Attachment—Additional Questions for the Record

Subcommittee on Health
Hearing on
"The Overdose Crisis: Interagency Proposal to Combat Illicit Fentanyl-Related Substances"
December 2, 2021

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The responses to the questions for the record are accurate as to the date of the hearing.

The Honorable Frank Pallone, Jr. (D-NJ)

1. As overdose deaths continue to rise in the United States, it is urgent that we consider additional public health approaches to help deliver care to Americans with substance use disorder. In midst of the COVID-19 pandemic, this matter is increasingly urgent. Public health experts have warned of new risks to Americans impacted by substance use disorder as well as new challenges to accessing treatment.

   One tool used across the states are harm reduction programs and syringe support services. For years, the Centers for Disease Control and Prevention (CDC) has provided guidance for these services, which offer linkage to substance use disorder treatment, provide access to and disposal of sterile syringes, and provide critical vaccination, testing, and linkage to care and treatment for infectious diseases.

   a. **What additional evidence-based harm reduction approaches will the Biden Administration seek to implement and what is the benefit of using such approaches**?

      Response:
      The Biden Administration has outlined a multi-pronged plan to reduce drug overdoses and deaths, including from fentanyl and other opioids. A major focus of this plan, administered by the Department of Health and Human Services (HHS), is to enhance development, implementation, and evaluation of harm reduction approaches.[1]

      Current National Institute on Drug Abuse (NIDA) research is assessing a variety of harm reduction approaches. One is expansion of access to naloxone, a medication that rapidly reverses opioid overdose. A current NIDA-funded study in this area will test an innovative program for pharmacists to see if it improves their knowledge about naloxone and their ability to educate patients taking prescribed or illicit opioids.[2] The study involves 160 pharmacies in the U.S. Northwest and New England and is expected to inform an evidence-based training course and toolkit for pharmacists who care for patients that could benefit

[1] Office of National Drug Control Policy. The Biden-Harris Administration's Statement of Drug Policy Priorities for Year One. https://www.whitehouse.gov/wp-content/uploads/2021/03/BidenHarris-Statement-of-Drug-Policy-Priorities-April-1.pdf
For the most current information, visit https://www.whitehouse.gov/briefing-room/statements-releases/2022/04/21/fact-sheet-white-house-releases-2022-national-drug-control-strategy-that-outlines-comprehensive-path-forward-to-address-addiction-and-the-overdose-epidemic/.
[2] NIDA Grant R01DA045745

from naloxone. Another study is using statistical modeling to estimate the public health impact of expanding naloxone availability through pharmacies and community-based programs in New York City, Massachusetts, and Rhode Island.[3]

Another harm reduction research area is identification of best practices for the use of fentanyl test strips (FTS). More than 60 percent of overdose deaths in the United States involve fentanyl and other synthetic opioids.[4] FTS provide a rapid, portable method to detect fentanyl in street drugs, and can help prevent overdose when combined with other evidence-based approaches.[5] To support this priority, NIDA is collaborating with the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the Substance Abuse and Mental Health Services Administration (SAMHSA) to facilitate evidence-based use of FTS in community and clinical settings.[6] NIDA also supports research to improve FTS technology and expand its use. For example, current FTS kits are more than 90 percent accurate for detecting fentanyl, but ascertaining their ability to detect novel fentanyl analogues requires additional research. A NIDA-funded project is exploring this question by comparing FTS to a highly sensitive but non-portable testing procedure.[7]

NIDA also funds research to improve effective implementation of FTS. This includes a clinical trial that will test whether a novel fentanyl overdose education program, including take-home FTS, can reduce overdose among young adults who use illicit drugs.[8] Another study will examine how FTS, as well as socioeconomic, demographic, and other factors, might influence positive behaviors (e.g., fentanyl avoidance, reduced drug use) and negative behaviors (e.g., fentanyl-seeking) among 700 adult users of illicit drugs in North Carolina and West Virginia.[9]

Finally, the HEALing Communities Study (HCS), funded through the Helping to End Addiction Long Term® Initiative (NIH HEAL Initiative®), is testing a variety of evidence-based approaches, including harm reduction interventions, in 67 communities hit hard by the opioid crisis. Study teams are working to increase distribution of naloxone and FTS in participating communities to reduce overdose deaths. The study is also investigating whether a hub-and-spoke healthcare model—connecting primary care centers (the hubs) to justice and social service settings (the spokes)—can bring evidence-based harm reduction strategies to underserved communities in New York.[10]

b. **Why are syringe service programs beneficial to communities and how will NIDA and help support expansion of such services**?

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[3] NIDA Grant U01DA047408
[4] National Center for Health Statistics. Provisional Drug Overdose Death Counts. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm
[5] Goldman JE, Waye KM, Periera KA. et al. (2019). Perspectives on rapid fentanyl test strips as a harm reduction practice among young adults who use drugs: a qualitative study. *Harm Reduction Journal*. 16(3) (PMID: 30621699).
[6] Centers for Disease Control and Prevention. (2021, April 7). *Federal Grantees May Now Use Funds to Purchase Fentanyl Test Strips*. Retrieved from https://www.cdc.gov/media/releases/2021/p0407-Fentanyl-Test-Strips.html
[7] NIDA Grant R03DA049998
[8] NIDA Grant R01DA047975
[9] NIDA Grant R01DA047334
[10] NIDA Grant UM1DA049415

Response:
Sharing and reusing syringes is associated with a high risk of blood-borne diseases—including HIV and viral hepatitis—soft tissue infections, and infection of the heart valves (infective endocarditis). In addition to providing clean syringes, many syringe services programs (SSPs) offer HIV, hepatitis B, and hepatitis C testing and linkage to care, vaccinations for hepatitis A and other infections, overdose-reversing medications such as naloxone, low-barrier buprenorphine treatment[11,12] and referrals for substance use disorder (SUD) treatment.[13] A large body of research provides evidence that SSPs reduce the risk of HIV,[14] hepatitis C (HCV, the most common form of hepatitis),[15] and soft tissue infections[16] among people who inject drugs.

SSPs do not increase crime or drug use in surrounding communities.[17,18] In fact, some programs have found that participants are more likely to enter SUD treatment, reduce or stop drug use, and engage in opioid overdose education and receive naloxone.[19,20] SSPs also appear to be cost-effective. A NIDA-funded modeling study found that scaling up SSPs nationally by just 50 percent could prevent 35,000 HIV infections over the next 20 years.[21] In Indiana, the state health department credited SSPs with halting an outbreak of HIV and HCV in 2015 and saving taxpayers an estimated $120 million; that county recently voted to close its SSP.[22]

NIDA is also supporting a national survey to characterize the variety of SSP models across the United States, and to evaluate community capacity and barriers to integrate SSPs with HIV/HCV testing and prevention and SUD medication services.[23] While SSPs appear to help

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[11] Hood JE, Banta-Green CJ, Duchin JS, et al. (2020). Engaging an unstably housed population with low-barrier buprenorphine treatment at a syringe services program: Lessons learned from Seattle, Washington. Substance Abuse. 41(3), (PMID: 31403907)
[12] Aronowitz, SV, Behrends, CN, Lowenstein M, et al. (2022). Lowering the Barriers to Medication Treatment for People with Opioid Use Disorder Evidence for a Low-Threshold Approach. Leonard Davis Institute of Health Economics: Center for Health Economics of Treatment Interventions for Substance Use Disorder, HCV, and HIV. Issue Brief. Retrieved from https://ldi.upenn.edu/our-work/research-updates/lowering-the-barriers-to-medication-treatment-for-people-with-opioid-use-disorder/
[13] Centers for Disease Control and Prevention. (2019, May 23)Summary of Information on The Safety and Effectiveness of Syringe Services Programs (SSPs). Retrieved from https://www.cdc.gov/ssp/syringe-services-programs-summary.html
[14] Broz D, Carnes N, Chapin-Bardales J. et al. (2021). Syringe Services Programs' Role in Ending the HIV Epidemic in the U.S.: Why We Cannot Do It Without Them. *American Journal of Preventive Medicine*. 61(5 Suppl 1) (PMID: 34686281).
[15] Platt L, Sweeney S, Ward Z. et al. (2017). Assessing the impact and cost-effectiveness of needle and syringe provision and opioid substitution therapy on hepatitis C transmission among people who inject drugs in the UK. *Public Health Research*. No. 5.5 (PMID: 28968044).
[16] Dunleavy K, Munro A, Roy K. et al. (2017). Association between harm reduction intervention uptake and skin and soft tissue infections among people who inject drugs. *Drug and Alcohol Dependence*. 1(174) (PMID: 28319754).
[17] Marx MA, Crape B, Brookmeyer RS. et al. (2000). Trends in crime and the introduction of a needle exchange program. *American Journal of Public Health*. 90(12) (PMID: 11111271).
[18] Fisher DG, Fenaughty AM, Cagle HH. et al. (2003). Needle exchange and injection drug use frequency: a randomized clinical trial. *Journal of AIDS*. 33(2). (PMID: 12794555)
[19] Surratt HL, Otachi JK, Williams T. et al. (2020). Motivation to Change and Treatment Participation Among Syringe Service Program Utilizers in Rural Kentucky. *Journal of Rural Health*. 36(2) (PMID: 31415716)
[20] Lambdin BH, Bluthenthal RN, Wenger LD, et al. (2020). Overdose Education and Naloxone Distribution Within Syringe Service Programs - United States, 2019. MMWR. Morbidity and mortality weekly report, 69(33), 1117–1121.
[21] Bernard CL, Owens DK, Goldhaber-Fiebert JD. et al. (2017). Estimation of the cost-effectiveness of HIV prevention portfolios for people who inject drugs in the United States: A model-based analysis. *PLoS Medicine*. 14(5) (PMID: 28542184)
[22] Indiana University School of Public Health. The Implementation of Syringe Services Programs (SSPs) in Indiana: Benefits, Barriers, and Best Practices. 2018.
[23] NIDA Grant R01DA027379

reduce rates of HIV and HCV without increasing drug use or crime, they have been deployed mostly in urban areas, and research is needed to determine their potential impact in rural areas with fewer resources and potentially greater drug-related stigma. The CARE2HOPE study will assess SUD treatment needs and resources in 12 rural Appalachian counties in Kentucky and will develop tailored community response projects to address injection drug use, HIV, and HCV.[24]

c. **What additional evidence-based harm reduction efforts should Congress, or the administration invest in**?

Response:
Additional research on existing and emerging harm reduction practices is necessary. This includes research on harm reduction strategies that are used in other countries but have not been widely adopted in the United States, research on clinical effectiveness of harm reduction practices; and research on strategies for implementing effective practices in diverse real-world settings. Through the NIH HEAL Initiative®, NIDA plans to establish a Harm Reduction Network consisting of several linked research projects that aim to increase our understanding of the effectiveness, implementation, and impact of existing and new harm reduction practices. Projects are expected to begin as early as September 2022.[25]

2. The Administration's fentanyl-related substances (FRS) proposal places all of these substances into schedule I as a class. As we have heard, the registration process under the Controlled Substances Act can present barriers to research. I was pleased that the FRS proposal acknowledges those potential barriers and want to better understand how they will help to facilitate additional research.

In your testimony, you suggest that the Administration's proposal would potentially expand the number of individuals registered to conduct research with Schedule I substances. However, there is criticism that the proposal may result in only well-funded researchers being able to access these substances. Do you agree with this criticism? If not, what is your response to it and how do you believe this will expand research opportunities broadly?

Response:
The Administration's proposal will help facilitate schedule I research in a number of ways. First, it would create an alternative registration process for schedule I research funded by the HHS or the Department of Veterans Affairs (VA), or conducted under an Investigational New Drug (IND) exemption from the FDA. This alternative process would be more closely aligned with the process for obtaining a schedule II registration, which investigators have indicated is easier than the schedule I process.

Under the alternative process, schedule I research applications would no longer be referred to HHS for a review of the protocol and determination of the qualifications of the investigator. Likewise, it would no longer be necessary for investigators to submit an amended application notifying the Department of Justice (DOJ) of research protocol changes as long as those changes do not modify the quantity of the substance used. Rather, researchers would submit a notice to DOJ containing:

[24] NIDA Grant UH3DA044798
[25] NIDA RFA-DA-22-046

the identity of the substance to be used; the quantity of the substance to be used; demonstration that the research is funded by HHS or by the VA or is conducted under an IND; and demonstration that the researcher is allowed to do the research under the law of the state where it will be conducted. If the researcher already holds a schedule I or II research registration he or she may commence the research 30 days after sending the notice described above—without waiting for a notification of approval from the DOJ. If the researcher does not already have such a registration, that notice would suffice to constitute the application, and DOJ must either grant the registration or issue a show-cause order denying the registration within 45 days. Removing the application referral and review steps and allowing current schedule I or II registrants to proceed with the research without an affirmative decision by the DOJ will greatly expedite the process.

Although the alternative registration process would apply only to research funded by HHS, the VA, or conducted under an FDA IND, there are several other provisions in the Administration's proposal that would apply to all schedule I researchers, irrespective of their funding source. For example, the proposal clarifies that separate registrations are not required for each individual researcher within an institution and that under specified circumstances researchers do not need to obtain separate registrations for each of their research sites (e.g., for each laboratory on a single campus). Not requiring separate registrations for each researcher and site will save both time and money associated with applying for multiple registrations.

The proposal also clarifies that schedule I researchers can continue to conduct research on substances newly added to schedule I while they apply for a modification of their registration, ensuring that time and resources are not lost while investigators apply for a modified registration. These provisions will apply to all investigators that conduct Schedule I research no matter how well-resourced they are.

3. **There has been criticism about the use of class-wide scheduling to combat illicit fentanyl. The class-wide scheduling of fentanyl-related substances has been in effect since 2018 and overdoses have nonetheless skyrocketed. As we know, overdoses are at an all-time high, and a significant driver of this trend is still illicitly manufactured fentanyl and fentanyl-related substances. What evidence is there that permanent class-wide scheduling of FRS will lead to reduced overdose deaths?**

Response:
Although multiple factors have contributed to the rise in opioid overdose deaths, illicitly-manufactured fentanyl, fentanyl-related substances, and other synthetic opioids are the major driver. Reducing the supply of illicitly manufactured fentanyl is one component of the nation's approach to combatting the overdose crisis, which also includes implementing evidence-based prevention, harm reduction, treatment, and recovery supports services as outlined in the HHS Overdose Prevention Strategy. Although we are not aware of any data directly analyzing the impact of fentanyl scheduling decisions on overdose mortality, the Government Accountability Office (GAO)'s April 2021 report, *Synthetic Opioids: Considerations for the Class-wide Scheduling of Fentanyl-Related Substances*, reviews data on law enforcement encounters with fentanyl-related substances before and after the implementation of the temporary fentanyl scheduling order in 2018. We refer you to GAO for more information on that analysis.

4. **This year the country has witnessed a high of 100,000 overdose deaths. I recognize that this is a complex and multifaceted problem that requires a multifaceted solution. What additional policies should be considered to reduce overdose deaths?**

   Response:
   Provisional data from the Centers for Disease Control and Prevention estimate that there were over 107,000 drug overdose deaths in the 12-month period ending in December 2021. An unprecedented level of drug overdose deaths must be met with an unprecedented public health response that pairs enhancement of proven policy strategies with rigorous evaluation of novel approaches.

   Proven strategies: President Biden has called for universal access to medications for opioid use disorder (MOUD) and the elimination of rules that place administrative burdens on providers who might prescribe MOUD. A robust research base has shown us that increased access to medication treatment for addiction and naloxone for overdose reversal saves lives,[26,27] increased access to SSPs reduces the spread of injection-related infection,[28] and increased access to contingency management results in very high treatment response rates.[29] It is critical to address barriers to the implementation of these interventions that exist at all levels. Persistent areas of need include ensuring adequate access to, coverage of, and reimbursement of evidence-based addiction care, naloxone, and syringe services.

   Novel approaches: There is a growing recognition that abstinence should not be the sole goal of addiction interventions, and alternative goals are essential for the development of interventions to reduce adverse consequences of drug use.[30] For example, outcomes such as reduced drug use and improved quality of life could facilitate entry into a wider range of treatment options. Patient-centered clinical trial endpoints, in particular, could lead to treatments that are more effective because patients will be more likely to utilize them. NIDA researchers are exploring strategies helpful for reducing drug use[31] as well as compounds that target neurobiological processes and symptoms such as disordered sleep that make recovery difficult.[32,33]

The Honorable Anna G. Eshoo (D-CA)

1. **Please describe how social media is used to facilitate the trafficking of fentanyl, fentanyl-related substances, and other opioids**.

   Response:
   Although the Ryan Haight Online Pharmacy Consumer Protection Act of 2008 (PL 110-425) was intended to curb the use of the internet as channel for sourcing illicit drugs, research shows that the online environment is populated with illegal internet pharmacies, dark web vendors, and social media posts from illicit drug dealers, all of which are implicated in illegal sales of fentanyl and other

[26] https://www.nap.edu/catalog/25310/medications-for-opioid-use-disorder-save-lives
[27] https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6423a2.htm
[28] https://www.ncbi.nlm.nih.gov/books/NBK184446/
[29] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6435332/
[30] Making Addiction Treatment More Realistic And Pragmatic: The Perfect Should Not Be The Enemy Of The Good | Health Affairs
[31] https://reporter.nih.gov/search/ORTgn7j7pU2Sss3XOthBbA/project-details/10137211
[32] https://reporter.nih.gov/search/C3fzb44A8U6ENCnBkITVAg/project-details/10454583
[33] https://reporter.nih.gov/search/C3fzb44A8U6ENCnBkITVAg/project-details/10092144

opioids.[34,35,36] Researchers have demonstrated that social media platforms are used by illicit drug sellers as direct-to-consumer marketing tools through fictitious advertising.[37,38,39] Although certain opioid keywords in hashtags are disabled on some platforms as a countermeasure, drug names are frequently misspelled by drug dealers and are relatively easy for social media users to find. [38,40] Posts typically include contact information such as a phone number or email address, and as such, it is difficult to surveil subsequent transactions.[41] Moreover, messages related to illicit drug marketing and sales are typically removed by the original posters after a short time, making them difficult to surveil.[41]

With NIDA support, researchers are refining detection methods by using a machine learning and multidisciplinary data analysis approaches to explore large volumes of data from Twitter and Instagram, aiming to characterize use of these platforms in promoting the marketing, distribution, and sale of synthetic psychoactive drugs (SPDs), including fentanyl and fentanyl related substances.[42] This study will describe the nature and magnitude of online marketing, sale, and distribution of SPDs; characterize the types of marketing strategies used, including messages used to influence knowledge, attitudes and perceptions pertaining to SPDs; and describe the association between SPD marketing and geographic and social network factors. This is a critical opportunity to better understand how social media contributes to the "digital risk" environment that can influence illicit drug initiation and addiction and enable illegal access to SPDs. The surveillance approach generated by this study holds promise for informing novel enforcement strategies as well as prevention and treatment interventions. Through an NIH Small Business Innovation Research award, this machine learning approach is being expanded to detect illegal opioid sales, with the aim of validating and commercializing this product for real-world use. [43] In addition, a recent NIDA supported study demonstrated the feasibility of using the publicly available Twitter Scraper for detecting Twitter content related to opioids, including messages about the procurement of illicit opioids online.[44] These methodologies may help ensure that the Ryan Haight Act is better implemented, monitored, and enforced in a constantly evolving digital environment in which social media use is ubiquitous.

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[34] Dasgupta N, Freifeld C, Brownstein JS. et al. (2013). Crowdsourcing black market prices for prescription opioids. *J Med Internet Res.* 15(8):e178. (PMID: 23956042)
[35] Pergolizzi, Jr. JJ, LeQuang JA, Taylor Jr. R, et al. (2017). NEMA Research Group The "Darknet": the new street for street drugs. *J Clin Pharm Ther.* 42(6):790–2.(PMID: 28921578)
[36] Broséus J, Rhumorbarbe D, Mireault C. et al. (2016). Studying illicit drug trafficking on Darknet markets: structure and organisation from a Canadian perspective. *Forensic Sci Int.* 264:7–14.. (PMID: 26978791)
[37] Mackey TK & Liang BA. et al. (2013). Global reach of direct-to-consumer advertising using social media for illicit online drug sales. *J Med Internet Res.*15(5):e105. (PMID: 23718965)
[38] Mackey TK, Kalyanam J, Katsuki T. et al. (2017). Twitter-Based Detection of Illegal Online Sale of Prescription Opioid. *Am J Public Health.* 107(12):1910–1915. (PMID: 29048960)
[39] Mackey TK, Kalyanam J, Katsuki T. et al. (2017) Detection of illicit online sales of fentanyls via Twitter. *F1000Res.* 6:1937. (PMID: 29259769)
[40] Li J, Xu Q, Shah N. et al. (2019). A machine learning approach for the detection and characterization of illicit drug dealers on Instagram: model evaluation study. J Med Internet Res. 15;21:e13803 (PMID: 31199298)
[41] Mackey T, Kalyanam J, Klugman J. et al. (2018). Solution to detect, classify, and report illicit online marketing and sales of controlled substances via Twitter: using machine learning and web forensics to combat digital opioid access. *J Med Internet Res.* 20(4):e10029 (PMID: 29613851).
[42] NIDA Grant R21DA050689
[43] NIH Contract: 75N95019C00069-0-9999-1
[44] Tofighi B, Aphinyanaphongs Y, Marini C. et al. (2020). Detecting illicit opioid content on Twitter. *Drug Alcohol Rev.* 39(3): 205-208 (PMID: 32202005).

NIDA-supported researchers also monitor social media to detect new and emerging drugs, and to understand how the internet and social media influences drug use. For example, the National Drug Early Warning System is developing an innovative machine learning approach to detect the emergence of novel psychoactive substances in real-time via social media and the darknet.[45] The annual Monitoring the Future survey of teens and young adults asks participants about their drug purchases through the internet more broadly in order to identify multiple digital risk environments.[46] Other studies aim to understand how social media marketing of cannabis, alcohol, and tobacco products influences substance use among youth and diverse populations.[47,48,49,50] Taken together, these studies hold promise to advance scientific knowledge about how the misuse of social media platforms may perpetuate the addiction crisis.

a. **Has the NIH observed an issue with private, peer-to-peer sales often facilitated in private groups**?

Response:
Social medica posts about illicit drug sales typically include contact information such as phone number or email address.[41] Sales are facilitated on social media, but subsequent transactions are difficult to surveil.

b. **Has the NIH observed formal, monetized advertisements on social media services for illicit drugs? Is this problem wide-spread**?

Response:
Advertisements for illicit drugs on social media platforms are disguised under fictitious advertisements. In April 2021, YouTube loosened its guidance about drug-related videos in order to expand monetization on content that may include recreational drugs and drug-related content, among other things. Research has not yet determined the impact of that change on illicit drug sales or use.

c. **To what degree and how often does the NIH coordinate with social media companies to combat the sale of opioids on social media**?

Response:
NIH funds independent grants and contracts to researchers and small businesses, and as such, does not partner with social media companies to combat the sale of opioids on social media.

d. **Which social media companies has the NIH worked with**?

Response:
NIH funds independent grants and contracts to researchers and small businesses, and as such, does not partner with social media companies to combat the sale of opioids on social

[45] NIDA Grant U01DA051126
[46] NIDA Grant R01DA001411
[47] NIDA Grant R56DA051232
[48] NIDA Grant R01DA049878
[49] NIDA Grant R01DA051000
[50] NIDA Grant F31DA053003

media.

e. **How does the NIH collaborate with social media companies**?

Response:
NIH funds independent grants and contracts to researchers and small businesses, and as such, does not partner with social media companies to combat the sale of opioids on social media.

f. **Have social media companies been receptive to the NIH outreach**?

Response:
NIH funds independent grants and contracts to researchers and small businesses, and as such, does not partner with social media companies to combat the sale of opioids on social media.

g. **Which social media companies have been the most productive partners on responding to issues involving illicit drug sales**?

Response:
NIH funds independent grants and contracts to researchers and small businesses, and as such, does not partner with social media companies to combat the sale of opioids on social media.

h. **Are there legal, technical, personnel, or other barriers to effectively coordinating to combating the sale of opioids on social media**?

Response:
NIH funds independent grants and contracts to researchers and small businesses, and as such, does not partner with social media companies to combat the sale of opioids on social media.

The Honorable Brett Guthrie (R-KY)

1. **As you know, methadone is still only given at treatment centers that must be visited once a day – which can be a burdensome and disruptive model to individuals' lives. However, there are products in development that would allow methadone to be given orally once per week – improving ability to receive and comply with treatment, reducing the risk of relapse, and providing a better quality of life. What actions can your agency take to speed development and uptake of these kinds of products, and how can the federal government at-large play a bigger role in supporting innovative dosage forms**?

Response:
NIDA's Division of Therapeutics and Medical Consequences[51] (DTMC) is leading efforts to support the discovery and development of new and improved treatments for opioid use disorder (OUD),

[51] https://www.drugabuse.gov/about-nida/organization/divisions/division-therapeutics-medical-consequences-dtmc

including extended-release formulations of existing FDA-approved medications (methadone, buprenorphine, and naltrexone). One of many medications in our drug development/testing pipeline is a long-acting formulation of methadone (oral once weekly therapy), developed by incorporating methadone into a gastric dosage form developed by Lyndra Therapeutics, Inc.[52]

Unfortunately, medications for OUD (MOUDs) are significantly under-utilized. To identify best approaches to speed the uptake of MOUD in diverse settings and diverse populations, NIDA funds implementation research in healthcare settings, justice settings, and community settings through the Clinical Trials Network (CTN),[53] the Justice Community Opioid Innovation Network (JCOIN),[54] and the HCS.[55] These studies are evaluating strategies for expanding OUD screening and treatment into emergency departments, primary care clinics, infectious disease programs, rural and American Indian/Alaska Native communities, and criminal justice settings.

NIDA also funds research on the provider- and systems-level barriers and facilitators to adoption of long-acting MOUD.[56] During the COVID-19 pandemic, people with OUD can now obtain a 14-28 days' take-home supply of methadone, which may particularly benefit people who live in rural areas or who otherwise have had trouble accessing treatment in the past. NIDA-funded research is examining clinicians' and patients' experiences with telehealth services for the treatment of OUD[57] and studying the implementation and outcomes of changes in OUD health services delivery policies, including effects on treatment rates and overdose rates.[58] This research will be critical for determining how to optimize access to effective MOUD through flexibilities in the provision of MOUD.

Incentives to encourage pharmaceutical industry investment in research and development of SUD treatments and to encourage payers to cover the cost of effective OUD medications could speed the development and adoption of evidence-based SUD practices. NIDA is exploring strategies to address significant barriers to the coverage of care for SUD to increase access to and utilization of MOUD, including innovative dosage forms. Research supports the benefits of increasing access to MOUD and reducing disparities in access.[59] [60] [61] Making federal flexibilities in the treatment for OUD permanent would build on the progress made during the COVID-19 pandemic to expand access to medication treatment.

The Honorable H. Morgan Griffith (R-VA)

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[52] NIDA Grant 4UH3DA050310-02
[53] https://www.drugabuse.gov/about-nida/organization/cctn/clinical-trials-network-ctn
[54] https://heal.nih.gov/research/research-to-practice/jcoin
[55] https://heal.nih.gov/research/research-to-practice/healing-communities
[56] NIDA Grant 1K01DA050771-01A1
[57] NIDA Grant 1R21DA053324-01
[58] NIDA Grant 1R01DA053232-01A1
[59] Institute of Medicine (US) Committee on Federal Regulation of Methadone Treatment, Rettig RA, Yarmolinsky A, eds. *Federal Regulation of Methadone Treatment*. Washington (DC): National Academies Press (US); 1995. (PMID: 25121195).
[60] Dick AW, Pacula RL, Gordon AJ. et al. (2015). Growth in Buprenorphine Waivers for Physicians Increased Potential Access to Opioid Agonist Treatment, 2002-11. *Health Aff (Millwood)*. 34(6):1028-1034 (PMID: 26056209).
[61] Jones CM, Campopiano M, Baldwin G. et al. (2015). National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment. *Am J Public Health*. 105(8): e55-e63 (PMID: 26066931).

1. **Do you believe that increasing access to long-acting injectable buprenorphine is vital to treating opioid use disorder and reducing drug overdose deaths? Why or why not**?

   Response:
   Yes. Buprenorphine is highly effective in reducing the morbidity and mortality among people with OUD. Long-acting formulations, available to patients stabilized on buprenorphine, eliminate the treatment barrier of daily dosing and can improve treatment retention and decrease risks of nonadherence, diversion, and misuse. Emerging evidence indicates that long-acting injectable formulations of buprenorphine (BUP-XR) improve medication satisfaction, patient-reported outcome measures (such as health status and quality of life),[62] and self-reported sustained abstinence in patients with OUD over a 12-month study period.[63] Additionally, compared to daily treatment with buprenorphine-naloxone, BUP-XR increased treatment retention rates at 8 weeks in individuals with OUD recently released from jail.[64]

   Preference for short-acting versus long-acting formulations of buprenorphine vary among individuals with OUD;[65] thus, expanding access to a variety of formulations of MOUD will allow patients to select formulations best aligned with their experiences, values, and treatment goals.

   NIDA funds several projects to compare the effectiveness of BUP-XR with other MOUD[66,67,68] and to assess the effectiveness of BUP-XR in criminal justice populations[69,70] and pregnant women with OUD.[71]

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[62] Ling W, Nadipelli VR, Solem CT. et al. (2020). Effects of monthly buprenorphine extended-release injections on patient-centered outcomes: A long-term study. *J Subst Abuse Treat*. 110:1-8 (PMID: 31952623).
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