Getting up to speed with the public health and regulatory challenges posed by new psychoactive substances in the information age

There is a need to review the various regulatory options that are available in order to address the challenge presented by a plethora of new psychoactive substances appearing on the market as well as to address the technology for rapid development and marketing of new ones.

Until about a decade ago, most new psychoactive substances that emerged were typically sold on the illicit market. They were usually produced in clandestine laboratories and called ‘designer drugs’, or were sourced from diverted medicines. This continues to be the case, with some of these drugs simply acting as temporary substitutes—often unknown to users—for established controlled drugs that are in short supply, such as 3,4-methylenedioxyn-N-methylamphetamine (MDMA). The sale of new drugs on an open market, beginning with 1-benzylpiperazine (BZP) and methylene, followed by mephedrone, marked the start of what is now called the ‘legal highs’ market.

We now know that many new drugs that are destined for the ‘legal highs’ market are produced in bulk in China and India and imported into Europe and elsewhere, where they are processed, packaged and sold. The marketing and distribution of these drugs has reached a new level of sophistication, including advertisement and sale on the open market, such as through the internet (with delivery via courier and postal services), as well as ‘head shops’ in towns and cities. They may also sold by street-level drug dealers [1].

Addiction has drawn together a collection of papers that have been published over the last few years, as a virtual issue1 which considers the challenges presented by these new psychoactive substances.

Only a few years ago the issue of the ‘legal highs’ market was regarded as an area of limited significance. Things change rapidly, however, and today the question of how to respond to the challenges posed by the emergence of new drugs has become one of major international concern [2]. The papers begin the task of elaborating the policy challenges we now face, particularly in relation to public health and regulatory responses. Before introducing them, however, it is worth taking a brief moment to reflect upon why these things have come to pass, and in so doing ground this virtual issue within the wider social and contextual factors that not only help to shape contemporary patterns of substance consumption but also impact upon almost all other aspects of our modern life.

Posting on an internet discussion forum on 26 September 2006, Mexican Seafood noted that some of his, or possibly her, friends had been smoking a herbal mixture called ‘Spice’ that was, by all accounts, surprisingly impressive. The post contained a list of the 14 herbal constituents it was claimed to contain and sought advice on their provenance. This was swift in coming, with MadScientist claiming early the next day that none of these substances contained CB1 agonists and that laboratory testing had not revealed any cannabinoids to be present. It was further speculated that the product might contain ‘additional active compounds as there were many legal and structurally distinct CB1 agonist available’. This post was followed within hours by claims from Shamantra that ‘Spice’ contained the synthetic cannabinoid HU-210 and speculating that none of the herbal substances claimed on the labelling were likely to be present. It was also noted that the effects were similar to, but longer-lasting than, hashish [3].

While not the first online discussion relating to ‘Spice’, the excerpts above are examples of how modern communication has impacted upon drug use trends [1]. It also serves to highlight the speed at which developments can now occur in the drugs field and by contrast how lumbering remain our efforts to track them. To put these posts into historical perspective, it was only in December 2008 that three synthetic cannabinoids, JWH-018, CP-47 497 and its active homologue, were identified in ‘Spice’ products [4]. Addiction was among the first journals to open the scientific debate on this topic, and by the time the editorial on ‘Spice’ products was published in 2010 nine synthetic cannabinoids had been reported to the European Union. Early warning system on new psychoactive substances [4]. By June 2013, more than 80 synthetic cannabinoids2

1The virtual issue can be viewed at http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1360-0443/homepage/the_legal_and_public_health_response_to_novelpsychoactive_drugs.htm
2The term ‘synthetic cannabinoids’ is used here to include synthetic cannabinoid receptor agonists (such as JWH-018 which is a CB1 and CB2 receptor agonist), allosteric modulators (such as Org 27569) that change the structure of the cannabinoid receptors leading to altered activity when a ligand binds to the receptors, and substances that act as inhibitors of the fatty-acid amide hydrolase (FAAH), which catalyses the intracellular hydrolysis of the endocannabinoid anandamide (such as URB597).
from 13 different chemical groups had been reported and, overall, more than 280 new drugs are currently being monitored by the Early warning system [5]. This total also includes phenethylamines, tryptamines, piperazines, synthetic cathinones and a range of other substances, such as medicines and their derivatives, that do not fit into the other chemical classes. Moreover, the emergence of new drugs has now been reported in most parts of the world [6].

With hindsight, these developments should not have been surprising. The twin engines of globalization and the new opportunities provided by developments in information technology have transformed many aspects of the modern world. They have profoundly changed how we work, communicate and play. Commerce and communication are no longer constrained by physical or geographical boundaries as they once were. Goods and ideas flow more quickly and more freely, and regulations and social control mechanisms of all description struggle to find traction in a world of open markets and unconfined communication, and unclear jurisdictions. This has meant that the back catalogue of pharmaceutical and medical research industries are easily accessible to those wishing to identify substances whose psychoactive potential may make them attractive, that new trends diffuse more rapidly, and a market-place for psychoactive substances has been created that exists, to a large extent, outside the established regulatory frameworks. The end result of all this is that the model on which drug control policies have been based historically appears to be, if not broken, then at least in serious need of repair. Existing national legislative approaches intended to restrict the illicit supply of a relatively limited number of substances increasingly appear poorly configured to meet the challenge posed by a global market place that is not only difficult to control but can also react rapidly to counter legal changes by simply producing new drugs [1].

Many of the papers and correspondence in this virtual issue address this issue of regulation. This reflects the fact that this new market is defined largely by the production of substances that are intended to fall outside the international drug control conventions and national legislation. It also reflects, however, the simple reality that until now we have very few empirical data to draw upon in this area to inform us about the implications of these changes. This is beginning to change as researchers start to explore the epidemiological issues and harms associated with the use of new drugs.

This is reflected in the virtual issue by a warning from Every-Palmer that synthetic cannabinoids such as JWH-018 may precipitate psychosis in vulnerable individuals [7]. This was a timely warning of an association that has subsequently been reported clinically [8]. It also speaks to the fact that synthetic cannabinoids are a diverse group of compounds about which we know very little with respect to either their acute or chronic toxicity. It would be naïve to assume that, just because products containing synthetic cannabinoids are sold as ‘legal’ replacements for cannabis, and contain substances that target some of the same receptor sites in the brain as Δ9-tetrahydrocannabinol, the health consequences of consumption will be necessarily analogous. Indeed, the case-series of acute intoxications by Hermanns-Clausen et al. suggest worrying associations with the use of these drugs and serious adverse events such as seizures and loss of consciousness [8]. These concerns must surely be amplified by the fact that not only are we seeing the emergence of more potent synthetic cannabinoids (at least in vitro) but also synthetic cannabinoids not described previously in the literature and on which we have no data [5].

The virtual issue also contains two papers that are among the first published exploring the subject effects and health risks of mephedrone [9–11], a drug that in a few years has gone from being virtually unknown to, in some countries at least, a commonly used stimulant on the illicit drug market [12]. Mephedrone was also the first synthetic cathinone to come to widespread attention, although it has now been joined by other drugs from this group, notably 3,4-methylenedioxyxypyrovalerone (MDPV) and 4-methylethcathinone (4-MEC). These papers help to illustrate why some substances have the potential to prove attractive to users and become established drugs in their own right, even competing successfully with stimulants such as cocaine, ecstasy and amphetamine. This is important for understanding their probable long-term public health impact, which will be mediated by the intrinsic properties of the drug, patterns and modes of use, availability, as well as population prevalence.

The fact that mephedrone has, to some extent, made the cross-over from ‘legal high’ to a drug of choice for some on the illicit market also provides an interesting backdrop to the papers and correspondence in this virtual issue that wrestle with the costs, benefits and unintended consequences that may arise from the different regulatory options for these new substances [13–22].

The appearance of new drugs is not a new phenomenon [23–26], yet in the past few years we have seen an unprecedented growth in their number, type and availability [1,5,27]. The scientific and patent literature, along with the ingenuity of chemists involved in the trade in new drugs, means that thousands more are possible [28]. Moreover, new drugs are also being marketed to broader groups beyond the traditionally targeted populations, such as psychonauts and clubbers, that have been studied in the past [29]. This includes problematic drug users who are injecting drugs such as
mephedrone [30,31] and life-style users who are sold new drugs often disguised as ‘food supplements’. These include 1,3-dimethylamylamine (DMAA), which is sold as a ‘pre-workout booster’ for gym-goers [32,33], and phenibut, which is marketed online as a veritable panacea that ‘improves mood, induces relaxation, enhances sexual desire’ [34]. It is important to note in this respect that γ-hydroxybutyric acid (GHB) began its recreational life as a ‘food supplement’ marketed to bodybuilders and life extensionists as a growth hormone releaser with the hope that it would build muscle, strip fat and turn back the clock [35,36].

Some new drugs appear to have a limited potential for diffusion, but they may still cause serious harm. A recent example of this was 5-(2-aminopropyl)indole (5-T; 5-API), associated with 24 deaths in four European countries over a 5-month period [37]*. Other new drugs may gain a foothold and diffuse to wider populations, posing significant public health and social harms [38]*. Stakeholders, including policy makers, practitioners and researchers, will increasingly need access to timely evidence-based information on new drugs, trends in their use, the harms they may pose and policy responses in order to take appropriate measures to minimize the harms. Alongside early warning systems [39]*, it will be essential that multi-disciplinary research, along with the rich analysis and debate that this often brings, continues to inform and shape the response to new drugs.

Declaration of interests

None.

PAUL GRIFFITHS, MICHAEL EVANS-BROWN & ROUMEN SEDEFOV

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), Lisbon, Portugal. E-mail: paul.griffiths@emcdda.europa.eu

References*


*The reference list was corrected on 22/07/2013 after original online publication 19/07/2013. A new reference (Measham et al.) has been inserted to replace reference 29. The reference which was 29 is now 37; the reference which was 37 is now 38; the reference which was 38 is now 39.