermarkets, liquor stores, temporary stores, or petrol stations.

(n) ***Advertising restrictions***. Approved products cannot be advertised on television, radio, the internet, or in a newspaper or periodical. Advertising of approved products is confined only to inside the premises of a retailer, and must be limited to objective information.

(o) ***Purchase age***. It is an offence to supply products to any person under 18 years old.

(p) ***Promotion restrictions***. Approved products cannot be offered for free, and cannot be sold as part of a promotion.

9.2.5.3 Regulations

The Act would also empower the Government to create regulations, which have not yet been promulgated. These regulations can cover:

(a) **Place-of-sale restrictions** (in addition to the current restrictions in the Act). Currently no such additional restrictions are proposed.

(b) **Labelling restrictions or requirements** (a mandatory health warning must be included in the regulations). The Authority has proposed creating regulations requiring a health warning, as well as other information including the recommended dosage.

(c) **Advertising restrictions** (in addition to the current restrictions in the Act). Currently no additional restrictions are proposed.

(d) **Packaging restrictions or requirements**. The Authority has proposed regulations for packaging, including requiring that they be child-proof and allowing the Authority to refuse packaging that associates with youth culture.

(e) **Signage requirements.** Currently no restrictions are proposed.

(f) **Internet sale restrictions and requirements**. The Authority has proposed requiring age verification process for internet sites.

(g) **Quantity, dosage, and serving restrictions or requirements**. The Authority is considering requirement that products be restricted to dose size, and that there be a split dose wherever possible.

(h) **Storage, display and disposal restriction or requirements**. Currently no restrictions are proposed.

9.2.5.4 Local Approved Product Policies

The Act would empower local authorities to create Local Approved Product Policies (**"LAPP"**). LAPPs may specify the location of premises from which approved products can be sold, by reference to one or more of:

(q) broad areas within the district;

(r) proximity to other premises from which approved products are sold within the district; or

(s) proximity to premises or facilities of a particular kind or kinds within the district (for example, kindergartens, early childhood centres, schools, places of worship, or other community facilities).

(t) LAPPs are not able to effectively prohibit the sale of approved products within a territorial authority's jurisdiction – they must be used for their legitimate purpose.

9.2.5.4.1 Insurance

Producers would insure their products and the premiums paid will be dependent on the available evidence of risk. It is suggested that this system will incentivise the production of increasingly safer products to be developed. The less you know about the risk profile of a substance the more the producer will have to pay. The lower the harm potential the more producers will pay.

We suggest not-for-profit insurance bodies insuring the consumer against any mishap resulting from the sale and use of the drug. The not-for-profit insurer would direct any surplus

funds received from their operations to a scientific charitable organization, which would fund and direct scientific research, and produce educational material.

The users would also pay a small portion of each purchase into the insurance. A commercial insurance body would naturally have as its mandate the maximization of profit, which would be achieved by selling more insurance – and therefore more of the NPS. For this reason, it is key that this insurance body should be a not-for-profit. The alternative would be to have the entire cost of insurance borne by the producer and allow for profit insurance companies to operate in this market, but this could have stifling effects on the creation of the market.

This insurance body, and the insurance policies it sells, would play many roles in making this system work:

a) The insurance body would channel its surplus funds into a charitable organization which would be in charge of research and education. The first research objective would be to establish a clinical practice manual for all NPS, so as to inform the medical community of the full information known about these substances. The second research objective would be to develop an antidote to each NPS that would rapidly cancel its effect. Such an antidote, if purchased with the NPS, could be both useful in the (rare) case of an adverse reaction, whilst the knowledge that he/she has an "escape" button available would provide an additional comfort to the consumer. Lastly, the insurance body's mandate would *create educational material* for users, so as to teach them the safe dosage and to prepare them for their first encounters with NPS. It would also encourage them to delay first use to an appropriate age and, if they do use, to do so in a responsible manner.

b) The NPS-consumer would be covered for any medical and related costs incurred as a result of taking the NPS, so long as the dosage guidelines specified in the policy had been followed. The medical community is constantly at a disadvantage when treating NPS-related complaints, because there is no clinical information as to how to treat them. Despite this, medical staff are responsible, by law and their oath, to safeguard the public's health. The extra treatments, advice or literature required to treat the consumer appropriately would be supplied by, and funded by, the insurance body.

c) The consumer of a regulated NPS would have the assurance that the NPS had been tested for safety; and, through the insurance policy, would have the *additional* assurance that if something untoward *did* result, he or she would be financially covered. This would also relieve the state of much of the burden of costs arising from problematic NPS-use.

d) That *additional assurance* is precisely what is lost to the consumer if he or she breaches the guide-lines set forth in the policy – for example with respect to dosage or frequency of consumption. This should motivate the consumer to moderate consumption in accordance with the policy.

The insurance body would continue to refine its knowledge of the individual differences in reaction to various NPS and the underlying physiological mechanisms, and could in principle develop into making personalized policies based on genetic analysis and personal history. The price of each policy would reflect the risk that a person runs in consuming the NPS. The insurance body would relieve the government of the burden of managing this complex

problem, and would fund the research that improves management from the premiums it collects.

The State would insist on the insurance policy being included in any regulated sale. This would then be somewhat similar to driving. When we drive illegally, we void the terms of our insurance and, on the other hand, it is illegal to drive without insurance. The double advantage to the consumer of the system here proposed is that he or she would be getting a substance with a defined ingredient and strength (as opposed to an unknown powder), and would additionally be insured against any accident so long as not breaching the policy.

In this way, NPS that have been safety-tested and use-insured will gradually enter the regulated market, thereby reducing potential harms and costs.

9.2.5.5 The New Zealand Experiment

New Zealand enacted legislation in 2013, which was widely viewed as progressive, in that it permitted products containing NPS to be sold legally where a product had been proven by the intended producer or supplier to pose no more than a low risk of harm to individuals using the product. Approvals were intended to be product-specific and not substance-specific.

The innovative approach was widely lauded as a positive move to combating the harms associated with NPS use. Unfortunately, due to a number of domestic political setbacks, not much has changed since.

"*During the establishment phase of the new regime, a number of importers, manufacturers, wholesalers and retailers were granted interim licences, and some products were given interim approvals, and were subsequently followed up to see if they were meeting their licence conditions and that their products were not causing adverse reactions*

The interim phase ended with the passing of the Psychoactive Substances Amendment Act 2014 on 8 May, which resulted in all interim product approvals and all wholesale and retail licences being revoked. It also placed a moratorium on processing applications for product approvals and for licences until regulations came into force" (71).

The Psychoactive Substances Regulatory Authority's approach to the interim licensing of psychoactive products was essentially to grant a licence where:

- The applicant could provide some evidence that the product had been on sale during the lead-in period to the commencement of the Act; and
- The Authority had not received sufficient evidence – primarily obtained through self-reports to the National Poisons Centre – that the product was responsible for one or more serious adverse effects, or an excessive number of minor effects.

It is questionable, bearing in mind the rate at which product compositions changed before the enactment of the Act, whether this methodology was really effective at identifying risky products or conceptually consistent with the intention of the Act. Nor did the Manufacturing Code of Practice come into effect until the interim regime was already well underway, which led to concerns about whether products even contained the substances claimed.

There have been no licences granted for any products since the amendment of the Act was made which halted the granting of interim licenses. Evidence from trials involving animal

testing[33] are no longer able to be used to determine low harm for a product (current threshold for a product to go to market), which has made it very difficult for any product to be approved, as current testing technology can't prove low harm without animal or human trials. Various alternative testing regimes have been proposed and are being considered, but as yet, none have been endorsed by the Psychoactive Substances Expert Advisory Committee.

Controlled drugs listed in the Schedules to the Misuse of Drugs Act 1975 are not able to go through this process.

There are also new, potentially harmful products that are entering the black market, but there is little understanding of what these substances are and the effect that they have. Because of this there have been increased reports of harm from new psychoactive substances with notable media attention around this, especially N-BOMe. Dealing in and use of these substances is an offence under the Psychoactive Substances Act, but nevertheless a number of such substances are also in the process of being scheduled under the Misuse of Drugs Act.

There has also been public resistance to the model. The Act empowered local councils to designate areas in which premises licensed to sell psychoactive products could trade, but did not permit councils to completely ban the sale of products in a district. Local politicians took the opportunity to suggest that they were being 'required' to authorise the sale of psychoactive substances in their communities, and made political mileage out of such claims.

Despite the problems in implementation with the New Zealand model, the authors believe that it still offers an interesting way of assessing whether new substances should be able to be legally sold.

[33] There are ethical concerns regarding testing on and dissecting animals as part of determining harms of recreational drugs which people are less concerned with when it is in relation to the testing of medicinal drugs.

Table 2. Proposed Regulatory Model

Stage in the chain	Regulatory aspect	Description
Production	Risk-assessment	Manufacturers would fund [pre-]clinical trials for new psychoactive substances. An independent regulatory agency would assess the risk posed by the substance on the basis of objective criteria.
	Licensed production	The regulatory agency would attribute production licenses and enforce quality, safety and product regulations.
	Traceability	Adequate reporting and monitoring coupled with accurate traceability technology which could include unit-dose packaging, RFID tagging, etc.
Supply	Type of outlet	Pharmacy or similar purposefully-designed outlets
	Trading hours	Trading hours limited by local authorities
	Density of outlets	Limit on density of licensed outlets decided by local authorities.
Accessibility	Price	Price and taxation structure that competes with the illegal market, restricts youth access and discourages consumption in general. Partially hypothecated tax: fiscal revenue from the sales of psychoactive substances must cover harm-reduction services.
	Taxation	
	Age	Minimum age of purchase: 18 years old
Demand and Harm reduction	Training for retailers	Licensing of retail subjected to training of specialised staff on drug use/abuse, counselling, treatment and harm-reduction
	Testing	Provision of pill-testing at large nightclubs and festivals
	Right to refuse sales	Specialised staff would have the right to refuse sales to purchasers deemed unfit (intoxication, disorderly conduct, intent to supply a minor, signs of abuse, etc.)
	Packaging	Plain and standardised packaging with uniform labelling requirements on product contents and health warnings.
	Advertising	Total ban on advertising and marketing
	Provision of information	Outlets would promote safer use and provide information on substances and harm reduction.
	Packaging requirements	Child-proof packaging
	Public campaigns / education	Harm-reduction initiatives, public education on psychoactive substances and public campaigns to aim to reduce consumption and promote responsible use.
Use and Consumption	Purchase limits	Purchases limited to 4 active doses per person per month
	Smoking bans	Smoking bans would apply
	Disorderly conduct	Laws on intoxication and disorderly conduct would apply to sanction unacceptable behaviour.
	Restrictions on potentially harmful behaviour	Driving / operating machinery illegal under the influence. (Standards would have to be developed by manufacturers to determine thresholds of impairment.)

9.3 Hypothesised impact

The recent challenge of NPS suggests a pivotal change in the behaviour of the illicit drugs market. While levels of use are relatively low, the nimbleness of the NPS market seriously questions the capacity of reactive prohibition to tackle drug-related challenges. In a context of strict regulation of 'traditional' psychoactive substances, we expect the demand for these novel substances to drop significantly and the importance and scale of the NPS regulatory framework would also substantially diminish, although not disappear[34]. So whilst the important issue is considered to be the creation of regulated markets for the traditional psychoactive substances, it is still necessary to address NPS as an interesting and unique part of any drug regulation framework.

Sensible drug policy should incorporate new evidence over time in order to adapt constantly towards an ever-improving solution. This is in contrast to the vast majority of drug policies worldwide, where the power of inertia combined with the inflexibility of the international drug control regime ensures that ineffective or harmful policies often remain in place for decades, irrespective of mounting evidence pointing to their manifest failure. It is important to review the policy, (e.g. on a 5 year basis) in order to estimate if it reaches its goal successfully and adapts to the arising challenges.

9.3.1 Impact of production controls

The new regulatory landscape would allow chemical entrepreneurs to enter the market while being mindful of the potential adverse effects associated to each product. In terms of production, this translates into the creation of a formal system of assessment *before* commercialisation. Both this process, and the licensing of the product on the basis of standard criteria would significantly increase the reliability and safety of the NPS market. While the administrative and regulatory architecture to frame pre-production and production operations in this new market will lead to certain costs, these are expected to be largely offset by law enforcement and public health savings, administrative and fiscal revenues and an overall increase in the wellbeing of users.

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[34] Evidence for this comes from the patterns of use of the NPS in the Netherlands, where a specific drug market exists, characterised by the fact that cannabis is legally available through the coffee shops and other, illicit drugs, are of relatively high purity, have a good quality and are obtained without particular problems. Consequently, the use of NPS in the Netherlands could be different from all the other European countries. Both Eurobarometer and GDS agree that about 7% of respondents have tried NPS in the last 12 months, which is much lower than in Ireland, Poland, Spain or even the UK, but is about average compared to other European countries (20, 28). There is no separate data for synthetic cannabinoids, which would be very interesting to compare, given the legal status of cannabis in the Netherlands and the fact that most users prefer 'real' cannabis (55). However, data from the Dutch Poisons Information Center (DPIC, information service to health care professionals on the management of suspected intoxications) demonstrates that most NPS-related emergency treatments involved 4-FA (4-Fluoroamphetamine), 2C-B and benzofurans. Drugs Information and Monitoring System (DIMS, organisation analysing drug samples in the Netherlands, in a similar way to WEDINOS scheme in the UK) received only a limited number of samples containing NPS. Curiously, the most of samples containing NPS submitted to the DIMS were sold not as such but as common illicit drugs, e.g. ecstasy or speed. This indicates that many people did not intend to purchase NPS separately, and were unaware of its presence. Most common NPS detected were also 2C-B, 4-FA and benzofurans, but very few synthetic cannabinoids (41).

Table 3. Hypothesised Impact on Production

Control Measures	Hypothesised behaviour change	Contextual Factors	Stakeholders affected	Costs / Benefits
Risk-assessment	Increased licit market	Thresholds of safety Assessment costs & requirements	Users State Licit producers	Administration costs Compliance costs Public health services savings CJS savings Administration revenues
Licensed production (plus traceability measures)	Increased licit market	Licensing costs & requirements Taxation Monitoring & Enforcement	Licit Producers State	Administration costs Public health services costs Fiscal revenue
	Decreased illicit market	Product satisfaction Enforcement	Users State Illicit producers	Public health services savings CJS Savings
Product & Quality controls	Reduction of contaminants and/or adulterants on the market	Monitoring Enforcement	Licit Producers Users State	Compliance costs Enforcement costs Increased enjoyment Public health services savings

9.3.2 Impact of supply controls

The creation of a tailored architecture of supply designed to reduce harms and limit consumption, especially among the vulnerable, would lead to significant gains for the public interest. Conversely, the most significant costs would be related to the establishment of an administrative and regulatory bureaucracy, as well as monitoring and enforcement activities associated to ensuring compliance and uprooting illegal competition.

Tested and regulated NPS will, if such a regime is introduced, appear on the market much more slowly, as the process of testing is very expensive. In the scenario described above, vendors will test the safety of the products prior to bringing them to market. Since not all substances will pass the test successfully, the rate at which NPS appear on the regulated market will diminish.

We expect the diversity and magnitude of the benefits to far offset the expenses. Social costs are expected to greatly decrease in a formalised market with adequate availability/accessibility standards, leading to savings in public health, a reduction of public nuisance, and increased enjoyment and wellbeing. Moreover, the State would derive considerable revenue from the NPS industry, both in the form of taxation and through the system of attribution of production licenses.

Table 4. Hypothesised Impact of Supply Regulations

Control Measures	Hypothesised behaviour change	Contextual Factors	Stakeholders affected	Costs / Benefits
Licensed outlets - Purposefully designed. - Limited density & trading hours. - Trained staff.	Increased licit market	Price Taxation Monitoring & Enforcement	Users State Families Young people	Administration costs Compliance costs Fiscal revenue Public health services savings Increased enjoyment
	Decreased illicit market	Product satisfaction Enforcement	State Community Illicit dealers	Public health services savings Public nuisance decrease CJS Savings
Age controls - Minimum age of purchase: 18y	Reduce uptake by young people	Compliance Monitoring Enforcement	State Licit Retailers Young People	Public health services savings Compliance costs Enforcement costs
Marketing controls - No advertising. - Plain packaging. - Child-proof packaging.	Reduced attractiveness of the products Reduced uptake by young people	Compliance Monitoring Enforcement	State Users Young people	

9.3.3 Impact of use-related controls

Controls focused on use and the user serve two main purposes when discussing a strictly regulated NPS market:

1. encouraging safer use; and,
2. limiting consumption, especially among the young.

Safer and responsible use would be promoted through restrictions on disorderly conduct and potentially harmful behaviour, such as driving or using heavy machinery under the influence, as well as targeted public information campaigns.

Table 5. Hypothesised Impact on Use

Control Measures	Hypothesised behaviour change	Contextual Factors	Stakeholders affected	Costs / Benefits
Licensed purchases **- Basic registration** **- Safety/Liability Waiver form**	Encourage safer use Reduce consumption Reduce diversion	Enforcement	Users State Society Young people	Administration & compliance costs Fiscal revenue Public health services costs Increased enjoyment CJS savings
Purchase/possession limits			Users State Young people	Public health services savings Enforcement costs Increased enjoyment
Laws on disorderly conduct	Discourage [public] use Reduce consumption		Users State Young people	
Restrictions on potentially harmful behaviour	Reduce accidents & fatalities		Users Society State	
Targeted information & awareness campaigns	Encourage safer use		Users Society State Young People	Implementation costs Public health services savings

9.4 Concluding Remarks

Whilst the development and consumption of substances which fall outside of the UN conventions is not strictly a new phenomenon, the sheer number of new substances which have been brought to market in the last decade or so marks a significant shift in both the nature of the market and consequently in the challenges posed to policy makers. The seemingly inexorable rise of the market for new psychoactive substances asks difficult questions of policy makers, who have traditionally responded to the use of recreational psychoactive substances (other than alcohol) with an iron fist.

The emergence of the internet as an easily available and anonymised market-place for the buying and selling of (often illegal) drugs, is just one example these changes. The internet has also enabled manufacturers and suppliers of NPS to remain one step ahead of legislation, as they are able to search the online scientific literature for potential new substances, and then market and sell their products with relative ease, all whilst remaining within the law.

Becoming frustrated at the apparent increase in the threat to public health, governments worldwide have reacted to reduce the size of their domestic market for NPS. Governments which have attempted to deal with the problem using various systems of reactive prohibition have failed to reduce the harms or the size of the market, and have therefore failed to have the impact they had hoped for. In most cases, it is clear that the vast but often hidden costs accruing to the prohibition of recreational drugs, far outweigh the apparent benefit.

The market for NPS has largely been created by the inadequate and harmful policies of prohibition. NPS policy needs to be designed with the realities of demand for psychoactive substances in mind. Policies should be designed to encourage the use of substances known to have low risk profiles in preference to more harmful substances or ones with unknown risk profiles. These known low risk drugs could be either traditional psychoactive substances or novel substances, which have undergone rigorous safety trials.

Instead of seeing the rise of the NPS market as a threat to health, and as an increased burden on an already cumbersome, ineffective and expensive global drug regime, it should be seen as an incentive to create a new international drug regime that provides legal markets to low risk psychoactive substances. The model proposed in this report is just one option, based on the New Zealand model, but even more important in our view is the formation of strictly regulated markets for the legal access to cannabis, MDMA and certain psychedelics, the provision of which would greatly lessen the demand for new psychoactive substances.

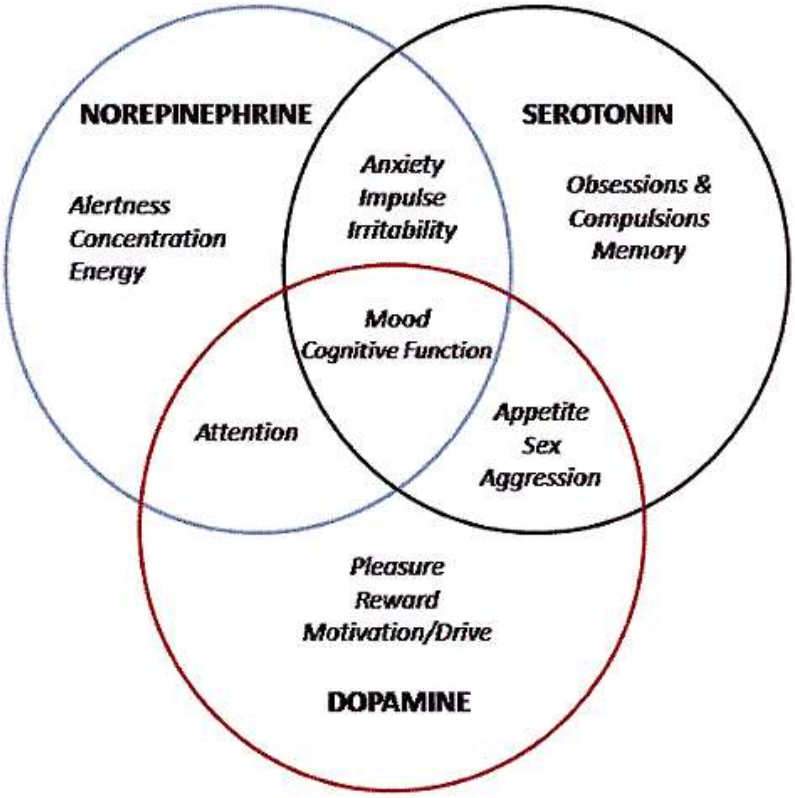
APPENDIX

Mephedrone Prohibition: A UK Case Study

In 2009, mephedrone was a legally available NPS in the UK and growing in popularity amongst clubbers. Mephedrone's rise to popularity was due to the combination of its legality and availability with the sharp decline in quality of MDMA/'Ecstasy' (72, 73). In 2010, increased media attention led to hurried policy action that may have produced more harms than benefits.

Mephedrone is one of the most commonly used NPS. According to the Crime Survey of England and Wales 2015 1.9% of people aged 16-24 have used it in the past year. 71% of mephedrone users tried it once or twice per year, so the number of frequent or problematic users is quite small compared to other drugs (19).

Mephedrone is a synthetic cathinone, similar in structure to the stimulant found in khat (the leaf from the *Catha edulis* plant) that has been chewed recreationally in East Africa and parts of the Middle East for centuries. In the brain, mephedrone acts on the three monoamine neurotransmitters (dopamine, serotonin, and norepinephrine, see below), increasing their availability with potencies comparable to MDMA.



Source: Deplin, http://www.deplin.com/LifeWithDepression/Causes (74)

Mephedrone produces relatively short-lasting stimulant effects, between those of MDMA and cocaine (75). The desired effects are increased confidence, euphoria, concentration, sociability, and wakefulness. Common side effects include excessive sweating, headaches, palpitations, nausea, bruxism (teeth grinding), suppressed appetite, and insomnia (76, 77).

In 2010, after two people were reported to have died from taking the substance, media attention turned to its easy availability and increasing popularity[35]. However, statistics for deaths with positive *post mortem* toxicology results for mephedrone painted a complex picture. In 87% of the deaths recorded in the National Programme on Substance Misuse Deaths (NPSAD), mephedrone was ingested with other substances. Moreover, in 60% of those deaths where mephedrone was present in toxicology reports, the cause of death cannot be attributed to mephedrone alone (79). The primary cause of death was accidental poisonings (63%), followed by suicide (mainly hanging) and high risk behaviour (driving or swimming). Some of the suicides were committed by people with a previous history of depression. These deaths highlight the fact that stimulants lower inhibitions and judgment, and reflect the dangers of ingesting drugs in combination with other substances and by people with pre-existing psychiatric vulnerabilities (80).

As a result of media attention on mephedrone-related deaths, the Government's Advisory Council on the Misuse of Drugs (ACMD) was asked to produce a report and to make a recommendation on how best to respond to the emergence of mephedrone. The report recommended the scheduling of mephedrone as a Class B Controlled Substance along with cannabis and amphetamines, with penalties for up to 5 years imprisonment for possession and 14 years for supply (81). The classification was announced hurriedly in a press conference that day, by the then Home Secretary, Alan Johnson.

It looked like a sensible, harm-reducing decision was taken, on the advice of the relevant scientific body, to ban a dangerous substance that had been linked to several deaths. This narrative is powerful because it is mostly true, and also fits well with the familiar argument that if something is potentially harmful it should be banned without further question.

This is not, however, a fair representation of what happened.

Eric Carlin (a member of the ACMD at the time that the draft report on mephedrone was being discussed, who later resigned in protest at the decision) writes of the decision-making process "[the ACMD] did not have sufficient evidence… to help us judge harms" (82). The report was carried out "without adequate consideration of how and why young people use this drug", and was "partially considered and inadequate". The ACMD was "unduly pressured by media and politicians to make a quick, tough decision to classify". This limitation is even acknowledged within the report itself, where it is stated in the introduction: 'There are no formal pharmacokinetic and pharmacodynamic studies on mephedrone. There are no published formal studies assessing the psychological or behavioural effects of mephedrone in humans. In addition, there are no animal studies on which to base an extrapolation of potential effects.'

The council decision was based largely on the impact that mephedrone had on the media and the consequent political and public pressure to ban it that this created. Toxicology examinations later showed that most of the deaths initially reported to have been the result of mephedrone were, in fact, not caused by mephedrone (80). Not only was the decision-making process woefully inadequate and biased towards prohibition, but, as is often the case, the decision itself was one that had its own harmful (though largely ignored) consequences.

[35] Ironically, a subsequent spike in use has been linked to this heightened press coverage (78).

Since 2008, a significant number of cocaine users instead chose to take mephedrone. In 2010 in England and Wales, the percentage of 16 to 24 year olds using mephedrone had *increased* to 4.4%, whilst the percentage using cocaine had *dropped* from a 2008/2009 peak of 6.6% to 4.4% (83). Despite rates of use being the same for each substance, there were 6 deaths in the UK where mephedrone was mentioned on the death certificate compared to 144 where cocaine was mentioned. Dr Les King concluded in a blog post for the Independent Scientific Committee on Drugs, that mephedrone had a significantly lower toxicity than cocaine, and that the substitution effect which encouraged people to swap cocaine for mephedrone was likely saving the lives of dozens of people who otherwise would have died from the fatal toxicity of cocaine (84). Once the ban came into force, it is thought that many users switched back to cocaine. Deaths involving cocaine increased steadily in the 1990s and 2000s, peaking in 2008, before declining between 2008 and 2011. Cocaine-related deaths in 2014/15 rose to 247 - up from 169 in 2013 (85).

The failure of the decision-making process to take into account the wider impact of the decision to ban mephedrone, may therefore have translated into a larger loss of life than would have been the case if it had not been banned. In terms of reducing harms from mephedrone use and scoring political points, this classification was a success, but in terms of reducing aggregate harms, the UK mephedrone ban was almost certainly a failure.

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