

Feature

Drugs: blanket ban or harm reduction?

As the commercial success of electronic cigarettes offers the opportunity to study harm reduction by replacement therapy, the UK government steers in the opposite direction and plans to expand the 'war on drugs' with a blanket ban on all psychoactive substances. **Michael Gross** reports.

The streets of London and other cities, along with summer music festivals, have recently witnessed a booming trade with balloons. Rather than with air or helium, these are filled with nitrous oxide, also known as laughing gas. Street traders can buy the gas in capsules available for cream dispensers, fill it into balloons and sell them for £3 to revellers in search of a bit of chemically-induced hilarity.

While the use of laughing gas appears to have been a growing fad last summer, it is by no means a new phenomenon. Medical students and members of the aristocracy used the gas to lighten up their parties over 200 years ago, and even the use of balloons for this purpose goes back to the 1970s.

The gas is known to be harmless, which is why it is commercially available for food production and widely used as an anaesthetic in childbirth. Fearless reporters who have tried the balloon-dispensing method in the street describe the resulting high as "barely there" with no consequences. The very few people who died after experimenting with industrial quantities of nitrous oxide were the victims of a lack of oxygen (and excess stupidity) rather than a psychoactive substance. So inhaling the gas from balloons is just harmless fun that nobody can argue with, right?

The UK's new Conservative government has announced new legislation to ban all psychoactive substances as a matter of principle, with specific exceptions made for established trades like coffee, alcoholic drinks, and tobacco. Intended to break out of the race against the creative development of new 'legal highs', the draft bill debated in the House of Lords on June 9th would ban entirely harmless diversions, like breathing in laughing gas, along with everything else that influences our minds.

More importantly, the plan undermines all plans for harm reduction in the drugs field, a strategy favoured by neuroscientists like David Nutt. The current commercial breakthrough of electronic cigarettes, or e-cigarettes, could provide a model of how drug replacement could work and what kind of scientific information would be required to ensure its success.

A new age of steam

Invented in China and first patented in 2003, e-cigarettes have become a major commercial success in recent years after manufacturers gave up the attempts to make them look like real cigarettes and offered opportunities to fine-tune the inhalation experience. They all include a battery-powered heating element that vaporises a liquid containing the nicotine and additional flavours. Modern ('third generation') vaporisers tend to be elaborate refillable devices with transparent tanks and a variable power setting.

Legislators, health officials and science have been left trailing behind as the e-cigarette boom took off. So far, legislation around the world varies chaotically from total bans to complete absence of regulation. The issue is complicated by the fact that two powerful economic interest groups — the tobacco and the pharmaceutical industries — offer competing products, but could be tempted to enter the market themselves. Thus, they may lobby governments against or for e-cigarettes depending on whether or not they have decided to engage with the new technology. There is very little product standardisation, and science is only just beginning to explore the potential of the devices for smoking cessation and their own risks.

In principle, the expectation is that smokers can reduce their risk exposure significantly by switching from the tobacco-burning to the

vaporising kind of nicotine intake. This is simply because most of the damage that smoking does is not due to the nicotine as such but to the tar-like condensation products that smokers inhale with the smoke and that settle in the airways. These condensates contain the substances that cause cancers and heart disease. By contrast, the electronic version does not involve any combustion and no chemical reaction with unwanted side products. What people breathe in is the mixture of chemicals that is in their liquid tank, so as long as those are safe, the process should be safe. One study that found dangerous levels of aldehyde in e-cigarette steam (N. Engl. J. Med. (2015) 372, 392–394) was recently shown to rely on unrealistic conditions (Addiction (2015) <http://dx.doi.org/10.1111/add.12942>). While it is possible to produce this result, the associated 'vaping' experience would be sufficiently unpleasant to ensure that users don't get exposed to these aldehydes.

Based on the general assumption that smoking-associated harm mostly originates from combustion products and on the first emerging studies of e-cigarette safety, experts have



Laughing Gas.

Laughing gas: After two hundred years of use, the UK government plans to ban the use of laughing gas for fun, although it remains legal in whipped cream and during childbirth. This line engraving by W. Cooke after John Haygarth was published in the *Gent's Magazine* in 1827. (Image: <http://wellcomeimages.org/>)



Building steam: Electronic cigarettes have seen a remarkable commercial success in recent years. Their usefulness in smoking cessation remains a subject of debate but offers the opportunity for scientific investigation into harm reduction by drug replacement. (Photo: TBEC Review.)

estimated that harm reduction will be at least 95% compared with the uptake of the same amount of nicotine through conventional smoking. Thus, encouraging smokers to switch could save many thousands of lives.

Critics of this assessment have expressed concern that the increasing visibility of e-cigarettes might encourage people who have never smoked to take up the electronic habit, such that their additional risk exposure would have to be balanced against the risk reduction of smokers switching. Given the arithmetic, however, it would take 20 non-smokers to take up e-cigarettes for every smoker who does to wipe out the benefits. Recent surveys show that there are hardly any users who come from the non-smoking side, so this fear appears to be unfounded at the moment. Advertising will of course have to be regulated to ensure that the industry does not try to entice children.

The small residual risk of e-cigarettes is still an open field for research however, as a recent conference of the American Thoracic Society has shown, where a number of presentations covered preliminary investigations into the effects of vaping (<http://conference.thoracic.org/2015/>). One study, for instance, showed that the vaping exposure corresponding

to the smoking of a single cigarette reduced the sensitivity of the cough reflex in an assay which uses an aerosol of capsaicin — the pungent substance in chilli peppers — to trigger coughing. Another presentation at the conference warned that the variability of device design and vaporisation conditions makes the medical effects unpredictable, as parameters such as coil temperature critically influence the composition of the vapour.

Standardisation of such parameters will be an issue when legislators catch up with the burgeoning popularity of vaping. The government of Wales has recently announced a ban of vaping in enclosed public places, which has been criticised as disproportionate, given the low level of potential harm to users and bystanders. Other legislators, including the European Commission, are also reportedly preparing regulatory measures which may include the classification of solutions with high concentrations of nicotine — more than 20 mg/ml, such as smokers would use as a help in giving up — as medical products, which would then be subject to much tighter regulations than simple consumer products.

As public opinion is still in flux, research remains in its infancy, and legal frameworks still need to

be written, it is unclear whether e-cigarettes will eventually make a big contribution to further reduce the prevalence of conventional smoking and its associated health problems. There appears to be a unique opportunity for science to study and accompany a large-scale drug replacement that users undergo voluntarily. Fundamental questions of drug addiction, such as what part of the behaviour is caused by the actual substance and what part by the social context, could be more easily studied with e-cigarettes, where the exposure is readily tuneable.

They could also serve as a model for the handling of other drugs that cause health issues. For instance, neurobiologist David Nutt, former drugs advisor to the UK government, has long argued to classify drugs on the basis of the actual harm they cause and to make harm reduction the guiding principle of drugs policy. In his research at Imperial College London, he is investigating safe alternatives to alcohol.

Reduce no harm

At this crucial junction in the history of drug use, as large-scale harm reduction appears to be within reach, the new UK government has stunned observers by storming off in exactly the opposite direction. Within weeks of coming to office, it proposed a new law that will impose a blanket ban on all substances that might in any way “affect the emotional state” of a user.

Under the Psychoactive Substances Bill, first debated in the House of Lords on June 9th, production, sale and provision (although not possession) of all psychoactive substances will be banned, with exemptions made only for specific product groups including alcoholic drinks, coffee, and nicotine, as well as for medicines and homeopathic products.

The draft bill has been widely criticised for its sweeping definitions, which risk banning all substances that could provide any kind of harmless pleasures. The text defines psychoactive substances as follows: “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. 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."

Several observers have argued that this definition includes activities like smelling the fragrance of a flower or using any other product that evokes a mental response by its smell. The barrister and blogger Matthew Scott has argued in the *Daily Telegraph* that: "Any substance which gives pleasure, of course, 'affects a person's emotional state'. The starting point of the Bill is that giving pleasure is sufficient justification for prohibition."

Psychoactive substances as defined by the bill lurk everywhere in our daily lives. "Butane gas, glue, petrol and some cleaning fluids have all been used for their psychoactive properties. As a result, the law as currently drafted will render their sale illegal. Indeed the Bill's artificial definition of the word 'consumption' to include inhaling 'fumes' could have been designed to criminalise petrol station operators and hardware stores," Scott notes. Ironically, e-cigarette refills with nicotine would be legal under the bill (due to the exemption for nicotine products, as long as they don't contain any other psychoactive substances), while those without might be banned from sale.

Robert Winston from Imperial College London called the draft bill "ludicrous" and "a thoroughly bad bill". The entrepreneur Richard Branson, who has engaged with a global campaign to stop the futile 'war on drugs', called the draft bill "an astonishing example of the continued madness of the drug wars" and concluded: "If our goal is to keep our children out of harm's way, the Psychoactive Substances Bill will achieve the opposite effect."

David Nutt has expressed his concern that the additional prohibition measures could further hamper brain science in the UK, adding to the severe limitations already imposed by the existing prohibition of the Misuse of Drugs Act 1971 (Curr. Biol. (2013)



Altered emotions: Under the UK government's proposed Psychoactive Substances Bill any product emitting a smell that affects our emotional state qualifies as a psychoactive substance, except if it serves as food or medicine. Strictly interpreted, that definition would include products like fragrant flowers, candles, air fresheners, and many of the things on display in this shop. (Photo: Cha già José.)

23, R585–R588). Amanda Feilding, director of the Beckley foundation, which supports medical research into psychoactive drugs, also expressed this concern.

Moreover, the overall direction of the bill is the exact opposite to the rational strategy of treating drug misuse as a medical problem and scaling responses according to the actual harm that drugs do, with the overall aim of harm reduction, as favoured by scientific experts including Nutt and Feilding. The root cause of the explosive growth in new, untested 'legal highs' is in the fact that well-known and relatively benign substances, including cannabis, are widely prohibited. A legalised and regulated supply of mild drugs, as is currently emerging in several US states including Alaska, Washington, Oregon and Colorado, as well as in Uruguay, would remove much of the incentive to play catch with the law by developing new substances.

At the first parliamentary debate on the bill, held in the House of Lords on June 9th, Lord Paddick from the Liberal Democrats criticised the draft bill severely and outlined the alternative: "We believe that there should be a health-based approach, aimed at reducing harm caused by

drug misuse, rather than a legalistic approach that is likely to further criminalise drug users. Successive governments have gradually eroded the link between criminal penalties and the harm caused by drugs by ignoring the scientific evidence and the advice that they have been given, to the extent that the drug laws in the UK are no longer considered by many people to have any credibility."

The clearest evidence that the government is blissfully unconcerned with the evaluation of actual harm that drugs do is its explicit inclusion of laughing gas in the prohibitions of the law. This inclusion clearly supports Scott's assertion that UK home secretary "Theresa May wants to ban pleasure". One could dismiss the bill as an obviously ridiculous fantasy of politicians removed from science and reality, but the unintended consequence of the bill, if it becomes law, will be that more people will get their (no longer legal) highs from criminal traders and run a higher risk of dying from tampered or mislabelled products. And this will be no laughing matter.

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