Neurochemical Approach to Scheduling Novel Psychoactive Substances in the United States

This project was supported by Grant No. G1399ONDCP03A, awarded by the Office of National Drug Control Policy. Points of view or opinions in this document are those of the author and do not necessarily represent the official position or policies of the Office of National Drug Control Policy or the United States Government.

Introduction

New novel psychoactive substances (also known as synthetic designer drugs) are being marketed and sold in cities, towns, and counties across the United States. These substances are not necessarily controlled under U.S. federal or state law but are designed to mimic the effects of illegal drugs. These substances fall into one of several categories – synthetic cannabinoids, those substances that mimic or purport to mimic the effects of marijuana; substituted cathinones, those substances that mimic or purport to mimic the effects of cathinone and methcathinone based drugs; and other synthetic substances, a catchall category for those synthetics which may be hallucinogenic, narcotic, psychedelic, or stimulant substances and do not fall into one of the other two categories. These substances have been known to cause increased heart rate and increased blood pressure (which may lead to heart attacks and strokes, chest pains, nosebleeds, and sweating), agitation, anxiety, nausea, vomiting, tachycardia, tremors, seizures, hallucinations, paranoid behavior, and non-responsiveness.

In most cases, the chemicals that make up these substances are shipped into the United States from countries overseas, notably South and East Asian countries. Law enforcement has identified four main countries where novel psychoactive substances are synthesized – China, India, Korea, and Pakistan. They are easy to obtain via the internet, and are typically shipped directly to the distributor or ordered by the distributor or users via the internet.

Most retailers sell these products in small doses in foil packets which are designed to attract teenagers and young adults. Synthetic cannabinoids are typically leafy, while substituted cathinones and other synthetics take many forms – pill, capsule, crystal, powder, tablet, and even liquid – and are typically smoked, snorted, injected, or swallowed. Synthetic cannabinoids are now also being sold in liquid form and smoked using e-cigarettes.

Novel psychoactive substances are cheap, easy to make, and return a high profit for manufacturers and distributors. One of the major issues with these drugs is the ease with which they can be purchased. Synthetic cannabinoids, substituted cathinones, and other synthetic substances are sold in convenience stores, gas stations, "head" shops, discount beer and tobacco shops, and on the internet. Typically, these substances are sold as herbal incense, bath salts, plant food, jewelry cleaner, iPod cleaner, scratch remover, and are labeled "not for human consumption."

U.S. federal and state legislatures have made efforts to schedule novel psychoactive substances. In response to those efforts, chemists immediately reconfigured the specific substances that were prohibited to produce "new" versions of these synthetic drugs. This was accomplished by altering the molecular architecture of the chemicals used in the products to produce a series of different compounds which are closely structurally related to the prohibited substances, but which are not listed in the state or federal schedules of controlled substances laws. The National Alliance for Model State Drug Laws has found that every U.S. state and the District of Columbia have outlawed specific versions of synthetic marijuana, synthetic cathinones, or other novel psychoactive substances, but minor variations in the chemical composition of these products create similar drugs not prohibited by current legislation. The question is how best to schedule

these substances in order to prevent manufacturers from being able to simply alter the chemical structure of a substance and turn a scheduled substance into a legal one.

Different Scheduling Approaches

Neurochemical Approach

In the United States, three states, the District of Columbia, and the federal government schedule synthetic cannabinoids using the neurochemical approach, that is, by scheduling these substances according to the effect they have on the brain rather than through either the listing of specific substances or through the use of class definitions.

The United States federal government defines "cannabimimetic agents" as "any substance that is a cannabinoid receptor type 1 (CB1 receptor) agonist as demonstrated by binding studies and functional assays within any of the following structural classes . . ." The classes include: 1) phenylacetylindoles; 2) naphthoylindoles; 3) naphthylmethylindoles; 4) naphthylmethylindenes; and 5) cyclohexylphenols. The definition also includes a list of fifteen specific cannabinoids.

Iowa, Maryland, Texas, and the District of Columbia definitions mimic that of the federal definition. In each case, the statutes in question include the five classes listed above as well as a list of specific cannabinoids included within the purview of "cannabimimetic agents." As of February 2015, the statutes in each of the three states and D.C. have not been tested in the state or District appeals courts, so it is unknown whether this approach would survive legal scrutiny. [1]

At the federal level, in all of the cases that NAMSDL has been able to locate, the defendants in those cases have been prosecuted under the federal controlled substance analogue statute if the substance is one that is not specifically scheduled by statute or regulation. Therefore, it is unclear at this point what level of proof would be required to prosecute a defendant using the neurochemical approach. The assumption, based on how the statute is written, is that it would require the prosecution to prove both that the substance fell within one of the five mentioned classes and that it was a CB1 receptor type substance.

The advantage of scheduling cannabinoids using the neurochemical approach is that it could theoretically eliminate the need for continually updating the schedules of substances each time a new cannabinoid is created or introduced into the market. The disadvantages of scheduling cannabinoids using this method include, as mentioned above, the uncertainty of what proof would be required to obtain a conviction under this statute as well as potentially being limited to the structural classes specifically mentioned in the statute. That disadvantage could be overcome by either not including the classes in the definition or by including all currently known classes of cannabinoids.

[1] Please note that NAMSDL does not have access to trial court documents, so any caselaw found is from the appellate or higher court level.

Additionally, the U.S. statute is limited to the CB1 receptor. Given how industrious these drug manufacturers have been in the past, it is within the realm of possibility that chemists could adapt future substances to attach to a different receptor in the brain, thereby avoiding the statute.

Analogue Approach

Under the federal controlled substance analogue statute, prosecutors must prove that a substance is both substantially similar structurally to a Schedule I or II controlled substance[2] and that it has either a substantially similar effect on the body as a scheduled substance or that a person represents or intends to have a substantially similar effect on the body as a scheduled substance.

The problem with prosecuting offenders under the analogue statute is that there is no clear guidance on what constitutes "substantially similar." U.S. law requires that defendants have notice that their actions are prohibited by law. This does not mean a defendant must have actual knowledge that his actions are unlawful, but that the law is clear that a certain action is criminal. Therefore, prosecutions under the analogue statute are prone to challenges based on vagueness because it does not state specifically in the statute the specific substances that are illegal. Thus far, all such challenges have been overruled. However, in some cases, substances have been declared to not be an analogue of a controlled substance because of the lack of structural similarity. For example, a substance can have an identical effect on the body as a controlled substance but differ by three molecules from a scheduled substance instead of only two and, therefore, be declared a "legal" substance.

The advantage to using the analogue method is that it covers every substance, regardless of type (e.g., cannabinoid, substituted cathinone, substituted tyrptamine, etc.), so long as the substance is structurally similar to at least one Schedule I or II controlled substance and it has a similar effect on the body as a Schedule I or II substance.

Class Definitions and Scheduling by Specific Substance

As a result of the issues with prosecuting offenders under state or federal analogue statutes, many states have opted to schedule synthetic cannabinoids through the use of class definitions or by scheduling each novel psychoactive substance individually by its specific chemical structure or trade/street name. At this time, the vast majority of states in the United States use one of these two scheduling approaches or both in combination.

The advantage of scheduling substances by class definition is that the only proof required is that the substance in question falls within a particular class. It is not necessary to show its structural similarity to another substance or its effect on the body. As of April 2014, the following classes have been scheduled in one or more U.S. states (including both cannabinoid and non-cannabinoid type novel psychoactive substances): adamantoylindoles, adamantoylindazoles, benzoylindoles, cyclohexylphenols, cyclopropanoylindoles, naphthoylindoles, naphthoylnaphthalenes, naphthoylpyrroles, naphthylmethylindenes, naphthylmethylindoles,

[2] Those substances that are either highly addictive and have no accepted medical value (e.g., methcathinone) or that are highly addictive and have limited medical value (e.g., morphine).

phenylacetylindoles, quinolinylindolecarboxylates, tetramethylcyclopropanoylindoles, tetramethylcyclopropane-thiazole carboxamides, substituted phenethylamines, and substituted tryptamines. In most cases, states have included specific substances as examples of the particular class in the definition.

The disadvantage to scheduling in this way is that if a substance doesn't fall within a particular named class and isn't otherwise specifically listed, the substance is "legal" until it is particularly scheduled, although the state or federal analogue statute could fill the void until the substance is scheduled.

Conclusion and Recommendations

Each of the foregoing approaches to scheduling synthetic cannabinoids has its advantages and disadvantages. It does not appear that there is a single simple solution to the problem of how best to schedule novel psychoactive substances in order to prevent the necessity of constantly updating the controlled substances schedules as new "legal" substances are created. The best option seems to be to use a combination of the above approaches so that all avenues are covered and successful prosecution of offenders is ensured.