

The new danger of synthetic drugs

A wave of novel drugs designed by chemists has travelled around the world, and policy makers have struggled to keep up with the threat. Carrie Arnold investigates.

17-year-old Henry Kwan died this June after jumping off a balcony. The teen from Sydney, Australia, had taken a synthetic form of the hallucinogen LSD and thought he could fly. It's the latest high-profile case of death following the use of a synthetic drug. The drugs, which are generally created in a laboratory as derivatives and analogues of a parent drug like cathinone or cannabis, have shown a startling rise in popularity over the past few years to become some of the most common misused substances.

Governments around the world are responding to the growing threat of synthetic drugs by banning their import, sale, and use. The problem, experts say, is that the laws are frequently on the side of the chemists developing these drugs. One small tweak, a single molecular change, and an illegal synthetic drug can suddenly become legal again. Increasing usage of these so-called legal highs, combined with an awareness of acute and chronic health effects, has left drug enforcement officials with knowledge of these drugs' dangers but no real way to ban them. But a few new ways of conceiving drug laws might start to have an effect on the ease with which these drugs can be found.

The problem of new synthetic drugs is reflected in the UN drug office's 2013 annual report released last week and the 2013 European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) Annual Report, released in June. The European Union (EU) seized 73 new types of synthetic drugs in 2012, compared with just 49 in 2011.

"Entrepreneurs are combing through the scientific and patent literature and picking the substances that aren't controlled by existing

laws. They're having them manufactured in countries such as China or India, and then ship them to the EU or the USA, where they're processed and packaged into a legal high", Michael Evans-Brown, a scientific analyst on the Action on New Drugs Team for the EMCDDA, tells *The Lancet*.

"People think that because they're legal, they must be safe'..."

These synthetic drugs fall into three broad categories: synthetic cathinones (known commercially as bath salts), synthetic cannabinoids (known as spice or incense), and synthetic amphetamine-like drugs. The cathinones and amphetamines are both stimulants and have similar effects. The most common signs of use are dilated pupils, hypertension, hyperventilation, paranoia, agitation, and hyperthermia. Synthetic cannabinoids have many of the same signs, as well as tremors and seizures.

This list of signs and symptoms, however, is at best a guess, says toxicologist and accident and emergency physician Jane Prosser of Weill Cornell Medical College in New York City, USA. "Something like synthetic cathinones is actually a broad range of compounds, so it's difficult to identify specific effects."

Nor does the drugs' packaging give much information as to what people are actually taking. The sachets look harmless, even fun. With names like Spice, K2, and Benzo Fury, they appeal to a youthful crowd, especially those that frequent nightclubs. Their status as a legal high probably adds to their appeal, says Les Iversen, a retired pharmacologist and current

chair of the UK's Advisory Council on the Misuse of Drugs. "People think that because they're legal, they must be safe", explains Iversen.

To officials in the UK, synthetic drugs did not trickle onto the scene. "The drugs started to appear at music festivals in the UK in the summer of 2009, and we started to see them becoming more and more popular. We recommended that the government make these illegal in April, 2010", Iversen says. "But by then, the drugs had become very firmly embedded in the drug culture."

Concern quickly followed the growing use of these drugs. One of the most attractive features to users was that these drugs were generally legal. Sold at petrol stations and convenience stores, sellers referred to the drugs as plant food or bath salts to avoid legal ire. The sachets also said that their contents were "not for human consumption".

"We need to stop pretending that these drugs are not for human use when we know that's what they're being produced for", Iversen says.

The most recent national statistics on synthetic cannabinoid use among young people in the USA, published

See [Editorial](#) page 1

For the [2013 UN World Drug Report](#) see <http://www.unodc.org/wdr/>

For the [EMCDDA report](#) see <http://www.emcdda.europa.eu/news/2013/6>

For the [US National Institute of Drug Abuse statistics](#) see <http://www.drugabuse.gov/related-topics/trends-statistics/monitoring-future>

For the [informal survey of UK club-goers](#) see <http://www.mixmag.net/words/features/mixmags-global-drug-survey-the-results>



Legal high packaging can look harmless and state "not for human consumption"

in December, 2012, by the National Institute on Drug Abuse, found that 11.6% of teens had used the drug within the past year. Synthetic cannabinoids were also responsible for 11 406 visits to hospital accident and emergency wards, and three-quarters of these visits were by young people aged 12–29 years. Aside from regular marijuana, synthetic cannabinoids were the most common drug used in this group. More detailed analysis revealed that males were twice as likely to use these drugs as females. Reported rates of bath salt use among young people are much lower—at about 1–3%.

Although formal epidemiological studies have not been published on the use of synthetic drugs in the EU and UK, anecdotal evidence suggests that synthetic cathinones are more popular there than synthetic cannabinoids—the opposite of the USA. An informal survey of club-goers in the UK found that 61% had used synthetic cathinones in the past month.

The sudden rise in the popularity of such synthetic drugs is matched with data from poison control centres and toxicologists about health risks from overdose and chronic use. The American Association of Poison Control Centers reported a 20-fold increase in calls about bath salts between 2010 and 2011. In 2012, the AAPCC reported 2656 calls about bath salts and 5205 calls about synthetic cannabinoids.

Treating these overdoses and toxic side-effects is clinically very difficult, Prosser notes. “It’s tough as a clinician because even if you do believe the patient is being honest with you, they don’t always know exactly what they’ve taken”, she says. “People will come in and say they used a drug, but they really have no idea.”

In March, 2011, the US Government became so worried about the rapid increase in synthetic drug use that the federal Drug Enforcement Agency (DEA) used its emergency powers to place five synthetic cannabinoids on

its Schedule I list of substances, which makes the manufacture, distribution, consumption, or possession of these drugs illegal unless specifically authorised to do so. In October of that year, the DEA also added five synthetic cathinones to that list. According to the National Conference on State Legislatures, 45 states have subsequently banned some type of synthetic drug as of December, 2012.

“It’s tough as a clinician because even if you do believe the patient is being honest with you, they don’t always know exactly what they’ve taken’...”

In June, 2012, the US Congress passed the Food and Drug Administration Safety and Administration Act. Tacked on to the end of that bill was the Synthetic Drug Abuse Prevention Act of 2012, which banned synthetic cannabinoids, methylenedioxypyrovalerone (MDPV), and mephedrone, the latter of which are synthetic amphetamines frequently found in bath salts. The bill became law in July, 2012, when it was signed by President Barack Obama.

What makes this bill unique—and a potential role model for other countries such as those in the EU—is how it bans the synthetic cannabinoids, Iversen says. “It’s really quite clever. The law says that any drug that acts on the CD1 cannabinoid receptor, which is the target for all these drugs, is automatically banned.”

Testing to see whether a synthetic substance binds to a receptor is cheap and easy. A technician can do the work in a test tube. This means it will be easier to enforce the laws, Iversen says, and harder for the chemists to evade the law. They can create whatever chemical magic they want, but if their substance binds to the cannabinoid receptor, then their product is automatically illegal.

Still, not everyone in the USA thought highly of the law. Even

before President Obama signed the bill into law, DEA officials were saying the bill didn’t go far enough. They wanted more synthetic substances added to the list. Additionally, drug possession and sales laws are determined at the state level, meaning that every state would have to develop adequate legal measures to give federal bans teeth.

Other countries, including New Zealand, Australia, and Japan, have also banned the drugs. They remain controlled substances in the UK. Besides banning the drugs outright, Simon Gibbons, a medicinal phytochemist at University College London, UK, notes several other tactics that can be used to help stem the tide of synthetic drug misuse. He advocates the education of young people as well as stricter advertising standards that will control how synthetic drugs are marketed. “Because these drugs are generally legal, we don’t have a basis to stop their import or sale”, he says.

Although long-term data for the addictive potential of these drugs remain scarce, researchers believe that users can readily become addicted to new synthetic drugs. The proliferation of treatment programmes and rehabilitation facilities specifically targeting users of these drugs would indicate this. Prosser also notes that the parent drugs are potentially addictive, which means that these newer synthetic derivatives are as well.

To truly combat this problem, lawmakers will have to develop novel types of legislation that can keep up with the pace of new drugs arriving on the market. These pieces of legislation will require scientists and policy makers to rethink their approach so they’re not merely responding to the creation of new synthetics. The drugs seem to be here to stay, and new policies are just beginning to catch up.

Carrie Arnold