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NOV 1 3 2017

The Honorable William H. Pryor, Jr.
Acting Chair
U.S. Sentencing Commission
One Columbus Circle, NE
Suite 2-500, South Lobby
Washington, DC 20002-8002

Dear Judge Pryor:

On October 11, 2017, the Commission published an issue for public comment on fentanyl and fentanyl analogues.1 The Drug Enforcement Administration is pleased to offer its perspective on these issues. Thank you in advance for considering our thoughts.

I. Chemistry of fentanyl and its analogues

Fentanyl is a powerful synthetic opioid that was first synthesized in Belgium during the late 1950s. Structurally, fentanyl belongs to the 4-anilidopiperidine class, which is a group of substances that have been well studied for their analgesic effects. Fentanyl analogues have chemical structures that are similar to that of fentanyl, but the chemical structure has been modified in specific locations. Some fentanyl analogues that have been identified in forensic evidence are found in the scientific and/or patent literature, which may also describe how to synthesize these substances.

The actual synthesis of fentanyl and fentanyl analogues requires some knowledge in synthetic organic chemistry. But, new fentanyl analogues can be designed easily and synthesized by using the same chemistry as that to make fentanyl and simply replacing one or more of the chemicals used in the synthetic process. For example, a group of fentanyl analogues (e.g., acetyl fentanyl, acryl fentanyl, butyryl fentanyl, furanyl fentanyl) can by synthesized from 4-anilino-N-phenethylpiperidine (4-ANPP), a Schedule II immediate precursor to fentanyl. The same idea can be, and has been, applied to other sections of fentanyl's chemical structure. Figure 1 shows one synthetic sequence to make fentanyl (there are several known synthetic routes). Using this pathway, different chemicals can be used to create structural modifications to the chemical structure of fentanyl. Some examples of these structural modifications (structures shown in Figure 2) have been highlighted in fentanyl-related substances recently controlled in the United States. Currently, there are 17 fentanyl-related substances controlled in

1 U.S. SENTENCING COMM'N, FEDERAL REGISTER NOTICE OF OCTOBER 2017 ISSUE FOR COMMENT, 82 Fed. Reg. 47322, https://www.ussc.gov/policymaking/federal-register-notices/federal-register-notice-october-2017-issue-comment.

Schedule I and besides fentanyl, five fentanyl-related substances are controlled in Schedule II, including their isomers, esters, ethers, salts, and salts of isomers, esters, and ethers.

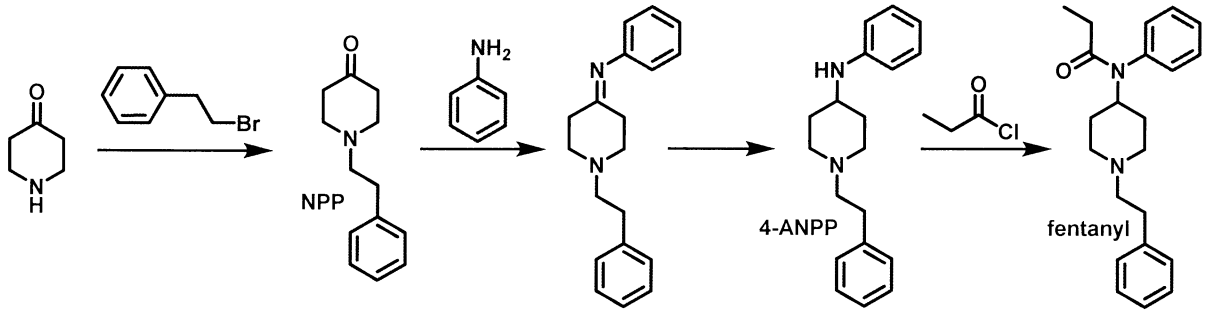

Figure 1: A General Synthetic Route to Fentanyl.

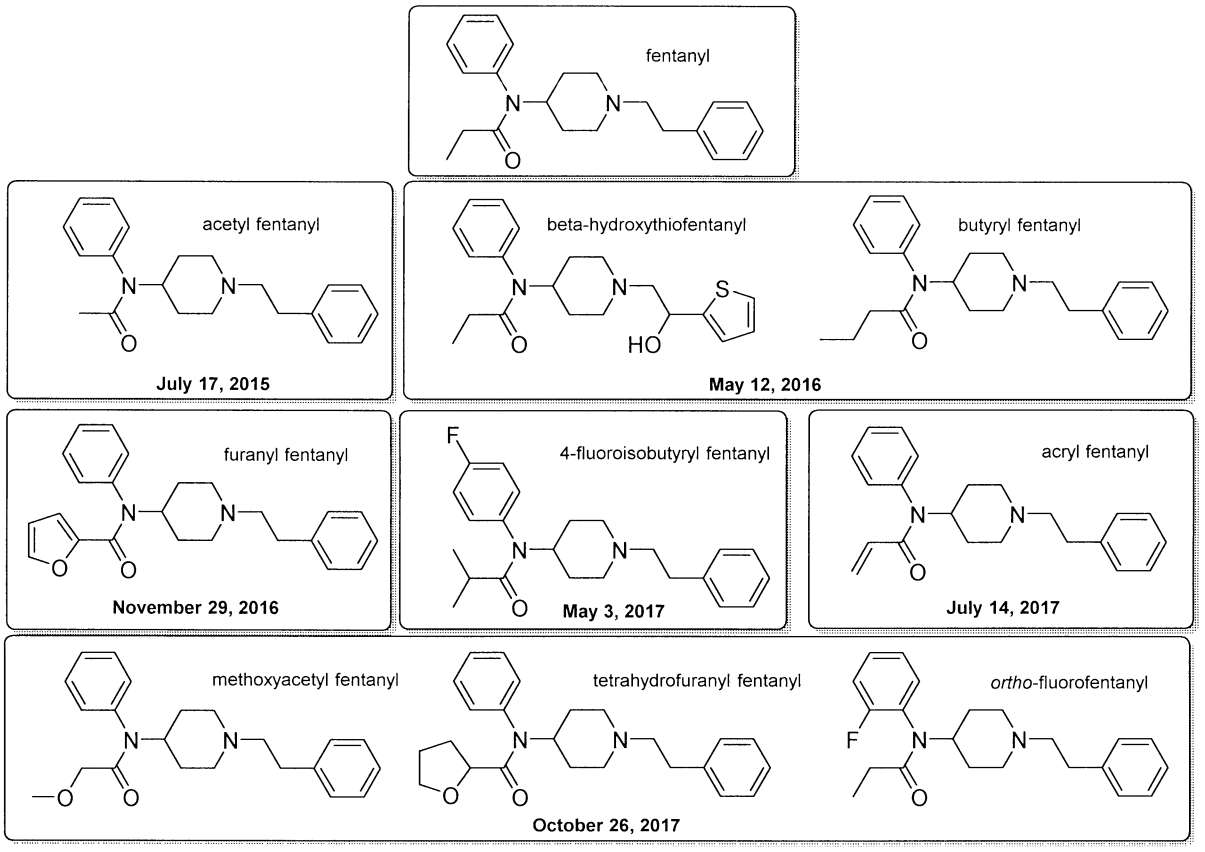

Figure 2: Examples of Fentanyl-related Substances Recently Controlled in the United States.[2,3]

2 The chemical structure of fentanyl is shown for reference.
3 July 17, 2015, 80 Fed. Reg. 42381; May 12, 2016; 81 Fed. Reg. 29492; November 29, 2016; 81 Fed. Reg. 85873; May 3, 2017, 82 Fed. Reg. 20544; July 14, 2017, 82 Fed. Reg. 32453; October 26, 2017, 82 Fed. Reg. 49504.

II. The U.S. Food and Drug Administration (FDA) approval of fentanyl and some of its analogues as pharmaceutical products for clinical use

Pharmacologically, fentanyl falls into a class of drugs known as "opioids." There are several varieties of opioids: natural (e.g., morphine, codeine); semisynthetic (e.g., oxycodone, hydrocodone, hydromorphone, oxymorphone); and synthetic (fentanyl, methadone, meperidine, tramadol). Opioids are commonly used by medical professionals to manage pain associated with various clinical conditions. Fentanyl was first introduced into medical practice as an injectable formulation in the early 1960s in Europe. In the United States, fentanyl was first approved as an injectable combination product (mixed with droperidol) in 1968. Four years later, a single-entity injectable formulation of fentanyl was approved for clinical use. Subsequently, various other formulations of fentanyl such as buccal tablets, transmucosal lozenges, transdermal films, sublingual spray and tablets, nasal spray, and transdermal iontophoresis, were approved by the FDA.

Upon the enactment of the Controlled Substances Act (CSA), fentanyl was placed in Schedule II due to its high potential for abuse and dependence and its approved medical use. Several other analogues of fentanyl, namely remifentanil, alfentanil, and sufentanil, also have been approved for medical use in the United States. Similar to fentanyl, these substances are also listed in Schedule II. Because of the risk for misuse, abuse, addiction, and overdose, marketing and clinical use of fentanyl pharmaceutical products are currently subject to an FDA-designated restricted program called Risk Evaluation and Mitigation Strategy (REMS). There are three different REMS programs that apply to fentanyl pharmaceutical products. Transmucosal fentanyl pharmaceutical products are only available through an FDA-designed restricted program called Transmucosal Immediate Release Fentanyl Risk Evaluation and Mitigation Strategy. Fentanyl transdermal formulations are subject to a program called Extended Release and Long-Acting Opioid Analgesics Risk Evaluation and Mitigation Strategy. Fentanyl iontophoretic transdermal system (IONSYS®) formulations are available through a program called IONSYS® Risk Evaluation and Mitigation Strategy, which is designed to mitigate the risks of respiratory depression resulting from accidental exposure.

Carfentanil, an analogue of fentanyl, has been approved for use in veterinary medicine to immobilize large animals (e.g., elephants). More recently, thiafentanil, another analogue of fentanyl, was approved for veterinary use for immobilization of captive non-food producing minor species of hoof stock. Both carfentanil and thiafentanil have been listed on Schedule II. Neither carfentanil nor thiafentanil have been approved in the United States for use in the medical treatment of humans.

It is important to point out that much of the fentanyl we are seeing on the streets today is not the pharmaceutical-grade fentanyl that is included in Schedule II. Rather, as explained in detail below, it is illicit and clandestinely manufactured fentanyl, as well as illicit and clandestinely manufactured fentanyl analogues.

III. Pharmacology of fentanyl and its analogues and other opioids

Scientific investigations have shown that strong opioid analgesics such as morphine, hydrocodone, and oxycodone produce pharmacological effects including euphoria, analgesia,

sedation, constipation, respiratory depression, and dependence. These effects are primarily achieved through activation of μ-opioid receptors, as opioids act as agonists at these receptors.[4] Fentanyl, and the clinically used analogues of fentanyl, are similar in their pharmacological effects to prescription opioid analgesics (e.g., oxycodone, hydrocodone, morphine) and heroin.

There are two main pharmacological effects of strong opioid analgesics that play a central role in understanding their adverse impact on public health: (1) opioid analgesics activate the reward pathways in the brain, thus producing intense euphoria and making them a highly addictive class of drugs; and (2) in high doses, opioid analgesics consistently depress the body's respiratory center. Deaths resulting from overdoses with these substances are most often due to respiratory depression, which leads to a complete failure of breathing. Additionally, the concomitant use of other central nervous system depressant drugs such as other opioids, sedatives or hypnotics, general anesthetics, phenothiazines (antipsychotics), tranquilizers, skeletal muscle relaxants, sedating antihistamines, or alcoholic beverages may enhance the depressant effects of opioid analgesics, including fentanyl and its analogues. Another important overdose risk factor is an individual's opioid tolerance. Those who have little or no tolerance are at a higher risk of overdose and death.

Fentanyl and fentanyl analogues used in clinical settings (e.g., sufentanil, alfentanil, remifentanil) and in veterinary medicine (carfentanil and thiafentanil) are high potency μ-opioid receptor agonists with rapid onset and short duration of action.[5] They are highly lipophilic and are rapidly distributed across the blood-brain barrier. Fentanyl is about 50 to 80 times more potent than heroin[6] and about 100 times more potent than morphine[7] as an analgesic. Alfentanil[8] and carfentanil9 are 600 and 10,000 times more potent than morphine, respectively. Thiafentanil is slightly less potent than carfentanil.[10] Sufentanil is 1,000 times more potent than morphine, while remifentanil is equipotent to fentanyl.[11] These pharmacological and physio-chemical properties of fentanyl and its analogues, in combination with their potential to cause respiratory depression, enhance the risk of life-threatening adverse effects when misused or abused.[12]

In vitro[13] and *in vivo* pharmacological studies of illicitly produced fentanyl analogues encountered thus far,[14] suggest that these fentanyl analogues also act as potent μ-opioid receptor

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4 GOODMAN & GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS (Laurence L. Brunton, John S. Lazo & Keith L. Parker, McGraw-Hill 11th ed., 2005).

5 H.B. GUTSTEIN & H. AKIL, GOODMAN & GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS (Laurence L. Brunton, John S. Lazo & Keith L. Parker, McGraw-Hill 11th ed., 2005).

6 C.W. Reichle, G.M. Smith, J.S. Gravenstein, S.G. Macris & H.K. Beecher, *Comparative Analgesic Potency of Heroin and Morphine in Postoperative Patients,* 136 J Pharmacol Exp Ther., 43-6 (Apr. 1962).

7 T.L. YAKSH & M.S. WALLACE, GOODMAN & GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS (Laurence L. Brunton, John S. Lazo & Keith L. Parker, McGraw-Hill 12th ed., 2011).

8 T. REISINE & G. PASTERNAK, GOODMAN & GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS (Laurence L. Brunton, John S. Lazo & Keith L. Parker, McGraw-Hill 9th ed., 1996).

9 P.G. Van Daele, M.F. De Bruyn, J.M. Boey, S. Sanczuk, J.T. Agten & P.A. Janssen, *Synthetic Analgesics: N-(1-[2-arylethyl]-4-substituted 4-piperidinyl) N-arylalkanamides,* 26 Arzneimittelforschung, 1521-31 (1976).

10 Department of Health and Human Services (HHS) Review (2011): Basis for the Recommendation to Place Thiafentanil and Its Salts in Schedule II of the Controlled Substances Act (CSA), at 2.

11 T.L. YAKSH & M.S. WALLACE.

12 H.B. GUTSTEIN & H. AKIL.

13 Studies are conducted by the United States Department of Veterans Affairs under an interagency agreement with the DEA

14 Studies are conducted by academic and research institutions under contracts with the DEA and by the National Center for Toxicological Research of the FDA under an interagency agreement with the DEA.

agonists. These preliminary findings help to explain why illicitly produced fentanyl analogues have caused overdoses and overdose deaths.

IV. Abuse and addiction potential of fentanyl, its analogues, and other opioids

Fentanyl, fentanyl analogues, and opioids in general are addictive drugs with a high potential for abuse. Illicit opioids and clinically used strong opioid analgesics (e.g., hydrocodone, oxycodone, morphine), activate μ-opioid receptors. Such activation is thought to be responsible for their high potential for abuse and addiction. According to the National Survey on Drug Use and Health,[15] in 2015 an estimated 12.5 million people aged 12 or older "misused"[16] pain relievers (opioid analgesics) in the past year, and 2.1 million people "misused" pain relievers for the first time. About 2 million people aged 12 or older had "pain reliever use disorder" in 2015.

Fentanyl also activates μ-opioid receptors and has high potential for abuse and addiction. As mentioned earlier, the fentanyl analogues that have been encountered by law enforcement in recent years also bind to and activate μ-opioid receptors. Therefore, they are likely to have high abuse and addiction potential similar to heroin, fentanyl, and other clinically used opioid analgesics. This is further supported by the marked increase in law enforcement encounters and deaths associated with illicitly produced fentanyl analogues in recent years.

It is worth noting that drugs with similar abuse and addiction potential may actually be abused at different rates. That is true because there are many other factors that contribute to the rate at which a particular drug is actually abused. For example, ease of drug availability, ease of drug manipulation such as extraction of active drug from pharmaceutical products, cost, profit margins, relative ease of clandestine synthesis and trafficking, and the availability of precursor and other chemicals for synthesis. The public health data, as discussed below, shows that the harms associated with fentanyl and fentanyl analogue abuse far exceed those associated with other opioid analgesics.

V. Current opioid-related public health crisis

The United States is in the midst of an unprecedented public health crisis that has resulted in approximately 64,000 people[17] losing their lives during 2016 and approximately 52,000 losing their lives during 2015.[18] Opioids, such as fentanyl, fentanyl analogues, heroin,

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15 Arthur Hughes, Matthew R. Williams, Rachel N. Lipari, Jonaki Bose, Elizabeth A.P. Copello & Larry A. Kroutil, *Prescription drug use and misuse in the United States: Results from the 2015 National Survey on Drug Use and Health*, National Survey on Drug Use and Health, September, 2016, https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR2-2015/NSDUH-FFR2-2015.htm.

16 Key Substance Use and Mental Health Indicators in the United States: Results from the 2016 National Survey on Drug Use and Health, defines misuse of substances as: "in any way that a doctor did not direct you to use them, " including (1) use without a prescription of the respondent's own; (2) use in greater amounts, more often, or longer than the respondent was told to take them; or (3) use in any way a doctor did not direct the respondent to use them. Rebecca Ahrnsbrak et al., *Key Substance Use and Mental Health Indicators in the United States: Results from the 2016 National Survey on Drug Use and Health,* Substance Abuse and Mental Health Services Administration, https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.htm.

17 *Overdose Death Rates*, National Institute on Drug Abuse, Sept. 2017, *available at* https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates.

18 *New Data Show Continuing Opioid Epidemic in the United States*, Center for Disease Control and Prevention, Dec. 16, 2016, *available at* https://www.cdc.gov/media/releases/2016/p1216-continuing-opioid-epidemic.html.

and prescription painkillers, have been driving the increased number of overdose deaths.[19] Fentanyl and its analogues have been major contributors to the increase.[20] In many cases, fentanyl and its analogues are mixed with other drugs, such as heroin. Thus, users often are unaware of what is actually in the substance they are ingesting until it is too late. In recognition of the unprecedented and continuing escalation in opioid-related overdoses, on October 26, 2017, the President of the United States declared the opioid crisis a national public health emergency.[21] Additionally, on November 9, 2017, the Department of Justice announced that the DEA will be taking immediate action to schedule all fentanyl-related substances on an emergency basis.[22]

VI. Patterns of abuse, trafficking and harms associated with fentanyl and its analogues

Over the past 20 years, the drug landscape in the United States has shifted, with the opioid threat reaching epidemic levels and impacting significant portions of the United States.[23] A major contributor to this epidemic has been fentanyl and its analogues, as well as other synthetic opioids. According to DEA investigations, fentanyl, its analogues, and their immediate chemical precursors are typically manufactured in China. The drug traffickers then often use freight forwarders to mail the fentanyl and its analogues out of China. Several DEA investigations have revealed that the original supplier will provide the package to a freight forwarding company or individual, who transfers it to another freight forwarder, who then takes custody and presents the package to customs for export. The combination of a chain of freight forwarders and multiple transfers of custody makes it difficult for law enforcement to track these packages. Often, the package will intentionally have missing, incomplete, and/or inaccurate information address information.

From China, the package is either mailed via parcel post to the United States or alternatively shipped directly to transnational criminal organizations (TCOs) in Mexico, Canada, and the Caribbean. Once in the Western Hemisphere, fentanyl and its analogues are introduced into the United States' illicit drug market through drug distribution networks. Fentanyl and its analogues are often mixed together with other drugs, most commonly heroin. However, we are also seeing instances of it being mixed with cocaine. Additionally, fentanyl and its analogues are pressed into pills that resemble prescription opioids such as oxycodone or hydrocodone. The tools and precursor chemicals needed to manufacture fentanyl and its analogues are available

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19 *Overdose Death Rates*, National Institute on Drug Abuse, Sept. 2017, *available at* https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates (reporting that of "the more than 64,000 drug overdose deaths estimated in 2016, the sharpest increase occurred among deaths related to fentanyl and fentanyl analogs (synthetic opioids) with over 20,000 overdose deaths").

20 R.M. Gladden, P. Martinez & P. Seth, *Fentanyl Law Enforcement Submissions and Increases in Synthetic Opioid-Involved Overdose Deaths – 27 States, 2013-2014*, 65 Morbidity and Mortality Weekly Report, 837-43 (2016); A.B. Peterson et al., *Increases in Fentanyl-Related Overdose Deaths – Florida and Ohio, 2013-2015*, 65 Morbidity and Mortality Weekly Report, 844-49 (2016); Nicholas J. Somerville et al., *Characteristics of Fentanyl Overdose – Massachusetts, 2014-2016*, 66 Morbidity and Mortality Weekly Report, 382-86 (2017); Deborah, Dowell, Rita K. Noonan & Debra Houry, *Underlying Factors in Drug Overdose Deaths*, The Journal of American Medical Association, E1-E2 (October 11, 2017).

21 *President Donald J. Trump is Taking Action on Drug Addiction and the Opioid Crisis*, The White House Office of the Press Secretary, Oct. 26, 2017, *available at* https://www.whitehouse.gov/the-press-office/2017/10/26/president-donald-j-trump-taking-action-drug-addiction-and-opioid-crisis.

22 *Department of Justice Announces Significant Tool in Prosecuting Opioid Traffickers in Emergency Scheduling of All Fentanyls*, U.S. Department of Justice, Nov. 9, 2017, *available at* https://www.justice.gov/opa/pr/department-justice-announces-significant-tool-prosecuting-opioid-traffickers-emergency.

23 National Drug Threat Assessment Summary, Drug Enforcement Administration, U.S. Department of Justice (2017).

online for relatively inexpensive prices. Additionally, fentanyl and its analogues are available for purchase online from anonymous "dark net" markets, as well as websites on the regular Internet. The pill presses used to create counterfeit pills laced with fentanyl are also easily obtained on the Internet, and they are commonly shipped into the United States directly from China, India, and Germany.

Trafficking in fentanyl and its analogues is particularly attractive to drug dealers, including TCOs, because of the substantial profit potential. Fentanyl and its analogues are extremely powerful, yet relatively cheap, opioids. For example, one kilogram of fentanyl purchased in China for $3,000 - $5,000 can potentially generate over $1.5 million in revenue on the illicit market in the United States.

Forensic laboratory data shows that law enforcement encounters of fentanyl and its analogues have markedly increased since 2012. According to DEA's National Forensic Laboratory Information System (NFLIS), law enforcement encounters of fentanyl increased by more than 50-fold from 694 reports in 2012 to 36,134 reports in 2016 (database queried October 30, 2017). Additionally, NFLIS reports for fentanyl analogues increased from 3 in 2012 to 6,926 in 2016. As of October 30, 2017, NFLIS reports for January - June 2017 for fentanyl and fentanyl analogues were 21,872 and 6,808, respectively.

Law enforcement and public health reports show that fentanyl analogues have been identified in counterfeit pharmaceutical opioid products.[24] In addition, reports indicate that fentanyl analogues are available in the illicit drug market in powder form, similar to fentanyl and heroin. Fentanyl analogues, with the exceptions of those that are approved by the FDA (carfentanil, alfentanil, sufentanil, thiafentanil, remifentanil), have no accepted medical use in treatment in the United States and are therefore not manufactured as legal pharmaceuticals. To date, DEA has not received information as to the diversion of legally produced pharmaceuticals containing thiafentanil, remifentanil, sufentanil and alfentanil in the United States. Carfentanil is legally available for veterinary use only.[25] Although recently carfentanil appeared on the illicit market, the DEA is not aware of diversion of legally manufactured carfentanil. DEA believes that the carfentanil encountered so far by the law enforcement is of illicit origin and is produced in clandestine labs.

The increasing trend in the use of novel psychoactive substances, including fentanyl analogues, is fueled by many factors including the relative ease of purchase through the internet. Clandestine chemists have exploited this mechanism for global marketing and sales of fentanyl analogues. Clandestine synthesis of the fentanyl analogues is likely on the rise due to several factors. The efforts to circumvent the restrictions associated with the sale of fentanyl in the United States have led to new replacement of fentanyl analogues, and because of the huge profit margins associated with this class of drugs, fentanyl analogues have become attractive for the clandestine chemists. Studies on structure-activity relationship show that minor substitution of this structural class retains pharmacological activity. The DEA has been tracking the increase in and evolution of fentanyl analogues that are being encountered in the recreational drug market in the United States. As noted above, since July of 2015, the DEA has issued six temporary

[24] Laboratory report obtained from Division of Forensic Science, Georgia Bureau of Investigation.
25 Manufacturer has switched to a newer alternative-thiafentanil and carfentanil is no longer being manufactured in the United States.

scheduling orders to schedule nine fentanyl analogues. These actions have been issued every few months in response to the appearance of new fentanyl analogue in the illicit drug market.[26]

The population likely to consume fentanyl and fentanyl analogues overlaps with the population consuming heroin and prescription opioids. Just as with heroin and prescription opioids, once an individual consumes fentanyl or a fentanyl analogue, he or she is at risk for addiction, overdose, and death. Harms associated with the use of fentanyl and its analogues are further heightened by the fact that users may unknowingly consume fentanyl or its analogues in products marketed as heroin or in counterfeit prescription pills. Because fentanyl and its analogues are obtained through unregulated sources, the identity, purity, and quantity of the drugs are uncertain and inconsistent, thus posing significant adverse health risks to the end user. Injection and insufflation are the most common routes of administration in deaths related to fentanyl and its analogues.[27] These routes of administration, combined with high potencies of fentanyl and its analogues, further increase the risk of overdoses and overdose deaths.

Fentanyl and its analogues also pose serious risks to law enforcement officers who may inadvertently come into contact with the drugs during arrests and searches. Indeed, law enforcement officers have required medical treatment after inadvertent exposure to fentanyl. The DEA, therefore, has issued a "Roll Call" video to all law enforcement officers nationwide that discusses the dangers of improperly handling fentanyl.

VII. Synthetic opioids that are structurally not related to fentanyl or thebaine-based opioids (e.g., morphine, codeine, oxycodone etc.)

The Commission should be aware of the increased trafficking and abuse of other synthetic opioids that are not structurally related to either fentanyl or thebaine-based opioids (e.g., morphine, codeine, oxycodone). Law enforcement agencies have encountered several such synthetic opioids recently, including MT-45, AH7921, and U-47700. These dangerous substances are available for purchase on the black market and online.

The above-mentioned synthetic opioids share pharmacological similarities with other opioid analgesics. These synthetic opioids have been shown to bind to μ-opioid receptors. In *in vivo* studies, MT-45, AH-7921 and U-47700 have been shown to be similar to morphine in their pharmacological effects. Overdoses and deaths have been associated with abuse of MT-45, AH-7921, and U-47700. In November 2016, DEA controlled U-47700[28] as a Schedule I substance pursuant to the temporary scheduling provision of the CSA because it posed an imminent hazard to public safety. Moreover, the United Nations Commission on Narcotic Drugs has added AH-7921, MT-45, and U-47700 to Schedule I of the Single Convention on Narcotic Drugs.[29] As a

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26 July 17, 2015, 80 Fed. Reg. 42381; May 12, 2016, 81 Fed. Reg. 29492; November 29, 2016, 81 Fed. Reg. 85873; May 3, 2017, 82 Fed. Reg. 20544; July 14, 2017, 82 Fed. Reg. 32453; October 26, 2017, 82 Fed. Reg. 49504.

27 Nicholas J. Somerville et al., *Characteristics of Fentanyl Overdose – Massachusetts, 2014-2016*, 66 Morbidity and Mortality Weekly Report (Apr. 14, 2017) ("Twenty-five percent reported witnessing or experiencing an overdose when fentanyl was insufflated (snorted), and the remainder reported the overdose always involved injecting fentanyl.").

28 81 Fed. Reg. 79389.

29 UN Commission on Narcotic Drugs, Scheduling Procedures, https://www.unodc.org/unodc/en/commissions/CND/Mandate_Functions/Mandate-and-Functions_Scheduling.html (stating that in 2015 the UN Commission added AH-7921 to Schedule I, in 2016 it added MT-45 to Schedule I, and in 2017 it added U-47700 to Schedule I).

signatory Member State to the Single Convention on Narcotic Drugs, the United States is obligated to control these three substances under its national drug control legislation. Accordingly, the DEA controlled AH-7921[30] as a Schedule I substance. And, it is in the process of controlling MT-45 and U-47700.

VIII. The Commission should consider establishing a class-based approach and increase the penalties for fentanyl and its analogues

DEA recommends establishing a class-based approach for synthetic opioids, which would include fentanyl, its analogues, as well as synthetic opioids such as AH-7921, MT-45, and U-47700. DEA has identified numerous fentanyl analogues currently available in the illicit marketplace. It is likely that new fentanyl analogues with additional structural deviations may enter the illicit market soon. As observed with other synthetic drug classes, manufacturers of fentanyl analogues routinely make small modifications to the chemical structure with the intention of providing the same pharmacological impact. Using a broad class-based approach would be straightforward and would reduce the need to present expert scientific witness testimony at sentencing when new fentanyl analogues and other synthetic opioids are introduced in the United States by drug traffickers.

IX. The Commission should increase penalties for those who traffic in fentanyl and fentanyl analogues

As the Department of Justice has previously stated, the Commission should increase the penalties for those who traffic in fentanyl and its analogues.[31] Additionally, the President's Commission on Combating Drug Addiction and the Opioid Crisis recently recommended "the enhancement of federal sentencing penalties for the trafficking of fentanyl and fentanyl analogues."[32] The current base offense level of 12 is plainly inadequate to account for the dangerous nature of fentanyl and its analogues. Under the current structure, a defendant in Criminal History Category I who sells 3 grams of fentanyl and pleads guilty receives an offense level of 10, falls within Zone B, and faces a guidelines range of 6-12 months, despite having placed hundreds if not thousands of deadly doses of fentanyl on the streets. The Commission should consider increasing the base offense level to ensure that those who traffic in fentanyl and its analogues fall within a sentencing range that fairly represents the severity and dangerousness of their conduct.

The Commission should also consider increasing the marijuana equivalency for fentanyl and fentanyl analogues. The current ratios fail to account for the current threat posed by illicit and clandestinely manufactured fentanyl and fentanyl analogues. When determining if the ratios should be adjusted, the DEA would urge the Commission to consider the following factors: (1) the current unprecedented threat to the public health and safety; (2) the continuing upward trend in the numbers of overdose deaths; (3) the clandestine and illicit manufacturing of the drugs, and the relative ease with which they can be obtained on the Internet; (4) the tremendous profit that

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30 81 Fed. Reg. 22023.

31 Letter to Judge William H. Pryor, Actin Chair, U.S. Sentencing Commission, U.S. Department of Justice (July 31, 2017), *available at* https://www.ussc.gov/sites/default/files/pdf/amendment-process/public-comment/20170731/DOJ.pdf.

32 *Report of the President's Commission on Combating Drug Addiction and the Opioid Crisis,* at 61 (Nov. 1, 2017), *available at* https://www.whitehouse.gov/sites/whitehouse.gov/files/images/Final_Report_Draft_11-1-2017.pdf.

can be generated by sales in the United States; and (5) the manner in which the drugs are mixed with other drugs, as well as the use of the drugs in the production of counterfeit prescription opioid pills.

With regard to the last factor identified above, the Commission should consider a sentencing enhancement for defendants who either (1) mix fentanyl and/or its analogues with other drugs and then misrepresent to the purchaser what is actually in the substance; or (2) produce counterfeit prescription opioid pills that contain fentanyl and/or its analogues and then misrepresent to the purchaser what is actually in the pills. Defendants who engage in this type of behavior pose an additional risk, and their sentences should reflect that additional risk.

We appreciate the opportunity to provide the Commission with our views, comments, and suggestions. We thank the Commission for taking up this important issue. As always, we look forward to working with the Commission during the remainder of the amendment cycle.

Respectfully Submitted,

Demetra Ashley
Assistant Administrator (Acting)
Diversion Control Division

cc: Commissioners
Ken Cohen, Staff Director
Kathleen Grilli, General Counsel