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October 26, 2017

Honorable William H. Pryor, Jr.
Acting Chair
United States Sentencing Commission
One Columbus Circle, N.E.
Suite 2-500, South Lobby
Washington, D.C. 20002-8002

Re: Public Comment on Synthetic Cathinones, Tetrahydrocannabinol (THC), and Synthetic Cannabinoids

Dear Judge Pryor:

Synthetic cathinones and cannabinoids are “understudied substances.”¹ Not enough information is available about these substances at this time for the Commission to make informed and just guideline amendments to address these drugs either individually or as a class. A far better approach is to amend Note 6 to give courts meaningful guidance on determining which of the listed substances are most similar to the unlisted substance. Specifically, we recommend guidance that will focus courts on the relative potency or impotency of unlisted substances and on medical and public health evidence of direct harms of the different drugs. With this approach, over time, courts and researchers will study these substances in a way that may, at some point, provide enough information for the Commission to specifically address them in the guidelines.

We recognize the strong urge to do something to address the harms from synthetic drugs. And we share it. Unfortunately, amending the guidelines to specifically address these synthetic substances individually or as a class will not deter their production, sale, or use. As discussed below, despite a strong belief by many that we can stop people from certain actions by lengthening the threatened punishment, the research shows that lengthening punishment does not deter.

¹ Congressional Research Service, *Synthetic Drugs: Overview and Issues for Congress* (May 3, 2016) (citing Office of National Drug Control Policy, *National Drug Control Strategy 2013*, at 10).

A critical difficulty in answering the Commission's issues for comment about these synthetic drugs arises from the structure of the current guidelines, particularly the Drug Quantity Table (DQT) and Drug Equivalency Tables (DET), which provide thresholds, ratios, and equivalencies that are illogical and unsupported by evidence. Our criticisms regarding the current drug guidelines are fundamental, and have been raised before, but are well illustrated by the difficulty of determining how the guidelines should best address synthetic drugs. First, the current Drug Quantity Table does not apportion punishment according to the relative harmfulness of various substances, or a particular defendant's culpability. Second, the guidelines' focus on quantity fails to fairly or effectively advance the purposes of sentencing. Third, the current guidelines reflect inconsistent decisions about fundamental matters—for example, which harms are relevant to sentencing, and the importance of potency and dosage amounts—which make it difficult to make rational suggestions about how unlisted substances should be addressed in the current drug guidelines.

As described in detail below, current thresholds, ratios, and equivalencies for synthetic drugs and potentially closely related substances are inaccurate and irrational, and exacerbate the difficulty of placing these synthetic drugs in the current guidelines. Because courts look to listed substances when establishing marijuana equivalencies for unlisted substances, it is crucial that the Commission address the unsound treatment of listed substances as soon as possible, whether the Commission specifically lists the synthetic drugs at issue, or not. We are particularly concerned about the equivalencies for MDMA, THC and the few cathinones addressed by the current DET.

If, despite the strong reasons to exercise restraint, the Commission decides to specifically address these substances in the guidelines, we urge caution in weighing the import of anecdote in this policy decision. As described below, empirical public health data on prevalence and emergency room episodes for "bath salts" and synthetic cannabinoids do exist, and provide crucial context for anecdotes or single case studies of health problems that can be caused by abuse of these substances. The available data show that, even allowing for a wide range of potential error in estimates, these substances are in the lowest tier of harmfulness. To avoid over-punishing these drugs, that evidence supports ratios no greater than 1:100 for the most common synthetic cathinones, and a presumption of 1:1 for a smokable synthetic cannabinoid sprayed onto psychologically inactive organic matter.

I. Longer Terms of Imprisonment Do Not Have a Deterrent Effect on Drug Trafficking or Use.

As the Commission considers appropriate guideline amendments for various drugs, we urge it to acknowledge research showing that setting high guideline recommended sentences will not have a deterrent effect. As discussed below, a broad consensus exists in the research that severe

sentences do not deter crime generally, nor drug crime specifically. Commission reports and data are consistent with this research.²

A comprehensive and rigorous review of the research led the National Research Council to conclude that “insufficient evidence exists to justify predicating policy choices on the general assumption that harsher punishments yield measurable deterrent effects.”³ With regard to drug crime, the Committee noted that “the best empirical evidence suggests that the successive iterations of the war on drugs—through a substantial public policy effort—are unlikely to have markedly or clearly reduced drug crime over the past three decades.”⁴ Nor is there “evidence of a specific deterrent effect on the experience of incarceration.”⁵ Moreover, “[m]ost drug policy analysts agree that ...imprisoning individual drug dealers seldom reduces the availability of drugs or the number of traffickers.”⁶

The Commission has acknowledged this research. For example, when explaining the Commission’s “drugs minus 2” amendment,⁷ the Honorable Patti B. Saris, then Chair of the Sentencing Commission, recognized the evolving knowledge about the effects of federal drug sentencing, including how “[s]ome prominent scholars have written that lengthy period of incarceration are unlikely to have a deterrent effect.”⁸ Chair Saris also noted that “real-life

² The Commission is statutorily obligated to consider a variety of factors in establishing categories of offenses and the imposition of sentences, but “only to the extent that they do have relevance.” 28 U.S. § 994(c). Among the factors listed is “the deterrent effect a particular sentence may have on the commission of the offense by others.” The Commission is also required to “establish sentencing policies and practices” that “reflect, to the extent practicable, advancement in knowledge of human behavior as it related to the criminal justice process.” 28 U.S.C. § 991(b)(2). Because advances in knowledge of human behavior show that severe sentences do not deter crime and are not associated with drug use or drug harms, the Commission should not determine drug quantity ratios based upon the belief that a particular sentence may have a deterrent effect.

³ Nat’l Res. Council, *The Growth of Incarceration in the United States: Exploring Causes and Consequences* 90 (J. Travis, et al., eds. 2014). The report also noted that “[n]early every leading survey of the deterrence literature in the past three decades has reached the same conclusion.” *Id.* See also Nat’l Inst. of Just., *Five Things About Deterrence* (Sept. 2014), <http://www.nij.gov/five-things/pages/deterrence.aspx>; Daniel S. Nagin, *Deterrence in the Twenty-First Century*, 42 *Crime & Just.* 199, 201 (2013); Gary Kleck & J.C. Barnes, *Deterrence and Macro-Level Perceptions of Punishment Risks: Is There a “Collective Wisdom”?*, 59 *Crime & Delinq.* 1006, 1031-33 (2013); Brennan Ctr. for Just., *What Caused the Crime Decline?* 26 (Feb. 2015), <https://www.brennancenter.org/publication/what-caused-crime-decline>; Andrew von Hirsch et al., *Criminal Deterrence and Sentence Severity: An Analysis of Recent Res.* (1999); Michael Tonry, *Purposes and Functions of Sentencing*, 34 *Crime & Just.: A Review of Res.* 28-29 (2006).

⁴ Nat’l Res. Council, *supra* note 3, at 154.

⁵ *Id.* at 156.

⁶ *Id.* at 88.

⁷ USSG App. C, Amend. 782 (Nov. 1, 2014).

⁸ Honorable Patti B. Saris, Chair, U.S. Sentencing Comm’n, *A Generational Shift for Federal Drug Sentences*, 52 *Am. Crim. L. Rev.* 1, 12 (2014) (citing Steven N. Durlauf & Daniel S. Nagin, *Imprisonment and Crime: Can Both*

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experience in the states, together with new academic research, has begun to indicate that drug sentences may now be longer than needed to advance the purposes for which we have prison sentences, including public safety, justice, and deterrence.”⁹

A Commission report acknowledged the absence of any demonstrable deterrent effect from a high drug-quantity ratio and lengthy sentences of imprisonment. The Commission’s 2007 report to Congress on crack cocaine noted “that it is nearly impossible to document any deterrent effect of the 100-to-1 drug quantity ratio because crack cocaine distributors rarely mention awareness of it or report changing business activities due to its existence.”¹⁰ The report also included information obtained from a public hearing that the “federal crack cocaine penalty structure has not disrupted drug markets,” because the supply did not decline, prices did not increase, and “former sellers lost to prison” were replaced.¹¹

Another Commission report noted that incarceration of retail-level drug traffickers will not curtail drug dealing:

Unlike repeat violent offenders, whose incapacitation may protect the public from additional crimes by the offender, criminologists and law enforcement officials testifying before the Commission have noted that retail-level drug traffickers are readily replaced by new drug sellers so long as the demand for a drug remains high. Incapacitating a low-level drug seller prevents little, if any, drug selling; the crime is simply committed by someone else.

USSC, *Fifteen Years of Guidelines Sentencing: An Assessment of How Well the Federal Criminal Justice System is Achieving the Goals of Sentencing Reform* 131 (2004).

A recent economic analysis from the Cato Institute also found “that the domestic War on Drugs has fostered and sustained the creation of powerful drug cartels” and has not accomplished its goal of “controlling the sale, manufacture, and consumption” of drugs.¹²

Other evidence shows that severe sentences are not associated with a decline in fatal overdoses.¹³ A recent report from the Center for Disease Control and Prevention found that “[t]he death rate

be Reduced?, 10 *Criminology & Pub. Pol’y* 13, 38 (2011) (finding that “lengthy” periods of incarceration are unlikely to serve a deterrent effect and that incapacitation effect is negated as prisoners get older).

⁹ *Id.*

¹⁰ USSC, *Report to Congress: Cocaine and Federal Sentencing Policy* B-15 (2007) (hereinafter *Cocaine Report 2007*).

¹¹ *Id.* at B-20.

¹² Christopher Coyne & Abigail Hall, Cato Institute, *Four Decades and Counting: The Continued Failure of the War on Drugs* 1 (2017).

due to drug overdose among adolescents aged 15-19 more than doubled from 1999 (1.6 per 100,000) to 2007 (4.2), declined by 26% between 2007 and 2014 (3.1), and then increased in 2015 (3.7).”¹⁴ From 1999 to 2015, the average sentence length for federal drug trafficking varied: it increased by 13.9% from 1999 (73 months) to 2007 (83.2 months); declined 18.2% between 2007 and 2014 (68 months); and then declined in 2015 (67 months).¹⁵ If severe sentences had any impact on the frequency of fatal overdoses, then the rate of fatal overdoses would have decreased between 1999 and 2007 as sentence length increased.¹⁶

Evidence shows that sentence length is not associated with the rate of drug use. This is apparent by comparing use of both crack and methamphetamine during periods where sentence lengths changed. As to crack cocaine, the Commission, relying on data from the National Survey on Drug Use and Health, concluded that the Fair Sentencing Act “did not disrupt the ongoing decline in the number of people who report using crack cocaine in the last year.”¹⁷ Additional data from the National Survey on Drug Use and Health, and the Commission, reveals that severe sentences are not associated with a decline in drug use. As Fig. I shows,¹⁸ from 2002 to 2007, the rate of crack cocaine usage was either .06 or .07. The rates from 2008 to 2016 varied from .03 to .05. During those 14 years, the average sentence length for drug trafficking in crack cocaine varied widely and was not associated with the frequency of drug use. Nor were severe sentences necessary for usage rates to drop. When the average sentence for trafficking in crack cocaine dropped from 129 months in 2007 to 104 months in 2011, the usage rate dropped from .06 to .03. And while the average sentences were even lower from 2012 to 2016, the usage rates were still lower than they were from 2002 to 2007.

¹³ “[C]orrelation is a necessary but not a sufficient condition to make causal inferences with reasonable confidence.” Karl Wuensch, *When Does Correlation Imply Causation?* (2001), <http://core.ecu.edu/psyc/wuenschk/StatHelp/Correlation-Causation.html>.

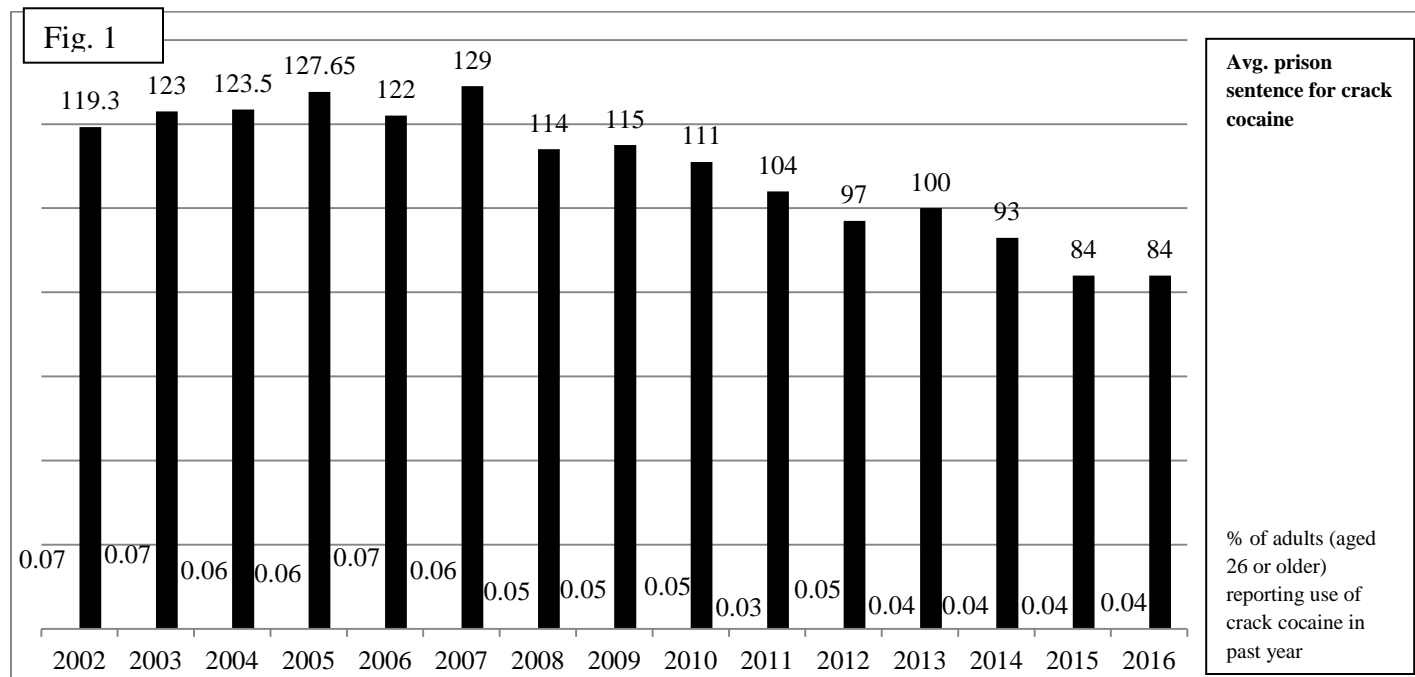
¹⁴ Nat’l Ctr. for Health Statistics Data Brief, No. 282: *Drug Overdose Deaths Among Adolescents Aged 15-19 in the United States: 1999-2015* (Aug. 2017).

¹⁵ USSC, *Sourcebook of Federal Sentencing Statistics*, tbl. 13 (1999, 2007, 2014, 2015).

¹⁶ Other data shows that the War on Drugs has resulted in more overdoses and drug-related illness “because prohibition’s added costs incentivize higher-potency drugs and their higher value per unit.” Coyne et al., *supra* note 12, at 4.

¹⁷ USSC, *Report to the Congress: Impact of the Fair Sentencing Act of 2010*, at 27 (2015).

¹⁸ Sources: SAMHSA, *2016 Nat’l Survey on Drug Use and Health: Detailed Tables*, tbl. 7.14D (2017); USSC, *Interactive Sourcebook*, fig. J FY 2002-2015.



The evidence regarding methamphetamine also shows no association between severe sentences and a decline in the availability of drugs or drug trafficking cases. Methamphetamine drug trafficking is still prevalent even though the Commission has repeatedly increased the recommended guideline sentence for such offenses. The Commission originally made penalties for methamphetamine more severe than for cocaine¹⁹ and later increased the penalties multiple times. In response to the Anti-Drug Abuse Act of 1988, the Commission chose higher penalties for methamphetamine²⁰ because, even though it recognized that “methamphetamine is a stimulant that produces effects upon its user similar to those of cocaine...., methamphetamine [was] viewed as posing a more serious drug control problem, in part, because it can be domestically produced by drug traffickers themselves....”²¹ In 1990, the Commission added a drug quantity ratio for methamphetamine (pure).²² In 1991, the Commission made 1 gm methamphetamine = 1 kg of marihuana; and 1 gm methamphetamine (actual) = 10 kg of marihuana.²³ Six years later, it doubled the marihuana equivalency as a result of the

¹⁹ The guidelines originally treated methamphetamine two times more seriously than cocaine. USSG §2D1.1 (1987) (1 gm of cocaine =0.2 gm of heroin; 1 gm of methamphetamine=2.0 gm of cocaine/0.4 gm of heroin).

²⁰ USSG App. C, Amend. 125 (Nov. 1, 1989) (1 gm of methamphetamine = 5.0 gm of cocaine/1.0 gm of heroin).

²¹ USSC, *Drug Working Group—Listed Chemicals Report 7* (1990).

²² USSG App. C, Amend. 318 (Nov. 1, 1990) (1 gm of methamphetamine (pure)=50 gm of cocaine/ 10 gm of heroin).

²³ USSG App. C, Amend. 396 (Nov. 1, 1991) (it also changed 1gm of cocaine to=200gm of marihuana).

Comprehensive Methamphetamine Control Act of 1996.²⁴ It also added additional penalties for environmental violations associated with manufacturing or drug trafficking,²⁵ the importation of methamphetamine and precursor chemicals,²⁶ manufacturing, and possession with intent to manufacture or distribute methamphetamine on premises where a minor is present or resides.²⁷

Notwithstanding repeated and sharp increases in recommended sentences, the availability of methamphetamine remains high. Almost twice as much methamphetamine was seized in North America in 2015 (55 tons) than in 2010 (28 tons).²⁸ The DEA found in 2016 that “[m]ethamphetamine seizures, survey data, price and purity data, and law enforcement reporting indicate methamphetamine continues to be readily available throughout the United States.”²⁹ “National-level use survey data [for methamphetamine] remains stable.”³⁰ The DEA’s National Drug Threat Survey shows that “29.8 per cent of responding [law enforcement] agencies reported that methamphetamine was the greatest drug threat in their areas.”³¹ Moreover, the percentage of responding United States law enforcement agencies reporting high availability of methamphetamine has increased annually, from 39.5 per cent in 2013 to 45.4 per cent in 2016.³² “Indeed, methamphetamine use in the United States continues to increase, with the annual prevalence of methamphetamine use among the general population aged 15-64 years rising from 0.5 per cent in 2012 to 0.8 per cent in 2015.”³³

II. Synthetic Cathinones and Cannabinoids Cannot Be Rationally Related to the Quantity-Based Penalties in the Drug Quantity and Drug Equivalency Tables.

This year’s priority concerning synthetic drugs has set a task for the Commission that is largely impossible to complete given the current structure of the drug quantity table. Synthetic cathinones and cannabinoids cannot be rationally related to the quantity-based penalties found in

²⁴ USSG App. C, Amend. 556 (Nov. 1, 1997).

²⁵ *Id.*

²⁶ *Id.*

²⁷ USSG App. C, Amend. 608, (Dec. 6, 2000); *id.*, Amend. 620 (Nov. 1, 2001); *id.* Amend. 705 (Nov. 1, 2007).

²⁸ United Nations Office on Drugs and Crime, *Market Analysis of Synthetic Drugs, World Drug Report 15* (2017), https://www.unodc.org/documents/scientific/Booklet_4_Market_Analysis_of_Synthetic_Drugs_ATS_NPS.pdf.

²⁹ U.S. Dep’t of Just., Drug Enforc. Admin., *2017 Nat’l Drug Threat Assessment* 67 (2017).

³⁰ *Id.*

³¹ *Id.*

³² *Id.* at fig. A9. *See also Market Analysis of Synthetic Drugs, World Drug Report, supra* note 28, at 16-17.

³³ *Market Analysis of Synthetic Drugs, World Drug Report, supra* note 28, at 17.

the current Drug Quantity Table (DQT), because the existing structure is itself fundamentally unsound. The current DQT does not apportion punishment according to the relative harmfulness of various drugs or a particular defendant's culpability. Rather than accomplish the purposes of sentencing in a rational manner, the DQT results in disparity, disproportionality, inefficiency, and injustice.³⁴

It would be easier to create a rational and defensible penalty structure for drugs from scratch than to relate synthetic drugs to the thresholds, ratios, and equivalencies in the current guidelines. The DQT and associated Drug Equivalency Tables (DET) are a result of piecemeal policymaking by Congress and the Commission, unguided by a coherent theory of sentencing. The DQT reflects a hodgepodge of thresholds established by 1) mandatory minimum penalty statutes contained in the Anti-Drug Abuse Act of 1986 (ADAA) and subsequent amendments that the Commission voluntarily incorporated into the DQT for some, but not all, drugs;³⁵ 2) specific statutory directives, often enacted by Congress in the midst of a media frenzy,³⁶ which the Commission was bound to follow;³⁷ and 3) to some extent, the Commission's own research and policy making. Unfortunately, even when not constrained by Congress, the Commission has not articulated and followed a consistent approach to assessing drug harms and setting the appropriate punishment for different drugs.

³⁴ See Letter from Marjorie Meyers, Chair, Federal Defender Sentencing Guideline Committee, to the Honorable William H. Pryor, Jr., Acting Chair, U.S. Sentencing Comm'n, at 2-5 (Mar. 10, 2017) (hereinafter *March Letter*).

³⁵ The Commission departed from the statutory thresholds in the case of LSD, due to the extreme anomalies created by different carrier mediums by which the drug is distributed. See USSG App. C, Amend. 488 (Nov. 1, 1993). The Supreme Court accepted the Commission's approach for guideline calculation purposes, but not for application of the mandatory penalty statutes. *Neal v. United States*, 516 U.S. 284 (1996).

³⁶ The deliberations surrounding enactment of the ADAA of 1986 have been described as "partisan bidding wars." Eric Sterling, counsel to the House Judiciary Committee at the time the Act was passed, described the process "like an auction house.... It was this frenzied, panic atmosphere—I'll see you five years and raise your five years. It was the crassest political poker game." Michael Isikoff & Tracy Thompson, *Getting Too Tough on Drugs: Draconian Sentences Hurt Small Offenders More Than Kingpins*, Wash. Post, Nov. 4, 1990, at C1, C2 (quoting Sterling). The sentencing provisions in the ADAA were called the product of "a flood of anti-drug hysteria." Eric Sterling, *Legislative Scatology* (Feb. 16, 2009), http://www.sterlingonjusticedrugs.com/2009_02_01_archive.html.

Legislation leading to directives to the Commission rather than mandatory statutory penalties also has been motivated by exaggerated fears. For example, the legislative history of the Ecstasy Anti-Proliferation Act of 2000, which directed the Commission to increase penalties for MDMA prior to any Commission study, claimed that MDMA "is a definite killer" and "can cause brain damage." 106 Cong. Rec. S4317-4318 (statements of Sens. Graham and Biden) (daily ed. May 23, 2000 (Senate)).

³⁷ *United States v. La Bonte*, 520 U.S. 751 (1997). The drug guideline has been subject to statutory directives concerning methamphetamine, amphetamine, powder and crack cocaine, MDMA/ecstasy, anabolic steroids, hydrocodone, and oxycodone, precursor drugs like ephedrine, and so-called "date-rape" drugs like flunitrazepam and GHB.

The absence of a clear and consistent rationale for drug sentencing leaves those responding to the Commission’s request for comments without guidance on the significance of information the Commission requests and how it relates to ranking drug harms in a proportionate manner. It also leaves the Commission vulnerable to receiving misleading or irrelevant information and to cognitive distortions such as the availability heuristic³⁸ or framing effects, by which extreme and unrepresentative examples are given undue weight. Defenders are concerned that the current amendment process for synthetic drugs will create a false impression—the appearance of reasoned, evidence-based policy making—when, in fact, incorporating synthetic drugs into the fundamentally flawed DQT and DET cannot result in proportional drug sentencing and sound sentence recommendations.

Because the Commission cannot rationally incorporate synthetic drugs into the fundamentally flawed DQT/ DET and the research available on new synthetic substances is limited, we discouraged the Commission from making such drugs a priority for the 2017 amendment cycle.³⁹ When the Commission nonetheless made synthetics a priority, we were gratified that MDMA was at least included in the priority. Many courts have found MDMA to be the most closely related substance to synthetic cathinone, even while finding the current equivalency for MDMA unsound. If the Commission would not reconsider the DQT/ DET as a whole, we believed it would at least reconsider the excessive penalties for the listed drug most often found closely related.

In August we submitted comment explaining in detail why the equivalency for MDMA “unquestionably needs to be revised.”⁴⁰ Unlike new synthetic drugs, considerable data on potential public health harms and prevalence of use are available for MDMA. These lead to the clear conclusion that “ecstasy is much less harmful than most other major controlled substances.”⁴¹ Yet when considering typical dosage amounts—which is necessary to make sense of the widely different marijuana equivalencies for substances like LSD and khat—MDMA is

³⁸ The “availability heuristic” occurs during decision-making when a “number of related events or situations might immediately spring to the forefront of your thoughts.” While it can be helpful sometimes, it can lead to incorrect decisions. “Just because something looms large in your memory does not necessarily mean that it is more common.” Kenrday Cherry, *What is an Availability Heuristic?* (Apr. 27, 2017), <https://www.verywell.com/availability-heuristic-2794824>.

³⁹ Letter from Marjorie Meyers, Chair, Federal Defender Sentencing Guideline Committee, to the Honorable Patti Saris, Chair, U.S. Sentencing Comm’n, at 8-11 (July 25, 2016).

⁴⁰ Letter from Marjorie Meyers, Chair, Federal Defender Sentencing Guideline Committee, to the Honorable William H. Pryor, Jr., Acting Chair, U.S. Sentencing Comm’n, at 6 (Aug. 7, 2017) (hereinafter *August Letter*).

⁴¹ *Id.*

punished more severely than many substances that are more harmful, including heroin, powder cocaine and methamphetamine mixtures.

Given this compelling evidence, we were surprised and dismayed that the Commission's final priorities for the current amendment cycle no longer include MDMA.⁴² We also do not believe the Commission can develop sound recommendations for synthetic cathinones without addressing the guidelines' unsound recommendations for the substance courts have most often found closely related.

A. The Current DQT Does not Fairly or Efficiently Advance the Purposes of Sentencing.

Despite its piecemeal development, the Commission has suggested that the drug guideline somehow advances all the purposes of sentencing, without explaining in meaningful detail how it advances even one.⁴³ Based on the sparse legislative history of the Anti-Drug Abuse Act of 1986, the Commission has sometimes suggested that the ratios, thresholds, and equivalencies in the DQT are designed to allocate punishment based on defendants' functional roles in drug trafficking, with penalties of at least five years for "serious" traffickers and ten-year minimums for "major" traffickers.⁴⁴ Research, however, has repeatedly shown that the current DQT does a poor job of allocating punishment according to defendants' roles and culpabilities, with large portions of the lowest-level couriers, mules, and street-level dealers receiving sentences as long or longer than those intended for serious and major players.⁴⁵

The present guideline also does not efficiently "protect the public from further crimes of the defendant" because it does not address rehabilitative needs or even target the longest sentences

⁴² USSC, Notice of Final 2017-2018 Priorities, 82 Fed. Reg. 39949 (June 21, 2017).

⁴³ See, e.g., USSC, *Report to the Congress: Mandatory Minimum Penalties in the Federal Criminal Justice System* 40 (2011) (hereinafter *Mandatory Minimum Report*) (noting that Commission considers § 3553(a) factors in developing guidelines); Brief for the USSC as Amicus Curiae in Support of Respondent, *Claiborne v. United States*, (No. 06-5618) and *Rita v. United States*, 551 U.S. 338 (2007) (No. 06-5754), 2007 WL 173622, 25-25 (asserting that "[t]he guidelines appropriately balance the statutory purposes of punishment").

⁴⁴ *Mandatory Minimum Report*, at 24 (describing Congress's "two-tiered penalty structure for discrete categories of drug traffickers").

⁴⁵ In 2010, nearly half of couriers (49.6%), and most street level dealers (65.5%) were held responsible for quantities of drugs qualifying them for a mandatory minimum penalty, even though Congress appears to have intended those penalties for serious or major traffickers. *Mandatory Minimum Report*, app., fig. D-2. See also *Cocaine Report 2007*, at 28-30 (showing large numbers of persons convicted of low-level crack and powder cocaine offenses exposed to harsh penalties intended for more serious offenses); USSC, *Report to the Congress: Cocaine and Federal Sentencing Policy* 42-49 (2002) (showing drug mixture quantity fails to closely track important facets of offense seriousness) (hereinafter *Cocaine Report 2002*); Eric L. Seigny, *Excessive Uniformity in Federal Drug Sentencing*, 25 J. Quant. Criminology 155, 171 (2009) (Drug quantity "is not significantly correlated with role in the offense.").

on the defendants most likely to recidivate or commit a violent act associated with drug trafficking.⁴⁶ Nor does incarceration of persons convicted of drug offenses reduce crime. Because drug offenses are driven by user demand, incarceration of a particular drug trafficker simply creates an employment opportunity for someone else, who readily replaces the incarcerated offender in the lucrative drug market.⁴⁷ And as previously discussed, no evidence shows that longer terms of imprisonment have a deterrent effect.

Finally, the offense levels provided in the DQT, which generally result in guideline ranges falling within Zone D of the sentencing table, do not meet “in the most effective manner,” the treatment and training needs of defendants.⁴⁸ Not only do community-based treatment programs generally offer better options, BOP’s overcrowding and staffing shortages still limit treatment and training programs.⁴⁹ Recently, only 23,000 inmates were enrolled in BOP’s occupational training programs, which have been shown to reduce recidivism.⁵⁰ And while 40% of inmates

⁴⁶ Persons convicted of drug offenses have lower rates of recidivism than several other offense types and higher offense levels are *not* correlated with increased risk of recidivism. USSC, *Recidivism Among Federal Offenders: A Comprehensive Overview* 20 (2016) (“The Commission did not find a strong correlation between the severity of the offender’s federal offense conduct, as determined under the sentencing guidelines, and future recidivism.” “Offenders whose federal offense involved firearms were most likely to be rearrested (68.3%), followed by those arrested for robbery (67.3%), immigration (55.7%), drug trafficking (49.9%), larceny (44.4%), other (42.0%), and fraud (34.2%).” See also USSC, *Measuring Recidivism: The Criminal History Computation of the Federal Sentencing Guidelines* 13 (2004) (“Offenders sentenced in fiscal year 1992 under fraud, §2F1.1 (16.9%), larceny, §2B1.1 (19.1%), and drug trafficking, §2D1.1 (21.2%) are overall the least likely to recidivate.” There is “no apparent relationship between the sentencing guideline final offense level and recidivism risk.”).

⁴⁷ USSC, *Cocaine and Federal Sentencing Policy*, at 68 (1995) (DEA and FBI reported dealers were immediately replaced) (hereinafter *Cocaine Report 1995*).

⁴⁸ Community residential treatment programs for individuals who receive probation or who are under supervised release offer better options and access to drug treatment than a lengthy prison sentence. See, e.g., Gary Zarkin et al., *Lifetime Benefits and Costs of Diverting Substance-Abusing Offenders from State Prison* (Oct. 2011), [https://psychonautwiki.org/w/index.php?title=Substituted_cathinone&_ =](https://psychonautwiki.org/w/index.php?title=Substituted_cathinone&_=) ; National Institute of Corrections, *Myths and Facts: Why Incarceration is Not the Best Way to Keep Communities Safe* 6 (2016) (“Community corrections has been shown to be effective in reducing future criminal activity by 10 to 30%”), <https://nicic.gov/myths-facts-why-incarceration-not-best-way-keep-communities-safe>.

⁴⁹ BOP is 13% overcrowded and anticipates a 2% increase in the next year. BOP, *Program Fact Sheet* (Sept. 2017), https://www.bop.gov/about/statistics/docs/program_fact_sheet_20170920.pdf; U.S. Dep’t of Justice, *Federal Prison System, FY 2018 Performance Budget: Congressional Submission, Salaries and Expenses* 7 (2017), <https://www.justice.gov/file/968971/download>.

BOP only has a 4.1-to-1 staffing ratio. *Program Fact Sheet*. Then Director of BOP, Charles Samuels, told Congress in 2015 that a 4.4-to-1 staffing ratio negatively impacted BOP’s ability to effectively supervise inmates and provide inmate programs. He also reported that staffing shortages hinder the ability of psychologists and others to provide needed services. *Oversight of the Bureau of Prisons: First-Hand Accounts of Challenges Facing the Federal Prison System, Hearing Before the Senate Committee on Homeland Security and Governmental Affairs*, 114th Cong. 3 (Aug. 4, 2015) (statement of Charles E. Samuels, Jr., Director, Federal Bureau of Prisons, U.S. Dep’t of Justice).

⁵⁰ *Performance Budget*, *supra* note 49, at 29.

have a drug use disorder, only 17,000 are projected to participate in the Residential Drug Abuse Program in FY2018.⁵¹ Lengthy sentences just result in years of incarceration without meaningful programming.

B. The Drug Quantity and Drug Equivalency Tables Do Not Result in Proportionate Punishment.

The Commission has sometimes characterized the offense level as measuring the seriousness of an offense, which criminologists conceive as the harms caused by an offense conditioned by a particular defendant's culpability for those harms.⁵² The DQT's consideration of drug type and quantity, in particular, has been described as aiming at proportionate punishment.⁵³ When not subject to statutory constraints, the Commission has often sought to assign thresholds and equivalencies to various drugs based on their relative harmfulness. For example, discussion of drug harms was central to the Commission's reports on cocaine sentencing, which reviewed empirical and medical evidence on the relative harmfulness of powder and crack cocaine.⁵⁴ Commission reports on MDMA ("ecstasy"),⁵⁵ methamphetamine,⁵⁶ and steroids also have reviewed various harms caused by these drugs and their trafficking.⁵⁷

Unfortunately, the Commission's harmfulness comparisons have been *ad hoc* and inconsistent.⁵⁸ The types of harms taken into account have been inconsistent, as has consideration of the important matter of dosage weight. A drug's prevalence of use, and indirect harms not fairly attributable to individual defendants, have confounded harms analyses. And while Commission

⁵¹ *Id.* at 38, 42.

⁵² See Amicus Brief in Support of Respondent, *supra* note 43, at 25 (describing how the "Guidelines assign each crime a score as a starting point in assessing the seriousness of the offense) (citing *USSC Fifteen Years of Guideline Sentencing: An Assessment of How Well the Federal Criminal Justice System is Achieving the Goals of Sentencing Reform* 12 (2004)). See also Paul J. Hofer & Mark H. Allenbaugh, *The Reason Behind the Rules: Finding and Using the Philosophy of the Federal Sentencing Guidelines*, 40 Am. Crim. L. Rev. 19, 62-67 (2003) (citing just desert theorists on the components of offense seriousness).

⁵³ *Mandatory Minimum Report*, *supra* note 43, at 349, n.845.

⁵⁴ *Cocaine Report 2007; Cocaine Report 2002; Cocaine Report 1995*.

⁵⁵ USSC, *Report to the Congress: MDMA Drug Offenses: Explanation of Recent Guideline Amendments* 6-10 (2001) (hereinafter *MDMA Report*).

⁵⁶ USSC, *Methamphetamine Final Report 2* (1999).

⁵⁷ USSC, *2006 Steroids Report*, at 23-26 (2006) (hereinafter *Steroids Report*).

⁵⁸ Paul J. Hofer, *Ranking Drug Harms for Sentencing Policy* (May 2015), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2612654.

reports have sometimes corrected mistaken ideas about the harmfulness of a particular drug,⁵⁹ the reports themselves have sometimes relied on evidence that later proved controversial, if not mistaken.⁶⁰

The role and relationship between the DQT and other guideline provisions are confused, resulting in double counting and excessive punishment. Ideally, the DQT would assess direct harms caused by the drugs themselves, since such harms would be common to all trafficking offenses involving a specific drug. Specific offense adjustments could then account for harms found in some, but not all, offenses involving a drug.⁶¹ But when establishing thresholds in the penalty statutes, Congress assigned prison terms based in part on factors thought to be “associated” with certain drugs, such as violence (crack),⁶² or use by role models, such as athletes (anabolic steroids),⁶³ or marketing to youth (ecstasy),⁶⁴ even though not all offenses involving those drugs involved those harms.

Other features of the DQT confound proportionate punishment, and add arbitrary variation in sentences unrelated to any purpose of punishment. As described in more detail in our March letter, Congress departed from prior Parole Commission practice and made mandatory minimum drug penalties depend on the weight of any “mixture or substance containing a detectable amount”⁶⁵ of most (but not all) drugs, rather than on the weight of only the active ingredient. This guarantees that offenses involving similar amounts of actual drug are often treated

⁵⁹ A perceived epidemic of “crack babies” contributed to the harsh treatment of crack cocaine under the Anti-Drug Abuse Act of 1986 and the original guidelines. The Commission later found that “research indicates that the negative effects from prenatal exposure to cocaine, in fact, are significantly less severe than previously believed.” *Cocaine Report 2007*, at 68.

⁶⁰George A. Ricaurte et al., *Severe Dopaminergic Neurotoxicity in Primates After a Common Recreational Dose Regimen of MDMA (“Ecstasy”)*, 297 *Science* 2260-63 (2002); George A. Ricaurte et al., *Retraction*, 301 *Science* 1479 (2003); Editorial, *Ecstasy’s after-effects*, 425 *Nature* 223 (2003) (“The retracted paper left the public with the impression that ecstasy is far more hazardous than it may actually turn out to be.”).

⁶¹ See, e.g., USSG §2D1.1(b)(13) (hazardous waste); §2D1.1(b)(2) (defendant used, threatened, or directed violence); §2D1.1(b)(9) (distribution of anabolic steroid to an athlete).

⁶² *Cocaine Report 2002*, at 90.

⁶³ *Steroids Report*, at 3-10.

⁶⁴ *MDMA Drug Offenses*, at 5 (the Commission also chose “a greater penalty structure for MDMA trafficking than for powder cocaine trafficking . . . because powder cocaine is not aggressively marketed to youth in the same manner as MDMA”).

⁶⁵ See 21 U.S.C. § 841.

disparately, and has the perverse effect of increasing punishments for persons lower in the distribution chain, where dilution of drugs is more common.⁶⁶

The Commission also has sent mixed signals about dosage weights. On the one hand, the Commission admits that the DQT and DET do not necessarily reflect differences in dosage weights, even for pharmacologically similar drugs.⁶⁷ On the other hand, the quantity thresholds for many drugs reflect the weight of a typical dose. The most severely punished drug per gram, by far, is LSD,⁶⁸ which necessarily reflects the minute amount of the drug in a typical dose. Conversely, the guidelines' marihuana equivalency for khat, the plant from which natural cathinones were first isolated, is low, with one gram of khat equating to just .01 gram of marihuana. This surely reflects the low concentration of cathinone in the plant material.⁶⁹ Similar reasoning underlies the different treatment of marihuana plants compared to the treatment of pure THC,⁷⁰ the most noteworthy active ingredient.

For a system that seeks proportionate punishment based on drug type and quantity, this inconsistent attention to dosage weights is surprising and has led to problematic results. For example, despite the guidance in Application Note 6 for courts to consider “whether a greater or lesser quantity of the controlled substance not referenced in this guideline is needed to produce a substantially similar effect,” some judges have ignored dosage when determining the “most closely related substances” for unlisted drugs. Only by ignoring dosage could a judge conclude that the proper marihuana equivalency for the weight of a synthetic cannabinoid sprayed on plant material is the corresponding weight of pure THC. The weight of a dose of the sprayed plant is 50 to 100 times greater than pure THC.⁷¹

⁶⁶ See Arthur Fries et al., Institute for Defense Analyses, *The Price and Purity of Illicit Drugs: 1981-2007* (2008) (reporting purity of seizures involving four quantity ranges of various drugs), https://obamawhitehouse.archives.gov/sites/default/files/ondcp/policy-and-research/bullet_1.pdf.

⁶⁷ USSG §2D1.1, comment. (n.8(B)) (“[b]ecause of the statutory equivalences, the ratios in the Drug Equivalency Tables do not necessarily reflect dosages based on pharmacological equivalents”).

⁶⁸ The marihuana equivalency ratio is 1 gm:100 kg. USSG §2D1.1, comment. (n.8(D)).

⁶⁹ One recent report found that 100 grams of khat leaves seized at various European airports contained between 36 and 114 milligrams of cathinone, depending on their freshness. Nasir Tajure Wabe, *Chemistry, Pharmacology, and Toxicology of Khat (Catha Edulis Forsk): A Review*, 3 *Addiction & Health* 137-149 (2011).

⁷⁰ The ratio for THC is 1 gm:167 gm. USSG §2D1.1, comment. (n.8(D)).

⁷¹ As described in our March letter and in greater detail later, the current marihuana equivalency for THC also fails to reflect actual concentrations of THC in marihuana. This can result in equating a single dose of synthetic cannabinoid sprayed on plant material to between 1000 and 2000 doses of marihuana. *March Letter*, at 13-14.

III. The Available Data Show that Synthetic Cathinones Are Less Harmful than Methamphetamine, Cocaine, PCP, and Heroin; and Synthetic Cannabinoids Should Not be Treated as Pure THC.

The Commission seeks comment on synthetic drugs’ “pharmacological effects, potential for addiction and abuse, the patterns of abuse and harms associated with their abuse, and the patterns of trafficking and harms associated with their trafficking.” It also requests comment on manufacturing, distribution, possession, and use; the characteristics of individuals involved in those activities; and the harms posed by those activities. The final question posed by the Commission is: “How do these harms differ from those associated with other controlled substances such as marijuana, cocaine, heroin, methamphetamine, or MDMA/Ecstasy?” Answering this question is difficult. It is conceptually challenging, and the difficulty is amplified by the lack of available evidence at this time regarding the harms from these synthetic drugs. Faced with these problems, it is understandable that one might be tempted to rely on anecdote. We urge the Commission to resist the pull of the anecdote, and to instead confront the challenging question by relying on actual evidence, limited though it may be.

Ranking harms for sentencing purposes. In the last decade, comparing the harms of different drugs for policy purposes has attracted attention from researchers around the world.⁷² The specific requirements of harm rankings for sentencing policy development and evaluation are coming into focus.⁷³ This work has demonstrated the need for a clear understanding of the types of harms that are relevant for sentencing purposes, and the types of empirical data that are available for making these rankings. Unless policymakers keep in mind the unique demands of harm rankings for sentencing purposes, and the limitations in the available evidence, they risk being misled by anecdotal reports and preliminary findings.

Defenders have previously encouraged the Commission to focus on the *direct harms* of the drugs themselves when determining the appropriate treatment of a substance under the DQT/ DET.⁷⁴ Virtually all trafficking activity, such as the marketing of some drugs to young people, the use of violence, unlawful importation, and mass-marketing by means of an interactive computer service, are accounted for elsewhere in the guidelines structure.⁷⁵ We also believe that

⁷² For a review of these efforts, and their relevance to sentencing policy, *see* Hofer, *supra* note 58.

⁷³ *Id.* *See also* Peter Reuter, *Should Offenses for Methamphetamine be Punished More Severely than Those for Crack Cocaine?* Statement prepared by Professor Peter Reuter, U. of Maryland, nationally recognized drug policy analyst, as an expert witness in a federal sentencing hearing in Hawaii (on file with the Sentencing Resource Counsel of the Federal Public Defenders).

⁷⁴ *March Letter*, at 6-7, 18-19.

⁷⁵ USSG §2D1.1(b).

establishing a defendant's proper sentencing liability requires that the harms be *caused* by the defendant's crime, not merely "associated" with general drug trafficking, as suggested in the issues for comment. Some harms "associated" with a drug are too remote to fairly affect the drug's proper treatment under the DQT. For example, punishments for all traffickers of a drug should not be increased because the drug is often used by disadvantaged populations, where collateral harms of addiction or abuse may be greater.⁷⁶ Even the overall or increasing popularity of a drug are not strictly relevant to the harms caused by a particular defendant.⁷⁷ Increasing the sentence of a drug defendant because many *other* people also sell the drug is like punishing a thief for crimes committed by other thieves.

The need for context: prevalence of use. Data on a drug's prevalence of use, while not directly relevant to ranking harm for sentencing purposes, are nonetheless crucial for assessing the significance of other public health data. Mere examples, or even counts, of problem outcomes like organ failure or overdose deaths are not useful *by themselves*; indeed, they may even be misleading. It is necessary to consider data on harmful outcomes *together* with data on prevalence of use in order to assess *how often* harmful outcomes occur. One example of such a measure is a risk ratio:⁷⁸ the portion of all users of a drug who experience a problem outcome, such as an emergency room admission or treatment episode. Such calculations have shown that drugs differ in their harmfulness, and that the current DQT does a poor job of assigning punishments proportionate to different drugs' harms.⁷⁹

⁷⁶ See, e.g., Joseph Palamar et al., *Powder Cocaine and Crack Use in the United States: An Examination of Risk for Arrest and Socioeconomic Disparities in Use*, 149 *Drug Alcohol Depend.* 108 (Apr. 2015) (crack users tended to be of lower socioeconomic status than power cocaine users); Nicole Piazza, *K2, Other Synthetic Marijuana Products Harming Low-Income Communities*, *NY Daily News* (July 12, 2016), <http://www.nydailynews.com/new-york/k2-synthetic-marijuana-products-harming-poor-article-1.2709009>.

The fact that a particular drug is used more frequently by poor individuals may leave the false impression that the drug is more harmful. This concern is relevant to synthetic cathinones and cannabinoids because of reports that these drugs have been popular among the homeless who are at high risk of poor health outcomes. See, e.g., *What is K2? 5 Facts and Synthetic Marijuana*, CBS New York (Aug. 6, 2015) (synthetic marijuana is "gaining popularity among the homeless in NYC because of its low-cost and availability").

⁷⁷ When the Commission lengthened sentences for MDMA, some Commissioners noted its use had been increasing in the preceding years, and hoped that by increasing penalties the Commission could help "nip the epidemic in the bud." See *MDMA Report*, at 6 (claiming that penalty levels chosen provide deterrence). But as noted above, there is no evidence of a deterrent effect from increased penalties, and the increases were never reversed in response to decreases in use.

⁷⁸ See Hofer, *supra* note 58; Reuter, *supra* note 73 (develops another type of risk ratio using as the denominator estimates of the total amount of methamphetamine and cocaine in circulation).

⁷⁹ See *August Letter*, at 7, Chart 1 (showing risk ratios and harms of various drugs).

The need for context data is apparent with a hypothetical example. Imagine two drugs whose use each result in five overdose deaths in a given year. Now imagine that one drug was used by just 100 people during that year, while the other was used by 100,000. The risk of overdose death for one drug is 1000 times greater than for the other—a fact clearly relevant to their comparative harm. A simple count of the number of overdoses caused by the two drugs fails to illuminate this crucial difference in lethality, and may create a false impression that the drugs are similarly harmful. Severely punishing traffickers of a drug used by millions, which rarely results in a problem outcome, would be as unfair as lenient treatment of traffickers of a rarely-used drug that nonetheless causes problems for a large portion of users. It also would promote disrespect for the law.

Unfortunately, little data are available on the use of synthetic cathinones or cannabinoids. The National Survey on Drug Use and Health, which provides the most comprehensive estimates of lifetime, past-year, and past-month use of a variety of legal and illegal drugs, does not ask about use of synthetic cathinones or cannabinoids.⁸⁰ Estimates of the size of the market for illicit drugs, prepared for the Office of National Drug Control Policy, are prepared only for cocaine, marihuana, heroin, and methamphetamine.⁸¹

The only prevalence information of which we are aware comes from the annual Monitoring the Future survey of adolescents. Beginning in 2012 this survey has asked 8th, 10th, and 12th graders enrolled in secondary school whether they used “bath salts” or synthetic marijuana in the past year.⁸² In recent surveys, the average percentage of 8th, 10th, and 12th grade students who reported using bath salts in the past year was 0.8 percent. The percentage using synthetic marihuana was 4.7 percent. Data from the Census Bureau indicates there were about 17 million adolescents enrolled in high school in the United States in 2011.⁸³ About 7% of high school age youth are not enrolled in school, making the total size of the high-school age population just over 18 million.⁸⁴ If we assume that the surveyed high school enrollees are reasonably representative of this population, we can estimate that about 145,000 high school-aged adolescents used bath salts at least once in recent years, and 854,000 used synthetic marihuana.

⁸⁰ See SAMHSA, *Results from the 2016 National Survey on Drug Use and Health: Detailed Tables* (2017), <https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.pdf>.

⁸¹ National Office of Drug Control Policy, *What America’s Users Spend on Illegal Drugs: 2000-2010* (Feb. 2014). https://obamawhitehouse.archives.gov/sites/default/files/ondcp/policy-and-research/wausid_results_report.pdf.

⁸² National Institute on Drug Abuse, *Monitoring the Future: 2016 Overview, Key Findings on Adolescent Drug Use*, tbl. 2.

⁸³ United States Census Bureau, *School Enrollment in the United States: 2011* 11, tbl. 3, <https://www.census.gov/prod/2013pubs/p20-571.pdf>.

⁸⁴ *Id.*, at 8.

Because some sense of the overall prevalence of use is crucial for evaluating reports of adverse reactions, it seems worthwhile to use this data to make a rough estimate of the overall use of bath salts and synthetic cannabinoids in the general population. According to the National Survey of Drug Use and Health, in 2011 about 38 million Americans age 12 and older used some type of illicit drug in the preceding year.⁸⁵ In that year, 4.177 million high school age youth were past-year illicit drug users, which is about 11 percent of the total population of past-year users.

Allowing for the possibility that synthetic drugs are somewhat more popular with high-school age users than illicit drugs in general, a rough but reasonable estimate is that high school age adolescents comprised between 10-20 percent of all past-year synthetic drug users in 2011. From the combined data, we can estimate that somewhere in the range of 725,000 to 1,450,000 people used bath salts in recent years, and between 4,270,000 and 8,540,000 used synthetic marijuana. This estimate, though far from perfect, nonetheless provides crucial context for the testimony and comment the Commission has received regarding potential adverse consequences of synthetic drug use.

Anecdotes Can Be Extremely Misleading. Some of the testimony offered at the Commission's October 2017 hearing raises concerns about how anecdotal information, without considering the broader context of use, may distort perception of the risk of new synthetic drugs. Witnesses from the Drug Enforcement Administration sought to dispel a "misconception" that NPS (new psychoactive substances) "carry a lower risk of harm."⁸⁶ They claimed that "published reports from law enforcement, emergency room physicians and scientists, accompanied with autopsies from medical examiners, have clearly demonstrated the harmful and potentially deadly consequences of using synthetic cathinones."⁸⁷ The testimony went on to claim that synthetic cathinones are "highly toxic" with severe adverse health effects.⁸⁸

The written testimony included five case studies, including a young man who died from cardiac arrest in a police car on the way to a hospital; another male who was pronounced dead upon arrival at a hospital in police custody; and another whose later death was ruled due to intoxication by *N*-ethylpentylone.⁸⁹ Our examination of several case studies involving synthetic

⁸⁵ SAMHSA, Types of Illicit Drug Use in Lifetime, Past Year and Past Month among Persons Aged 12 or Older: Numbers in Thousands, 2011 and 2012, <https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs2012/NSDUH-DetTabs2012/HTML/NSDUH-DetTabsSect1peTabs1to46-2012.htm#Tab1.1A>.

⁸⁶ Statement of Terrence Boos & Cassandra Prioleau Before the U.S. Sentencing Comm'n, Washington, D.C., at 2 (Oct. 4, 2017).

⁸⁷ *Id.*

⁸⁸ *Id.*

⁸⁹ *Id.* at 10-11.

cathinones indicates that identifying the precise role of the drug as a cause of death is often very difficult, with complications created by multiple drug use, de-hydration or over-hydration, environmental stress, and pre-existing conditions.⁹⁰

Another problem is that adverse reactions are most common among users who ingest amounts far exceeding typical doses. One of the witnesses at the recent hearing devoted most of her time to describing a case of multiple organ damage following ingestion of “bath salts.”⁹¹ The young man, who had *injected* an unknown amount of the especially potent MDPV, required lengthy hospitalization, including dialysis, before eventual recovery. The published report of the case notes: “It is unknown whether these end-organ effects were due to direct cellular toxicity induced by MDPV or a result of the patient's marked agitation and hyperthermia.”⁹² Other case reports similarly note that ingestion of extremely large amounts can lead to adverse consequences. One subject was reported to have ingested a “tea bag” amount of methylone, which would be about ten times the typical dose.⁹³

Synthetic cathinones, especially when consumed in large amounts, can undoubtedly contribute to a variety of dangerous health consequences. The problem with relying on such information to determine drug harms is that many substances, both legal and illegal, including alcohol and over-the-counter analgesics can cause such health effects. One researcher found that ten times the typical dose of alcohol, if taken quickly on an empty stomach, is potentially lethal, as recent cases of “hazing” deaths due to alcohol poisoning confirm.⁹⁴ Even water can kill you if over-indulged.⁹⁵ If the Commission were to set penalties for drugs based on the most extreme

⁹⁰ See, e.g., Katalin Kovacs et al., *A New Designer Drug: Methylone Related Death*, *Orvosi Hetilap* 153, 271-76 (Feb. 2012),

https://www.researchgate.net/publication/221817471_A_new_designer_drug_Methylone_related_death; AJ Dickson et al., *Multiple-Drug Toxicity Cause by the Coadministration of 4-Methylmethcathinone (mephedrone) & Heroin*, 34 *J. Anal. Toxicol.* 162-68 (Apr. 2010); PD Maskell, *Mephedrone (4-methylmethcathinon)-Related Deaths*, 35 *J. Anal. Toxicol.* 188-91 (Apr. 2011).

⁹¹ Testimony of Heather Borek Before the U.S. Sentencing Comm’n, Washington, D.C. (Oct. 4, 2017), <https://www.ussc.gov/education/videos/public-hearing-october-4-2017>.

⁹² Heather Bortek & Christopher Holstege, *Hyperthermia and Multiorgan Failure After Abuse of “Bath Salts” Containing 3,4-Methylenedioxypyrovalerone*, 60 *Annals of Emergency Medicine* 103-105 (2012).

⁹³ C. Boulanger-Gobeil, et al., *Seizures and Hyponatremia Related to Ethcathinone and Methylone Poisoning*, 8 *J. of Med. Toxicology* 59 (Mar. 2012).

⁹⁴ Robert S. Gabel, *Comparison of Acute Lethal Toxicity of Commonly Abused Psychoactive Substances*, 99 *Addiction* 686-696 (2004)

⁹⁵ Shawn Radcliffe & Stephanie Watson, *What is Overhydration* (2017), <https://www.healthline.com/health/overhydration#overview1>.

examples of the health consequences of overdoses, there would be little basis for differentiating among drugs, and every substance would be punished severely.

We strongly discourage the Commission from relying on anecdotal information or subjective impressions when assessing the harms of these or any drugs. We are especially dismayed at the lurid language used by some witnesses, who described over-heating caused by cathinone use as “boiling from the inside,”⁹⁶ or the behavior of some users of “flakka” as “zombies” who “run around naked.”⁹⁷ Commission experience with reports of “crack babies,” the neurotoxicity of MDMA, “meth mouth,” and other drugs described in the midst of media attention as the “worst drug ever,”⁹⁸ should result in healthy skepticism about impressions based on sensationalized news reports, or on the extreme cases—often involving multi-drug use or pre-existing health problems—that appear in emergency rooms or coroners’ reports.⁹⁹ Policy based on such examples can result in sentences that are too severe, but difficult to change.

Despite the dire warnings and lurid examples, the effects of synthetic cathinones “have not been thoroughly investigated.”¹⁰⁰ Unlike the research available for many other drugs, there are not

⁹⁶ USSC, *Public Hearing on Synthetic Cathinones* (Oct. 4, 2017).

⁹⁷ See, e.g., Transcript of Public Hearing Before the U.S. Sentencing Comm’n, Washington, D.C., at 156 (Apr. 18, 2017) (testimony of Osvaldo Tianga describing users of “flakka”—a synthetic cathinone—as “zombies” who run “around naked, acting very psychotic, paranoid”). See also Statement of Captain Osvaldo Tianga Before the U.S. Sentencing Comm’n, Washington, D.C., at 1 (Apr. 18, 2017).

A scholar who receives funding from the National Institute of Drug Abuse, however, has noted how “[s]tories of horrific crimes resulting from drug use have been propagated by the media for over a century,” and discusses how the adverse effects of flakka have been exaggerated. Joseph Palamar, *Flakka is a Dangerous Drug, But It Doesn’t Turn You into a Zombie*, The Conversation (Nov. 28, 2016), <https://theconversation.com/flakka-is-a-dangerous-drug-but-it-doesnt-turn-you-into-a-zombie-69533>. See also Natashia Swalve and Ruth DeFoster, *Framing the Danger of Designer Drugs: Mass Media, Bath Salts, and the “Miami Zombie Attack,”* 43 *Contemp. Drug Probs.* 103 (2016) (research finding that “media coverage of the Miami Zombie Attack framed a novel drug in incomplete and problematic terms” and “dramatically underrepresented the role of mental health in the attack and led to inadequately informed health legislation”).

⁹⁸ Former Drug “Czar” Barry McCaffrey described methamphetamine as “the worst drug that has ever hit America. A ferociously addictive drug that is spreading . . . It’s hard to imagine overstating the magnitude of the meth problem.” The Free Library, *Special Report on Methamphetamine* (October 2, 2000), [https://www.thefreelibrary.com/Special Report on Methamphetamine.-a065645163](https://www.thefreelibrary.com/Special+Report+on+Methamphetamine.-a065645163).

⁹⁹ *Cocaine Report 2002*, at 21-30.

¹⁰⁰ Public Hearing Before the U.S. Sentencing Comm’n, Washington, D.C. (Oct. 4, 2017) (Cassandra Prioleau, Ph.D.). The Congressional Research Service also reports that the National Office of Drug Control Policy considers synthetic cathinones such as methylone “understudied substances.” Congressional Research Service, *Synthetic Drugs: Overview and Issues for Congress* (May 3, 2016) (citing Office of National Drug Control Policy, *National Drug Control Strategy 2013*, at 10), <https://fas.org/sgp/crs/misc/R42066.pdf>.

adequate studies of the toxicity and disease burden of synthetic cannabinoids or cathinones,¹⁰¹ or of “safety”¹⁰² or “capture”¹⁰³ ratios, which compare drugs on the risk of overdose death and addiction. Prevalence of use data are only available for past-year use by high school students, which as noted above, provide a meager basis for estimating overall use.

Making the most of the limited public health data. The only public health data available for these new synthetic substances concern emergency room episodes in which the drugs were mentioned as a reason for the visit. The Substance Abuse and Mental Health Services Administration (SAMHSA) reported in 2013 that “bath salts” were mentioned in nearly 23,000 emergency room visits in 2011.¹⁰⁴ One third of the time, bath salts were the only substance mentioned, half the time bath salts were mentioned with other drugs other than marijuana, and 15 percent of the time bath salts were mentioned with marijuana or synthetic marijuana.¹⁰⁵ We can provide some context for this finding by using the past-year use estimate for bath salts discussed above. These 23,000 emergency room mentions were from an estimated population of between 725,000 to 1,450,000 past-year bath salt users. This yields a risk ratio for emergency room visits by past-year “bath salts” users of between .016 and .032.

SAMHSA also provided emergency room data for synthetic cannabinoids for 2010 and 2011. They reported that “[t]he number of emergency department (ED) visits involving synthetic cannabinoids increased significantly from 11,406 in 2010 to 28,531 visits in 2011.”¹⁰⁶ Synthetic cannabinoids were the only substance involved in between half and two-thirds of the visits in 2011, depending on the age of the patients. Again using the rough estimates described above of between 4,270,000 and 8,540,000 past-year users of synthetic cannabinoids, we obtain a risk

¹⁰¹ Jan van Amsterdam et al., *Physical Harm Due to Chronic Substance Use*, 66 Reg. Toxicology & Pharmacology 83-87 (2013).

¹⁰² Gabel, *supra* note 94.

¹⁰³ James Anthony et al., *Comparative Epidemiology of Dependence on Tobacco, Alcohol, Controlled Substances, and Inhalants: Basic Findings from the National Comorbidity Survey*, 2 Experimental and Clinical Psychopharmacology 244 (1994).

¹⁰⁴ SAMHSA, *The DAWN Report 1* (Sept. 17, 2013), <https://www.samhsa.gov/data/sites/default/files/spot117-bath-salts-2013/spot117-bath-salts-2013.pdf>. The Drug Abuse Warning Network, which collected data on drug-related emergency room visits was discontinued after 2011. Data on “bath salts” and synthetic cannabinoids from the replacement system do not appear to be available at this time.

¹⁰⁵ *Id.*

¹⁰⁶ SAMHSA, Donna M. Bush and David A. Woodwell, *Update: Drug-Related Emergency Department Visits Involving Synthetic Cannabinoids* (Oct. 16, 2014), <https://www.samhsa.gov/data/sites/default/files/SR-1378/SR-1378.pdf>.

ratio of between .003 and .007 for emergency room visits by past-year synthetic cannabinoid users.

Table 1: Emergency Room Risk Ratios 2011

| Substance | 2011 Past-year Users (in thousands)¹⁰⁷ | 2011 Emergency Room Mentions¹⁰⁸ | Risk Ratio ER/Past Year Users |
|------------------------|--|---|--------------------------------------|
| PCP | 119 | 75,538 | .635 |
| Heroin | 620 | 258,482 | .414 |
| Cocaine | 3,857 | 505,224 | .131 |
| Methamphetamine | 1,033 | 102,961 | .100 |
| “Bath Salts” | 725-1,450 | 23,000 | .016 - .032 |
| Marijuana/Hashish | 29,739 | 455,688 | .015 |
| MDMA | 2,422 | 22,489 | .009 |
| Synthetic Cannabinoids | 4,270-8,540 | 28,531 | .003 - .007 |
| LSD | 880 | 4,819 | .005 |

To put these risk ratios in context, Table 1 provides 2011 emergency room risk ratios for past-year users of various illegal drugs.¹⁰⁹ PCP and heroin put their users at far greater risk of an

¹⁰⁷ SAMHSA, *Results from the 2012 National Survey on Drug Use and Health: Detailed Tables*, tb. 1.1A, <https://www.samhsa.gov/data/sites/default/files/NSDUH-DefTabs2012/NSDUH-DefTabs2012/HTML/NSDUH-DefTabsSect1peTabs1to46-2012.htm#Tab1.1A>.

¹⁰⁸ U.S. Dep’t of Health and Human Services, *Drug Abuse Warning Network, 2011: National Estimates of Drug-Related Emergency Department Visits*, <https://www.samhsa.gov/data/sites/default/files/DAWN2k11ED/DAWN2k11ED/DAWN2k11ED htm#3.1>.

¹⁰⁹ This table is an adaptation of Table 6 from Hofer, *supra* note 58. For reasons explained in that paper, the number of past-month users makes a better denominator for the risk ratio. But the Monitoring the Future Survey on which the estimates of the number of 2011 users of “bath salts” and synthetic cannabinoids are based asked only about past-year use, so past year numbers were used for all drugs in this table. While the ratios are significantly reduced

emergency room visit than any other drugs. Cocaine and methamphetamine are in the next tier. “Bath salts” and synthetic cannabinoids are in the lowest risk tier, more similar in risk to marijuana and MDMA than to any of the other major drugs of abuse.

Obviously these risk ratio estimates for the synthetic drugs are based on extrapolations from limited data. We wish there were better prevalence estimates, and measures of other adverse outcomes, such as treatment episodes or overdose deaths. As was noted in testimony before the Commission, mislabeling and consumer confusion about drugs sold as “molly” or “ecstasy” means there may be overlap in the data for bath salts and MDMA. Tablets and powders sold as “ecstasy” may have synthetic cathinones as a major ingredient. Counts of emergency room mentions depend on the verbal reports of patients concerning the substances they have ingested, and the patients simply may not know.

Nonetheless, we believe these data provide important context that can help correct any misperceptions created by single case studies and anecdotes. The data should help assure Commissioners that, while potentially very harmful when abused, it is very unlikely that these synthetic drugs are among the most harmful controlled substances in circulation. In terms of the risk of a trip to the emergency room, these synthetic drugs are far less dangerous than PCP or heroin, and substantially less dangerous than cocaine and methamphetamine.

IV. The Commission Should Address Synthetic Cannabinoids and Cathinones by Amending Application Note 6 and Correcting Current Problem Equivalencies Rather than Adopting Set Ratios or a Class-Based Approach.

The Commission requests comment on whether, and if so, how the guidelines should be amended to account for synthetic cathinones and cannabinoids. Defenders previously encouraged the Commission to modify Application note 6 to focus on direct harms¹¹⁰ and suggested that the Commission could adopt a single ratio for synthetic cathinones.¹¹¹ After further research and considering that these drugs have different potencies, we believe the best option is to modify Application Note 6 and tailor its criteria to better promote proportionate sentencing.

A. Modify Application Note 6 to §2D1.1.

The first two prongs of the test in Note 6 closely track the definition of “controlled substance analogue” in 21 U.S.C. § 802(32)(A). As noted in the attached statement of Dr. Anthony P DeCrapio, serious questions have been raised about the validity of these criteria, even for the

with this method (due to larger numbers of past-year users) the overall ordering of different substances was not greatly affected.

¹¹⁰ *March Letter*, at 15-20.

¹¹¹ *August Letter*, at 20.

definition of an analogue, and an expert panel was established to focus on how to evaluate controlled substance analogues.¹¹²

We recommend deleting the first two prongs from Note 6. The first prong directs courts to consider whether the unlisted substance “has a chemical structure that is substantially similar” to a listed substance. We believe this criterion is responsible for much of the highly technical expert testimony in these cases, but that it is largely unhelpful for determining the appropriate equivalency. Determinations of substantial similarity based on molecular structure are subjective and disagreements among experts are common.¹¹³ Moreover, given current scientific knowledge, the relationships between molecular structure, psychopharmacological effects, and the important matter of a substance’s potency are highly uncertain. Of course, molecular structure affects a substance’s psychopharmacological effects and potency, and ultimately its potential harms, but we believe those issues are better addressed directly.

The second prong directs courts to consider “the stimulant, depressant, or hallucinogenic effects on the central nervous system.” Psychoactive substances affect the “nervous system” —different brain areas, neuron types, and the activity of neurotransmitters—in complex ways that are subject to active investigation but remain poorly understood. The terms “stimulant, depressant, or hallucinogenic” refer less to a drug’s effects on the “nervous system” than to the drug’s behavioral manifestations and the subjective experience of taking the drug. Unfortunately, test tube investigation, for example, into a drug’s binding affinities, or even animal studies using classical discrimination and reinforcement methods, are unreliable guides to a drug’s effects and harmfulness to humans.

Note 6 should instead focus more on how novel substances are used, their relative potencies, and most important, their medical and public health harms.

The third prong of Note 6 takes a step in the right direction. This prong departs from the statutory definition of analogues and directs judges’ attention to relative potency: “(C) Whether a lesser or greater quantity of the controlled substance not referenced in this guideline is needed to produce a substantially similar effect . . .” As described in comments submitted earlier this year, Defenders believe more consistent attention to different drugs’ potency and typical dosage

¹¹² Declaration of Anthony P. Decaprio, *United States v. Lane*, No. 2:12-cr-01419-DGC) (D. Ariz.-Phoenix April 8, 2013) (attached as Appendix A).

¹¹³ *Id.* See also Linda Jackson, Va. Dep’t of Forensic Science, *Presentation: SWGDRUG Draft Recommendations on Analogues and Structural Class Determinations* at National Institute of Standards and Technology Emerging Trends in Synthetic Drugs Workshop (May 1, 2013) (noting that “[e]valuation of similarity is a subjective matter and opinions may differ”), <https://www.nist.gov/sites/default/files/documents/oles/00-Day-2-Drug-Workshop-Handouts-scan-combined.pdf>.

amounts is essential for rationalizing and improving the DQT and DET.¹¹⁴ We therefore agree with this part of Note 6 and appreciate the Commission's recognition of the importance of potency. But the current Note needs to be clarified and strengthened to ensure that judges understand, appreciate, and consistently take account of potency when determining equivalencies.

As noted above and discussed further below, judges have sometimes decided, at the government's urging, that the "most closely related substance" to synthetic cannabinoids sprayed on inert plant material is *pure* THC, and have equated one gram of "Spice" or "K2" with one gram of pure THC and 167 grams of marijuana. This makes clear that the current note is inadequate for ensuring the proper consideration of potency and for avoiding gross disparities and injustice.

B. A Class-Based Approach Is Not Workable.

Because of the importance of potency, we do not think that a categorical or "broad class-based approach" is possible for either synthetic cathinones or cannabinoids because of the substantial variation in potency of different substances within each class. Of course, particular users' dosage amounts vary based on many factors unrelated to the drug itself, including the user's body weight, any developed tolerance, mode of ingestion, and desired intensity and length of intoxication. But as noted previously, it is impossible to make sense of the different thresholds and ratios in the statutes and guidelines for drugs such as LSD or the plant khat without recognizing the importance of potency.

Another highly important factor affecting dosage size is the purity of the drug, i.e., how much it has been diluted, mixed with, or sprayed onto inactive ingredients. As we have noted many times over the years, one of the biggest problems of the current drug statutes and guidelines is inclusion of the weight of any "mixture or substance containing a detectable amount of the controlled substance" when assigning base offense levels in the DQT. Defenders find it troubling that the Commission has never explained to Congress how this rule makes rational sentencing based on drug type and quantity impossible, and has never recommended changes to the statutes, or amended the guidelines to adopt a standardized approach for all drugs as it does for LSD. The irrationality of directing judges' attention to drug potency, while simultaneously ignoring drug purity, may help explain some judges' indifference to potency, despite the third prong of Note 6. The manner in which the guidelines address potency and purity is incoherent.

Despite the many factors that can affect a particular user's preferred dosage, researchers have developed a concept of "typical effective dose." This has been described as "the estimated

¹¹⁴ *March Letter*, at 6-12.

quantity for an average healthy 70-kg human who has not developed tolerance to the substance, who does not have residues of the substance in the body from previous administrations.”¹¹⁵ In addition, users compare notes and report common dosages for different drugs on websites such as The Vaults of Erowid¹¹⁶ and PsychonautWiki.¹¹⁷ These provide a crowdsourced resource on typical dosage sizes.

These resources make clear that the particular substances within the broad category of synthetic cathinones and cannabinoids vary dramatically in common dosage amounts. For example, the cannabinoid page of PsychonautWiki includes a list of natural and synthetic compounds with links to pages that provide dosage amounts ranging from “threshold” to “common” to “heavy.”¹¹⁸ Common pure dosages for smoked synthetic cannabinoids range from 1-2 mg for THJ-2201 to 5-10 mg for JWH-073—a difference of a factor of five. Similarly, the substituted cathinone page lists substances with common pure oral dosages ranging from 5-10 mg for alpha-PHP to 150-250 for Mexadrone—a difference of a factor of 30.¹¹⁹

The Drug Enforcement Administration also has recently acknowledged that “[e]ach synthetic cannabinoid variety has differing effects, potencies, and toxicities”¹²⁰ and that the “constantly changing [synthetic drugs] on the markets pose differing levels of harm to users.”¹²¹

Given the wide dosage ranges and varying harms, we do not believe a categorical approach can avoid unwarranted disparities and ensure individualized sentencing that takes proper account of the relative potency and harmfulness of the particular substances trafficked by a particular defendant. Rather than impose crude and false equivalency, based on the limited research now available on these substances, we believe the Commission should clarify the importance of potency by revising Note 6, with the aim of achieving similar treatment for similar numbers of doses of similarly harmful drugs.

Correcting problem equivalencies: cathinones. As described earlier, sound guideline recommendations for these synthetic substances cannot be achieved by equating them to listed

¹¹⁵ Robert S. Gabel, *Comparison of Acute Lethal Toxicity of Commonly Abused Psychoactive Substances*, 99 *Addiction* 686, 690, tbl. 1., n. a (2004), <https://rgable.files.wordpress.com/2012/02/toxicity-addiction-offprint.pdf>.

¹¹⁶ <https://erowid.org/psychoactives/psychoactives.shtml>.

¹¹⁷ https://psychonautwiki.org/wiki/Psychoactive_substance_index.

¹¹⁸ <https://psychonautwiki.org/wiki/Cannabinoid>.

¹¹⁹ [https://psychonautwiki.org/w/index.php?title=Substituted_cathinone&_ = .](https://psychonautwiki.org/w/index.php?title=Substituted_cathinone&_=)

¹²⁰ 2017 *National Drug Threat Assessment Summary*, at 118.

¹²¹ *Id.* at 123.

substances that are sentenced improperly under the current guidelines. In the case of synthetic cathinones, based in part on the questionable first two criteria in Note 6, courts have most often found that MDMA is the most similar listed substance. Some courts and prosecutors have properly noted that typical dosage amounts for a synthetic like methylone are twice as large as for MDMA, and have adjusted the marihuana equivalency by reducing the marihuana equivalency by half, from 500 gms per gram of cathinone to 250 gms.¹²² But, as described in detail in our August comment, the marihuana equivalency for MDMA is grossly excessive, so equating methylone to it, even with a dosage adjustment, does not lead to sound sentence recommendations.¹²³

Methcathinone is a synthetic cathinone already listed in the DET, with an equivalency of 1 gm methcathinone to 380 gm marihuana. As noted in Dr. Dudley's testimony,¹²⁴ several other cathinones are Schedule IV and V substances, which would appear to qualify for a marihuana equivalency of .00625 gm., although some courts have held that Schedule IV and V substances cannot be the "most closely related substances" despite the equivalency provided in the DET.¹²⁵

For reasons not explained in the guidelines or elsewhere, the plant khat (with active ingredients that include natural cathinone, cathine, and norephedrine) is given an equivalency of .01 gm marihuana per gm of khat. This means it takes 38,000 grams of khat to have the same 380 gm marihuana equivalency of 1 gm of methcathinone. Given the range of concentrations of cathinone in khat reported in the literature,¹²⁶ 38,000 grams of khat would contain between 13,680 to 43,320 mg of cathinone (ignoring the other active ingredients). Assuming a typical

¹²² *August Letter*. at 18 and n.72.

¹²³ *Id.* at 6-18.

¹²⁴ Statement of Gregory Dudley, Ph.D., Before the U.S. Sentencing Comm'n, Washington, D.C., at 4 (Oct. 4, 2017).

¹²⁵ *See, e.g., United States v. Giggey*, 867 F.3d 236, 241 S (1st Cir. 2017) (citing *United States v. Brewer*, 2016 WL 3580614, at *11 (D. Me. June 28, 2016) (J. Woodcock) (holding that only a Schedule I or II controlled substance can be considered the most closely related drug to a controlled substance analogue not referenced in the guidelines)); *Treiu Thuy Duong v. United States*, 2017 WL 4310216, at *7 (MD. Pa. Sept. 28, 2017).

¹²⁶ Wabe, *supra* note 69.

dose of 150 mg of cathinone,¹²⁷ 38,000 grams of khat yields between 91 and 289 doses of cathinone. One gram of methcathinone typically yields 6-7 common doses.¹²⁸

We question whether there is any logic behind these equivalencies in the guidelines. Especially given the current excessive marijuana equivalency for MDMA, it might appear that methcathinone should be the most closely related substance to other synthetic cathinones of ordinary potency. But methcathinone is also punished excessively compared to khat, the natural substance on which the synthetic cathinones are based. We conclude that the equivalences for MDMA and natural and synthetic cathinones listed in the current DET *provide no sound guidance regarding the proper equivalence for unlisted synthetic cathinones.*

Rather than base synthetic cathinone equivalencies on a hopelessly flawed foundation, we recommend turning instead to data on relative harmfulness of all drugs, including those already listed in the DET. The data reviewed above show that synthetic cathinones are far less harmful than PCP or heroin, and significantly less harmful than methamphetamine or cocaine. Both powder cocaine and synthetic cathinones are typically “keyed” or “snorted.” According to Psychonautwiki, typical dosage sizes for insufflated cocaine are 30 to 50 percent *smaller* than for the common synthetic cathinones methcathinone and methylone. If the Commission chooses to adopt a class-based approach, the available data show that a *reasonable equivalence for common synthetic cathinones would be half that of cocaine: 1 gm cathinone to 100 gms marijuana.*

Correcting problem equivalencies: THC and cannabinoids. Our March comment detailed severe problems with the marijuana equivalencies for THC and why the Commission should change the ratio.¹²⁹ The DET provides an equivalency for either organic or synthetic THC of 167 grams of marijuana per 1 gram of THC. The origin and basis for this equivalency is unknown, but current research shows that it is wildly off the mark in terms of the pharmaceutical equivalency between pure THC and marijuana. For a given amount of marijuana to contain a similar dose of THC under this equivalency, the marijuana would need to contain about 0.6 percent THC. The University of Mississippi’s Potency Monitoring Project tests marijuana seized

¹²⁷ See PsychonautWiki (identifying dosage amounts for various synthetic cathinones), [https://psychonautwiki.org/w/index.php?title=Substituted_cathinone&_ =](https://psychonautwiki.org/w/index.php?title=Substituted_cathinone&_=). Common oral dosages range from 5-10 mg for the most potent alpha-PHP to 150-250 mg for mextedrone. The most typical lowest common dosage size is 150 mg. *Id.*

¹²⁸ We have not found comparative data on common dosage sizes specifically for methcathinone, so we again use the most typical lowest common oral dosage of 150 mg. One report describes 280 mg taken orally as a high dose. <https://erowid.org/experiences/exp.php?ID=66893>. Other reports involved 20- 50 mg insufflated. <https://erowid.org/experiences/exp.php?ID=33366>; <http://www.bluelight.org/vb/threads/145111-Methcathinone-First-Time-Goofy-Speed> Insufflated doses are typically less than half oral doses. *See also* <https://erowid.org/experiences/exp.php?ID=33366> (reporting dosages ranging from 10 to 200 mg at a time).

¹²⁹ *March Letter*, at 32.

by the DEA in all 50 states, using a validated gas chromatography with flame ionization detector method. While the potency of different marihuana strains differs significantly, the average potency in 2014 was about 12 percent.¹³⁰ Other studies show that the “average THC content in marijuana today is over 14 percent.”¹³¹

This means that to similarly punish THC and marihuana crimes that yield similar numbers of doses for the most typical potencies of marihuana, the equivalency between THC and marihuana should be about 7 or 8 grams of marihuana per 1 gram of THC, not 167 grams.¹³² Under the current equivalencies, THC defendants are sentenced as if they trafficked in amounts of marihuana about 21 to 24 times too large. *The marihuana equivalency for organic and synthetic THC in the DET should be radically reduced.*

Incredibly, the government has argued, and many courts have found, that this excessive marihuana equivalency for pure THC should be applied to synthetic cannabinoids, *even when sprayed on inert plant material.*¹³³ Different brands, and even batches of the same brand, of smokable synthetic cannabinoids can vary significantly in potency. We believe a revised Note 6 should alert judges to consider these variations when determining the appropriate equivalency. Research has shown that concentrations of synthetic cannabinoids in “spice” and similar mixtures are typically in the range of one to two percent by weight. This means the current marijuana equivalency for THC, when used in “spice” cases, equates one dose of synthetic cannabinoid to between 1000 to 2000 doses of marihuana.

The variety of synthetic cannabinoids is daunting and research on their pharmacological properties is incomplete. Some test tube and animal research suggests that some synthetic cannabinoids are significantly more potent in their pure form than pure THC.¹³⁴ On the other hand, the concentration of synthetic cannabinoids in the organic products on which they are diffused is often much less than the concentrations of organic THC in marihuana. This makes

¹³⁰ Mahmoud A. ElSohly et al., *Changes in Cannabis Potency Over the Last 2 Decades (1995–2014): Analysis of Current Data in the United States*, 79 *Biological Psychiatry* 613 (2016).

¹³¹ *United States v. Hossain*, 2016 WL 70583, at *6 (S.D. Fla. Jan 5, 2016).

¹³² *See id.* (finding that THC ratio should be one to seven). *See also* Statement of Gregory Dudley, Ph.D. Before the U.S. Sentencing Comm’n, Washington, D.C. at 2 (Apr. 18, 2017) (recommending 1:7 ratio).

¹³³ *See* Brad Gershel, *Sentencing Synthetic Cannabinoid Offenders: “No Cognizable Basis”*, 54 *Am. Crim L. Rev.* 50 (2017).

¹³⁴ Brian Burrows et al., *Synthetic Cannabinoids: a Summary of Selected Phenomena With Respect to Behavioral Pharmacology and Abuse Liability in Handbook of Cannabis and Related Pathologies* 691–99 (2017); Marisol Castaneto, et al., *Synthetic Cannabinoids: Epidemiology, Pharmacodynamics, and Clinical Implications*, 144 *Drug Alcohol Depend.* 12-41 (2014).

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recommending a precise marihuana equivalency appropriate for all forms of synthetic cannabinoids especially problematic.

The most important reforms are: 1) reduce the marihuana equivalency for THC; and 2) amend the commentary to make clear to judges that equating highly diluted synthetic cannabinoid to pure THC is not appropriate. Given the variety of synthetic cannabinoids, and their inconsistency in potencies and concentrations, we believe the best approach would be to begin with a presumption that the proper equivalency for a smokable synthetic cannabinoid sprayed onto psychologically inactive organic matter *is marihuana itself* on a one to one basis. Revised commentary to Note 6 can alert judges to take account of concentrations or substances that make a particular synthetic marihuana more potent than is typical of organic marihuana.

V. Conclusion

As always, we appreciate the opportunity to submit comments on the work of the Commission. We look forward to continuing to work with the Commission on important matters including those related to the fair and just sentencing of individuals convicted of federal drug offenses.

Very truly yours,

/s/ Marjorie Meyers

Marjorie Meyers

Federal Public Defender

Chair, Federal Defender Sentencing Guidelines Committee

cc : Rachel E. Barkow, Commissioner
Hon. Charles R. Breyer, Commissioner
Hon. Danny C. Reeves, Commissioner
Zachary Bolitho, Commissioner *Ex Officio*
J. Patricia Wilson Smoot, Commissioner *Ex Officio*
Kenneth Cohen, Staff Director
Kathleen Cooper Grilli, General Counsel

APPENDIX A

**UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF ARIZONA**

United States of America,
Plaintiff,

Court File No.: CR-12-1419 PHX DGC

-vs-

Michael R. Lane, et.al.

DECLARATION OF ANTHONY P. DECAPRIO

State of Wisconsin }
County of Dane }ss

The undersigned, first being duly sworn, states upon oath:

1. Background and Qualifications: My name is Anthony P. DeCaprio. I am an Associate Professor of Chemistry and Biochemistry and serve as the Director of the Forensic and Analytical Toxicology Facility and the Forensic Science Certificate Program for the International Forensic Research Institute at Florida International University. I received a B.S. degree in biology from Rensselaer Polytechnic Institute in 1975 and a Ph.D. in toxicology from Albany Medical College in 1981. I worked as a research toxicologist with the New York State Department of Health, Wadsworth Laboratories from 1981 to 1995. Since then, I have served in academic appointments at UAlbany and UMass Amherst prior to joining FIU in 2008.

I have 30+ years of professional scientific experience in the fields of chemistry and analysis of drugs, analytical/forensic toxicology, neurotoxicology of drugs and chemicals, and biomarkers of drug and chemical exposure. I have published over 70 original research papers in peer-reviewed journals, written several chapters for reference works in toxicology, and edited a book on biomarkers in toxicology. I provide expert peer-review services for numerous journals and funding agencies. I have delivered more than 80 research papers and invited lectures at universities, conferences, and private-sector companies. I am Certified in General Toxicology by the American Board of Toxicology and am a full member of the Society of Forensic Toxicologists and Society of Toxicology. I regularly teach undergraduate and graduate courses in analytical chemistry and forensic toxicology. I have performed extensive research on α -PVP, MDPV, MDMA, and other “designer drugs” of the phenethylamine and cathinone class. My qualifications and experience are detailed in my curriculum vitae, which is attached.

Below I explain my opinions regarding the analogue status of **α -pyrrolidinovalerophenone (α -PVP)** under Title 21 U.S.C. §802(32)(A).

2. General Opinions Regarding DEA Drug Analogue Scheduling Based on “Structural Similarity”:

The first criterion (*i.e.*, “Prong 1”) for inclusion of a compound as a controlled substance analogue is defined by Title 21 U.S.C. §802(32)(A) as a substance: *(i) the chemical structure of which is substantially similar to the chemical structure of a controlled substance in Schedule I or II.* Since no definition of “substantially similar” is provided in the statute or other regulations, the determination of whether or not two compounds fulfill this criterion is subject to variable interpretation, perspective, and opinion and is therefore a subjective process. The process is most subjective if it involves only simple comparisons of two-dimensional (2D) drawings of the structures, which is the basis of the method currently used by DEA. In their approach, considerations of similarity involve only judgments as to whether the molecules have the same “core structures” and of the relative importance of additional chemical groups attached to the core structure in terms of imparting either “similarity” or “difference”. For the most part, in their available Analogue Status documents the Agency appears to minimize the structural significance of any modifications to the core structure. In my opinion, no qualified chemist would rely upon such cursory comparisons in providing a judgment regarding structural similarity, as they are not based on testable scientific assumptions.

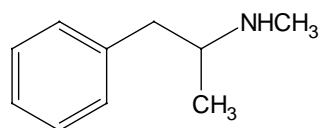
Three-dimensional (3D) drawings, models, or other depictions provide much more structural information than 2D drawings. This is because 3D representations allow for at least some understanding of how the molecule appears in space, *i.e.*, where each part of the molecule is located in comparison to other regions of the molecule. In virtually all cases, the 3D orientation of the compound governs how (and if) a drug interacts with a biological receptor. In the case of drugs of abuse, it is this interaction that determines whether the drug will have psychotropic properties and, if so, what they are. In contrast, 2D diagrams of molecules show atomic connections but not shape and represent an oversimplification of the true structure. Therefore, particularly when communicating with non-chemists, 2D structures can be misleading and inaccurate.

While 3D depictions are certainly more useful than 2D drawings in comparing the structures of two potential drug molecules, “similarity” can only be objectively determined by the use of mathematical models that employ computational chemistry techniques. Such models compare many physical and chemical properties of two drugs to provide a quantitative estimate of their relative similarities and differences. For example, the “Tanimoto score”, which is a relatively simple computational model, has been used for a number of years to compare similarity of chemical entities. This model takes as data input the 2D or 3D “chemical fingerprints” of two molecules and then calculates a similarity score. Even such a basic model is far preferable to simple visual inspection and subjective judgment for assessing structural similarity. In contrast, most models currently used by pharmaceutical companies to judge molecular similarity are

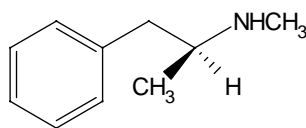
considerably more complex, sophisticated, and reliable.

The DEA approach is also flawed in that it assumes that the more similar the chemical structure, the more similar the pharmacological activity of a pair of drugs. While this assumption may be intuitive and true in a very general way, examples of very minor structural changes, at least as judged by 2D drawings, that are associated with inactivity or substantially different activity of the modified (but still structurally similar) drug are common in pharmacology. An extreme example of this phenomenon involves the case of enantiomers, which are drugs that are mirror images of each other, *i.e.*, identical in 2D structure but differing only in the arrangement of groups attached to a single carbon.

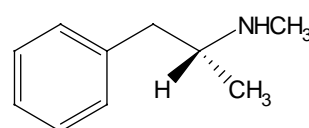
As an illustration, methamphetamine exists in two enantiomeric forms, dextromethamphetamine and levomethamphetamine. The diagrams below show 2D and 3D representations of the molecules. In the 3D diagrams, the dark wedges indicate chemical bonds pointing out of the page while the dashed wedges indicate bonds pointing into the page. Dextromethamphetamine is a potent stimulant and dopaminergic drug, while levomethamphetamine is a much weaker stimulant with a different profile of biological activities. As is obvious from examination of the diagram, the 2D representations do not convey any structural differences between the molecules. Thus, two drugs that would legitimately be considered “substantially similar in structure”, and therefore analogues according to the DEA approach, can still have very different pharmacological effects.



methamphetamine 2D representation



3D “dextro” enantiomer

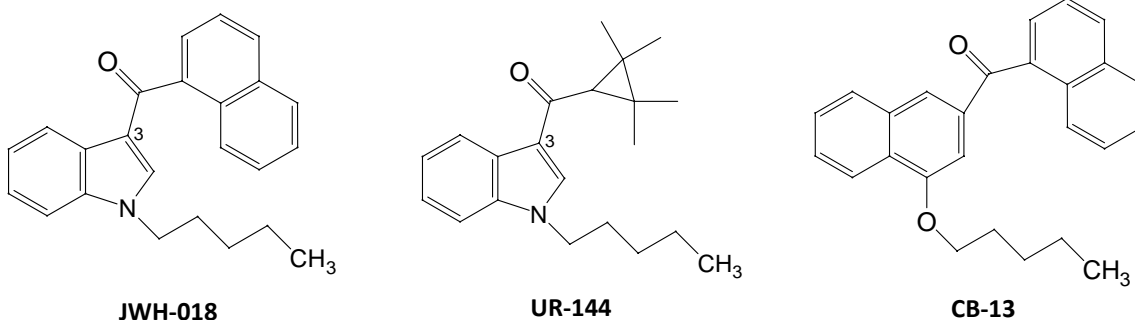


3D “levo” enantiomer

Interestingly, DEA has scheduled dextromethamphetamine in Schedule II, while levomethamphetamine is an over-the-counter drug in Schedule V.

There are other examples of inconsistencies in application of the structural similarity criterion of the analogue statute. The Agency considers the synthetic cannabinoid UR-144 to be an analogue of the Schedule I compound JWH-018, due to substantial similarity in structure (see below). In contrast, they consider the compound CB-13 as not substantially similar in chemical structure to JWH-018. In my opinion, neither of these compounds is similar enough to JWH-018 to fulfill the analogue criterion. The difference between JWH-018 and CB-13 can be related to the difference between pyrrole and phenol. Both pyrrole and phenol are flat, electron-rich aromatic rings, but pyrrole is a five-membered heterocycle (a ring containing at least one non-carbon atom) whereas phenol is larger and provides more conformational freedom to the attached alkyl

chain. Likewise, the difference between JWH-018 and UR-144 can be related to the difference between naphthalene and tetramethylcyclopropane. Both are hydrocarbons, but naphthalene is flat and aromatic whereas tetramethylcyclopropane is globular, aliphatic, and “strained” (*i.e.*, it has unusually weak carbon–carbon bonds). In my opinion (which is probably in agreement with that of the majority of chemists), the structural and chemical differences between JWH-018 and CB-13 are less than those between JWH-018 and UR-144, which is the opposite of DEA’s conclusion.



In summary, it is my opinion that the DEA approach to classifying drugs as analogues of Schedule I substances based on substantial similarity in chemical structure is not supported by valid and rigorous scientific principles. The DEA approach to analogue scheduling has been criticized by others (*e.g.*, see King *et al.*¹) and is currently being evaluated by an expert review panel (<http://www.druganalogs.org/mission.html>) seeking to recommend an objective scientific method for structural similarity assessment for drugs. Finally, this approach has not been subjected to formal peer-review, nor has it been assessed for reliability, both of which are normal (and vital) parts of the process of general acceptance by the scientific community.

3. General Opinions Regarding DEA Drug Analogue Scheduling Based on “Pharmacological Similarity”:

The second criterion (*i.e.*, “Prong 2”) for inclusion of a compound as a controlled substance analogue is defined by Title 21 U.S.C. §802(32)(A) as a substance: *(ii) which has a stimulant, depressant, or hallucinogenic effect on the central nervous system that is substantially similar to or greater than the stimulant, depressant, or hallucinogenic effect on the central nervous system of a controlled substance in Schedule I or II.*

The psychotropic effects of the cathinone class of drugs are due primarily to their action in affecting “transporter” molecules in the brain, specifically the dopamine, norepinephrine, and serotonin transporters (termed DAT, NET, and SERT, respectively). Inhibition of such transport molecules by competitive substrate binding or by induction of “reverse transport” by certain of these drugs may cause increased levels of these monoamine neurotransmitter molecules to occur

in brain synapses, thus leading to stimulatory, hallucinogenic, and/or euphoric effects on the central nervous system. In order to assess the ability of cathinones and related drugs to produce these effects, initial studies often employ measurement of binding affinity with the various transporter molecules and additional experiments to determine whether such drugs can release dopamine, norepinephrine, and/or serotonin from nerve cells. These experiments are performed *in vitro*, *i.e.*, in an artificial “test tube” system outside of a whole animal or human being.

The ability of a drug to bind to a specific receptor or transporter molecule can be measured by determining the K_i , the “equilibrium dissociation constant”. This parameter is defined as the concentration of the drug needed to occupy one-half (50%) of the specific binding sites at equilibrium. The smaller the value of K_i , the higher the affinity of the drug receptor. K_i values are often employed in drug development and other biomedical studies to provide some indication of how effectively a drug will (or will not) activate a particular receptor. This may (or may not) be correlated with a specific biologic, pharmacologic, or toxicologic effect. Thus, the appropriate use of such assays is only to indicate which compounds may be considered for further testing in either animal models or humans. In addition, there are significant problems with attempting to extrapolate *in vitro* binding or neurotransmitter release data determined for one drug to another untested, but chemically related compound. This is because small structural differences in drug molecules can lead to large changes in transporter or receptor binding affinity, thus potentially leading to major pharmacological differences. Specific examples of this phenomenon in the case of the cathinones are discussed later.

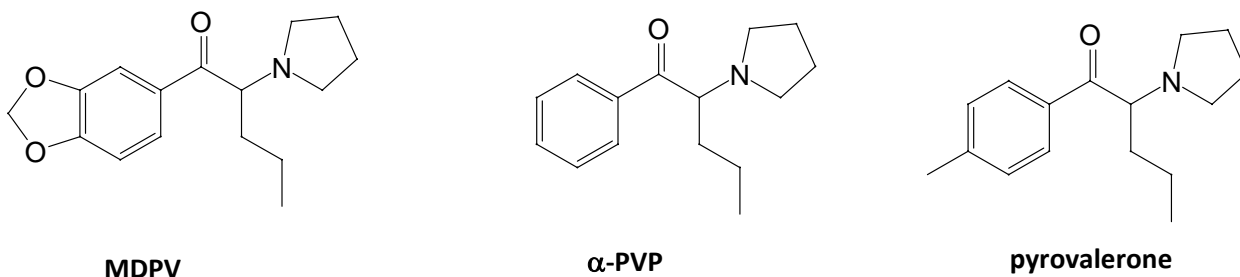
As it is impossible to predict with confidence how *in vitro* data will translate into pharmacological effects in living systems, the objective and accurate prediction of drug activity in humans based on *in vitro* data alone is unreliable. Thus, at the very least, a sound and reliable analogue drug scheduling approach should involve assessment of stimulant, depressant, or hallucinogenic effects in animal models, as corroborated if possible by existing human data. Prong 2 of the statute does, after all, specify that these effects be demonstrated “... *on the central nervous system...*”, a requirement that cannot be achieved by *in vitro* testing or structure-activity considerations alone.

4. Specific Opinions regarding the “Structural Similarity” of α -PVP and MDPV:

In his Declaration, Dr. DiBerardino states that α -pyrrolidinovalerophenone (α -PVP) is an analogue of the Schedule I substance methylenedioxypropylamphetamine (MDPV) based on structural similarity. While both compounds are considered to be cathinones due to the presence of the β -carbonyl group, there are structural differences between the molecules that are not insignificant. Specifically, MDPV contains the methylenedioxy functional group attached to the benzene group on the left-hand side of the molecule (see below) which is not present in α -PVP. While Dr.

DiBerardino states that this structural difference is “minor”, in my opinion it would likely impart structural and chemical characteristics to the molecule distinct from those of α -PVP. This is due to the presence of the two additional oxygen atoms in MDPV that would, among other effects, increase the relative polarity of the molecule. For example, α -PVP and MDPV (in addition to pyrovalerone) are readily separated using the technique known as gas chromatography. A widely accepted principle in basic chemistry is that structurally similar compounds are difficult to separate from each other by chemical or physical techniques such as gas chromatography. In contrast, easy separability is consistent with structural and chemical dissimilarity.

In my opinion, a stronger case for similarity (*i.e.*, using the DEA approach based only on 2D structural representation) might be made by comparing α -PVP with the drug pyrovalerone, which differs only by the presence of a single methyl group on the benzene ring (see below). While I would still consider such a simple comparison scientifically unsound, DEA has placed pyrovalerone in Schedule V, a decision that is clearly inconsistent with their determination for α -PVP (and many other related drugs). Such inconsistencies suggest a lack of sound scientific basis for their determinations based on analogue comparisons.



5. Specific Opinions Regarding the “Pharmacological Similarity” of α -PVP and MDPV:

In her Declaration, Dr. Prioleau states that α -PVP is likely to have substantially similar pharmacological effects as MDPV. Her opinion is primarily based on the results of *in vitro* (*i.e.*, test tube) studies examining transporter binding affinities and other related parameters associated with potential increases in monoamine neurotransmitter levels. The only peer-reviewed, published study where α -PVP was directly tested in such an assay is that by Meltzer *et al.*², where its affinity for DAT, SERT, and NET was compared to a variety of other pyrovalerone type drugs (but not including MDPV). None of the other peer-reviewed articles cited in the Declaration include actual data for α -PVP itself. However, the Meltzer paper does report that α -PVP exhibited similar affinity to DAT and NET as was observed for pyrovalerone, which, as discussed previously, is a DEA Schedule V compound. Furthermore, Dr. Prioleau cites NIDA data that are unpublished, have not been subjected to peer review, and are not generally available to the scientific community. Such data cannot be used to support an opinion that purportedly has an objective scientific basis.

Data presented in a recent paper not cited by Dr. Prioleau (Simmler *et al.*)³ demonstrated that MDPV exhibited relatively potent binding to DAT and NET, but not to SERT. In contrast, the structurally related cathinones ethylone and butylone were relatively poor binders for DAT and NET while exhibiting higher affinity for SERT. As another example of the generally poor correlation between chemical structure and receptor binding affinity, Meltzer *et al.* reported that their compound designated as O-2512, which bears some structural similarity to MDPV, exhibited poor affinity for all three receptors. In summary, when the bulk of available data are considered it becomes apparent that even small structural differences among related drugs can result in large differences in relative receptor affinity and other related parameters as measured by *in vitro* assays. This makes the scientifically objective and accurate prediction of psychotropic drug activity in humans based on *in vitro* structure-activity data alone an unreliable process.

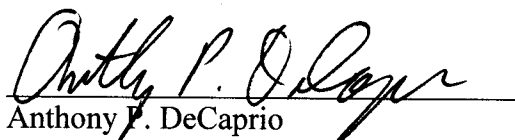
In contrast to the limited *in vitro* data discussed above, there are no *in vivo* data (*i.e.*, data collected from either experimental animal or human studies) available with which to objectively assess the potential pharmacological effects of α -PVP. Without such data, it is my opinion that classification of α -PVP as an analogue of MDPV or any other controlled substance based on a purported substantial similarity in psychotropic effect is not scientifically supportable.

¹King, L.A., Nutt, D., Singleton, N., and Howard, R. (2012). Analogue controls: An imperfect law. *Report by the UK Drug Policy Commission; Independent Scientific Committee on Drugs.*

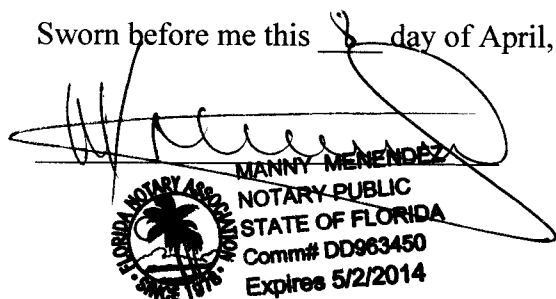
²Meltzer, P.C.; Butler, D.; Deschamps, J.R.; Madras, B. K. (2006). 1-(4-Methylphenyl)-2-pyrrolidin-1-yl-pentan-1-one (pyrovalerone) analogues: A promising class of monoamine uptake inhibitors. *J. Med. Chem.* **49**, 1420-1432.

³Simmler, L.D.; Buser, T.A.; Donzelli, M.; Schramm, Y.; Dieu, L.H.; Huwyler, J.; Chaboz, S.; Hoener, M.C.; Liechti, M.E. (2013). Pharmacological characterization of designer cathinones in vitro. *Br. J. Pharmacol.* **168**, 458-470.

Further Declarant sayeth not


Anthony P. DeCaprio

Sworn before me this 8 day of April, 2013


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