

STATEMENT
OF

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BEFORE THE

HOUSE JUDICIARY COMMITTEE
SUBCOMMITTEE ON CRIME, TERRORISM, AND HOMELAND
SECURITY

FENTANYL ANALOGUES: PERSPECTIVES ON CLASSWIDE
SCHEDULING

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Chair Bass and Ranking Member Ratcliffe, thank you for the opportunity to participate in this hearing. I am the Assistant Secretary for Health at the Department of Health and Human Services (HHS), as well as the Senior Advisor to the Secretary for Opioid Policy. I appreciate the opportunity to speak with you today about the opioid overdose epidemic, and specifically the role of fentanyl and fentanyl analogues.

America's Overdose Epidemic

America's drug overdose epidemic is the most daunting public health challenge of our time. Between 1999 and 2018, over 770,000 people died of drug overdoses in our country, the majority of which were opioid-related¹. And, although in 2018, we witnessed the first decrease in overdose deaths in over two decades, still, more than 68,500 mothers, fathers, sons, daughters, friends and colleagues died of drug overdoses, more than 47,600 of which were caused by opioids².

In the first waves of this crisis, opioid deaths were caused predominantly by misuse of prescription opioids, heroin, or both. But in 2016, the predominant cause of opioid deaths became "synthetic opioids," including illicit fentanyl and derivatives of fentanyl known as fentanyl analogues, illegally manufactured and transported into our country, either through international mail, express consignment facilities, or smuggling across the border.

The Food and Drug Administration (FDA) -approved, pharmaceutically manufactured molecule known as fentanyl is an extremely powerful opioid, and when I was engaged in clinical practice as a physician, I used it safely and effectively nearly every day on children undergoing surgery, or in severe pain in my intensive care unit.

¹ Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018. Data are from the Multiple Cause of Death Files, 1999-2017, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program.

² Ahmad FB, Escobedo LA, Rossen LM, Spencer MR, Warner M, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2020.

But because of its potency and potential for respiratory depression or respiratory arrest, only highly trained specialists were allowed to prescribe and utilize this drug, and only in carefully controlled settings. Contrast that to illicitly manufactured, non-prescription fentanyl and fentanyl analogues, entering our country in the thousands of pounds, with some shipment having the potential to kill millions or tens of millions of Americans, which drives the bulk of the opioid overdose crisis today.

Our most recent data unfortunately demonstrates that deaths caused by illicit fentanyl and chemical analogues of fentanyl are still increasing at about 10 percent, year over year, and threaten the overall progress we have made against prescription opioids and heroin³. And we are seeing new and highly dangerous patterns of use, including polysubstance use of both methamphetamine and fentanyl or fentanyl analogues –a particularly dangerous and potentially deadly combination.

With the leadership of President Trump and Congress, HHS has implemented unprecedented and effective efforts to combat this crisis, including encouraging appropriate prescribing practices that have reduced the total amount of opioids prescribed by more than 32 percent since January 2017⁴; a greater than 400 percent increase in naloxone prescriptions⁴, in addition to more than double that amount directly distributed to first responders and community organizations; an estimated 1.28 million people receiving medication-assisted treatment, also known as MAT⁵; and investing billions of dollars in enhanced data and basic, translational, and clinical research.

The Challenge of Fentanyl Analogues

In addition to these public health measures implemented by HHS and other sectors in our nation, we must prevent these dangerous drugs from coming into our country, through the mail, express consignment carriers, or across our borders.

³ Ahmad FB, Escobedo LA, Rossen LM, Spencer MR, Warner M, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2020.

⁴ IQVIA National Prescription Audit. Retrieved November 2019. Note: These data are for the retail and mail service channels only and do not include the long-term care channel

⁵ IQVIA National Prescription Audit; SAMHSA Opioid Treatment Program Self-Report; N-SSATS.

A significant factor that complicates enforcement against illicit fentanyl and related compounds is that there are a myriad – thousands and perhaps tens of thousands - of potent opioids that can be created by chemical manipulation of the basic fentanyl structure. These are called analogues. While some have been identified and undergone the formal process for scheduling as controlled substances, under the Controlled Substances Act (CSA), the power of chemistry has led to a deadly game of “whack a mole” such that when an analog is identified and undergoes the process of scheduling, clandestine manufacturers are able to synthesize a different, potentially even more deadly chemical that evades enforcement, and at a much faster rate than the chemical can be identified and undergo the rigorous process of scheduling.

For this reason, HHS supports the permanent scheduling of these fentanyl analogs as a class, but with critical protections and facilitation of potentially vital research on this and other classes of molecules.

The Process of Scheduling Controlled Substances

HHS plays an important role in scheduling controlled substances. In order for a substance to be permanently scheduled under the CSA, the FDA conducts a scientific and medical evaluation, also known as an “eight factor analysis,” on the specific drug (molecule). Following consultation with the National Institute on Drug Abuse, FDA makes a recommendation to the Assistant Secretary for Health (ASH) on the appropriate level of permanent controls for a substance with the potential to be abused. The ASH, who has the delegated authority from the HHS Secretary for matters related to scheduling, then conveys the HHS recommendation to the Drug Enforcement Administration (DEA) for action.

The CSA also allows the DEA to place certain substances not already scheduled, and not subject to an approved or investigational new drug application, into schedule I on a temporary basis to address an imminent hazard to the public health. Under these circumstances, HHS receives notice from the Attorney General (through DEA) of the

proposed action. FDA then reviews the records of drugs approved or being investigated for therapeutic use, communicates the findings to the ASH, and the ASH conveys to DEA whether or not HHS has any objection to the proposed temporary order to place the substance in schedule I.

In this regard, on November 6, 2017, the DEA Acting Administrator notified the HHS Acting Assistant Secretary for Health, of the DEA's intent to publish in the Federal Register a Notice of Intent to issue a temporary order adding all fentanyl-related substances (a.k.a. fentanyl analogues) to schedule I of the CSA. The Acting ASH responded on November 29, 2017, that according to FDA, there did not at that time appear to be any approved new drug applications or active investigational new drug applications for these fentanyl-related substances and that HHS did not object to the temporary placement of these substances in Schedule I of the CSA. DEA subsequently issued the temporary order on February 6, 2018. HHS was not asked for, and did not produce, an “eight-factor analysis,” on fentanyl-related substances as a class. Such an evaluation for permanent scheduling of a class of substances, rather than specific substances, would be a significant change from the normal process of scheduling, and might not be feasible for the FDA to develop.

The Need to Advance Research

As the leading cause of overdose deaths in our nation, and in many nations around the world, fentanyl and fentanyl analogues are our highest priority to keep off our streets. The chemical structures and pharmacological activity targeted by illicit opioid manufacturers overlap not only with illicit, and potentially dangerous, schedule I substances, but also with many molecules that may be shown by future research to have a potential for legitimate therapeutic uses. Research with fentanyl-related substances and other synthetic opioids is important in the development of new and improved treatments for opioid addiction and overdose, chronic pain, and other neurologic and psychiatric conditions, as well as to understand the effects these

substances have on human health. That is why we must ensure access to these substances for legitimate research to develop new therapies and improve scientific understanding of their effects on human health.

Currently, obtaining or modifying a schedule I (and, in some cases, a schedule II-V) research registration involves significant administrative challenges. Under the law, scientists who wish to conduct research on schedule I substances, including fentanyl-related substances pursuant to the temporary scheduling order issued by the DEA, must hold a schedule I research registration. Obtaining a schedule I research registration is a multistep process that involves review and approval of a scientist's research protocol by multiple regulatory or review bodies, including the DEA, FDA, institutional review boards (for research with humans), and institutional animal care and use committees (for research with animals). The DEA conducts background checks on individuals who would be granted access to the substances for which a registration is sought and may perform site inspections to ensure that appropriate security safeguards are in place to mitigate against diversion. In addition to obtaining a federal schedule I registration, researchers may be required to obtain a separate registration from their state licensing authority before their federal application can be processed.

Researchers have reported that obtaining a new registration can take more than a year. Adding new substances to an existing registration can also be time-consuming. These challenges can impede critical research on schedule I substances and deter or prevent scientists from pursuing such work. HHS has worked closely with our colleagues at the Office of National Drug Control Policy (ONDCP), the Department of Justice (DOJ), and DEA on the following proposals to mitigate potential negative impacts on research or development of therapeutics, including those mentioned above.

Working together this summer, we reached an interagency solution that balances the need to control these substances as a class, with the researcher access necessary to study these substances. We submitted the results of our work to House and Senate

Committee staff in early September.

1. Allow HHS to identify a substance with no potential for abuse, based on consideration of certain of the eight factors, and require DOJ to remove the substance from schedule I within 90 days. Additionally, allow HHS to identify a substance with a low potential for abuse, based on consideration of the same factors, and allow DOJ 180 days to decide whether to remove the substance from scheduling for research purposes only.
2. Allow individuals conducting research with a substance subsequently placed into schedule I who hold a registration to conduct research with any other schedule I or schedule II substance to continue work on the newly scheduled substance until their new or amended registration application is approved or denied. These individuals will have to submit their new or amended registration application within 30 days of the substance being added to schedule I.
3. Clarify that individuals who are agents or employees of the person holding the research registration are not required to have a separate registration.
4. Allow registered researchers to store, administer, and otherwise work with any substances for which they hold a researcher registration at multiple practice sites, on a single contiguous campus so long as the registrant notifies the Attorney General prior to conducting research at those sites.
5. Allow a researcher who is registered to do research with a controlled substance, and who needs to perform limited manufacturing activities on small quantities of that substance consistent with their research protocol (for example, creating a particular dosage formulation for research purposes), to do so without having to obtain a separate manufacturing registration.
6. Require the Attorney General and the HHS Secretary to conduct a review of the

process for obtaining or modifying a research registration under the CSA to identify redundancies, inefficiencies, or burdens on persons seeking registrations that can be reduced while ensuring public safety, and subsequently require the Attorney General and the HHS Secretary to issue joint guidance clarifying the registration process.

7. Clarify that if a person is registered to conduct research with a controlled substance and applies to conduct research with a second controlled substance that is in the same schedule or in a schedule with a higher numerical designation, an inspection that was performed for purposes of the existing registration shall be sufficient to support the application.

Thank you for the opportunity to testify today on this important topic. I am happy to answer any questions you have.