Committee on Energy and Commerce
Subcommittee on Oversight and Investigations
Hearing: "Fentanyl: The Next Wave of the Opioid Crisis"
March 21, 2017

Questions for the Record for Dr. Wilson Compton, Deputy Director, National Institute on Drug Abuse (NIDA), National Institutes of Health

Questions from Chairman Tim Murphy

1. **Question: Last fall, the Canadian press reported that a type of test strip to indicate the presence of fentanyl was being made widely available for a low price ($5 Canadian). These kits or test strips were first announced in Vancouver, British Columbia, but later reports have identified them to pharmacies in Winnipeg, Manitoba (the middle of Canada). Yet there appears to be little if any public reaction, response, or similar kits detected or reported in the US.**
    a. **Does NIDA have any familiarity with these test kits?**
    b. **Is NIDA supporting research into these types of test kits?**

    Answer: Our understanding is that these test strips are enzyme immunoassay kits originally developed to test for the presence of fentanyl in urine that are being used to test for fentanyl in drug samples diluted in water. These kits are available for sale in the United States as well, from Diagnostic Automation/Cortez Diagnostics Inc., Confirm Biosciences, and NarcoCheck, and are sensitive to a variety of newer fentanyl analogs. At this time, there are no NIDA projects researching the adaptation of these kits to identify fentanyl in drug samples.

2. **Question: What challenges does fentanyl present in a treatment setting and how does that compare to treating a patient that is addicted to opioids or heroin?**

    Answer: The high potency of fentanyl and its rapid onset of effects are likely to increase the risk for overdose, as well as for addiction and for withdrawal symptoms. Thus, fentanyl users may be more likely to have severe opioid use disorders, compared with users of other types of opioids, but the treatment strategy is the same. It is also important to note that most individuals who illicitly use fentanyl also use other opioids; polydrug use is very common. Furthermore, users may be unaware that fentanyl was in the substances that they consumed.

    Medication-assisted treatment (MAT) is the standard of care. Evidence strongly demonstrates that methadone, buprenorphine, and injectable extended-release naltrexone all effectively help maintain abstinence from other opioids and reduce opioid use disorder symptoms. These medications should be administered in the context of drug use monitoring along with appropriate counseling and psychosocial supports to improve

outcomes and reduce the potential for relapse. However, there have been few cases of illicitly manufactured fentanyl users treated with MAT, and given that fentanyl use may lead to a more severe opioid use disorder, higher doses may be required to restore balance to the brain circuits impaired in these patients and to support recovery.

3. **Question: How could the NIDA-funded National Drug Early Warning System be used to enhance fentanyl surveillance?**

   Answer: The NIDA-funded National Drug Early Warning System (NDEWS) uses multiple sources of data to monitor fentanyl use and informs our understanding of the extent of the problem. NDEWS is a unique approach to understanding drug use (including fentanyl) patterns and trends in sentinel communities and across the nation. This program identifies emerging issues and disseminates information to a broad range of stakeholders. Key components of NDEWS include:

   a. leveraging existing data from law enforcement, public health, and research sources to monitor indicators of drug use, availability and consequences, in combination with novel data available via the internet and media;
   b. establishing collaborations with researchers in local communities to produce annual Sentinel Community Site Drug Use Patterns and Trends Reports and serving as contacts for emerging issues through the year. For example, NDEWS Sentinel Community Site Advance Report 2016: Selected Findings for Heroin, Fentanyl, and Methamphetamine
   c. an open virtual NDEWS Network of more than 1,500 members, including researchers, practitioners, and concerned citizens, providing the opportunity for NDEWS to share information and query the Network about emerging drug trends, and for Network participants to alert others to significant drug-related issues in their areas as they arise, query each other about what they have seen, and exchange scientific information and resources;
   d. the ability to conduct a limited number of "hot spot" studies in collaboration with local researchers to obtain more detailed information on emerging issues, including analysis of existing bio-specimens for the detection of drug metabolites–for example, New Hampshire HotSpot Report: The Increase in Fentanyl Overdoses (2016);
   e. the dissemination of information though several mechanisms including project website, annual Sentinel Community Site reports, special reports addressing priority topics and a webinar series addressing timely drug topics.

4. **Question: How can real-time monitoring of the fentanyl threat be expanded?**

   This question is best addressed by CDC. Please see their QFRs for a response.

5. **Question: Is NIDA supporting any research on understanding the differences between fentanyl analogues and their responsiveness to naloxone?**

Answer: While no NIDA projects are currently researching the efficacy of naloxone for treating overdoses related to fentanyl analogues, the National Institutes of Health (NIH), of which NIDA is a component, has just launched an Opioid Research Initiative to target research advances toward an end to the opioid crisis. Overdose Treatment Options is one of the three key pillars of this Initiative (along with Pain Management and Opioid Addiction Treatment), which will focus on developing new stronger, longer-acting antagonists to address the higher-potency synthetic opioids and reduce opioid overdose mortality.

6. **Question: Is NIDA supporting any behavioral research on effective prevention messaging?**

   Answer: NIDA is not currently supporting projects on prevention messaging that address fentanyl specifically, or opioids more broadly. The prevention messaging grants that NIDA supports primarily address tobacco, alcohol and marijuana use. However, NIDA is supporting a research study that is exploring the acceptability and feasibility of using social media-based interventions for opioid misuse and overdose prevention among patients on chronic opioid therapy (5R21DA039458-02).

7. **Question: Is NIDA supporting any research on the development of a low-cost rapid field test to detect the presence of fentanyl?**

   Answer: As noted in our response to question 1, NIDA is not currently funding any research to develop a field test for detecting fentanyl in drug samples. However, we are funding a project to develop a more rapid test for screening biosamples (e.g. blood or urine). Routine drug screens in hospitals often fail to detect synthetic drugs, so clinicians might be unaware of what caused an overdose. Mass spectrometry has the potential to be a useful tool to detect synthetic drugs, but it is rarely used at the point of care due to the complexity of conducting the analyses. A NIDA-funded study (DA043037)[1] is addressing this issue by exploring the use of "paper spray" mass spectrometry, which simplifies the testing process to make it more feasible in healthcare settings or potentially for emergency responders in the field. Researchers are developing and testing a disposable paper spray cartridge, which automates the preparation of the sample for testing. If the technology becomes widely used, the timely information on synthetic drug usage has the potential to improve the quality of care, and will be very useful for monitoring and surveillance of the fentanyl threat across the country.

8. **Question: The trends in medical prescriptions for fentanyl and related opioids are decreasing. Is NIDA supporting research to evaluate what programs have been effective in these areas?**

   Answer: Federal and state efforts have begun to curb the rate of opioid prescribing in the last few years. In states with the most comprehensive initiatives to reduce opioid

overprescribing, the results have been encouraging. The state of Washington's implementation of evidence-based dosing and best-practice guidelines, as well as enhanced funding for the state's Prescription Drug Monitoring Program (PDMP), helped reduce opioid deaths by 27 percent between 2008 and 2012.[2] In Florida, new restrictions were imposed on pain clinics, new policies were implemented requiring more consistent use of the state PDMP, and the Drug Enforcement Administration (DEA) worked with state law enforcement to conduct widespread raids on pill mills, which resulted in a dramatic decrease in opioid prescribing and in overdose deaths between 2010 and 2012.[3] These examples show that state and federal policies can reduce the availability of prescription opioids and related overdose deaths. NIDA is currently funding work to further explore the effectiveness of policies and programs intended to reduce opioid prescriptions, which includes research on:

- The impact of opioid prescribing practices on clinical outcomes[4]
- The impact of PDMP use on opioid prescribing and related health outcomes[5]
- Improving data extraction from PDMPs to identify patients who are doctor shopping[6]
- The impact of clinical guidelines and training on opioid prescribing and health outcomes[7]

9. Question: What has research shown about what is driving the increasing rates of heroin use?

Answer: Heroin produces its effects through the same opioid receptors as prescription pain relievers do, and research has shown that increases in heroin use have largely been driven by the increase in misuse of prescription opioids. Between 1999 and 2011 there was a fourfold increase in opioid prescribing that was paralleled by increases in prescription opioid misuse, addiction, and overdose.[8] While only about 1-3 percent of people who misuse prescription opioids transition to heroin in any given year,[9,10] 80 percent of heroin users today initiated opioid misuse with prescription opioids.[9] Those who transition to heroin are likely to use multiple other drugs and to have severe prescription opioid use disorders, suggesting that the transition to heroin is part of a broad drug misuse pattern.

Increases in heroin use may also be driven by increases in heroin availability and purity, along with its relatively low cost.[8] Mexican potential pure heroin production increased from an estimated eight metric tons in 2005 to 70 metric tons in 2015—more than a 10-fold increase. Domination of the U.S. market by Mexican and Colombian heroin sources, along with technology transfer between these suppliers, has increased the availability of easily injectable, white powder heroin.[11] In a recent survey of patients receiving treatment for opioid use disorder, accessibility was one of the main factors identified in the decision to start using heroin.[12] While some have speculated that regulatory changes aimed to restrict prescription opioid availability have led to increased heroin use, this was not the primary driver as heroin use began to rise before these policy shifts.[8]

10. Question: Does fentanyl adulteration of heroin and other drugs of abuse raise concerns about increases in the rates of addiction and overdoses?

Answer: Yes. Fentanyl taken alone or in combination with other drugs exhibits properties that are associated with a heightened risk of addiction and overdose. Fentanyl is extremely fat-soluble, so it crosses the blood-brain barrier very rapidly and exerts potent subjective effects within seconds.[13] Faster euphoric effects are associated with increased addictive potential of drugs.[14] Fentanyl also quickly and potently reduces the rate of breathing, and circumstances surrounding fentanyl overdose—including lack of fentanyl metabolism and death with the needle still in the vein—indicate that such overdoses can occur very quickly.[15,16] Acute chest wall rigidity caused by IV fentanyl use could also contribute to heightened risk of rapid overdose death. A recent study of injection drug use determined that fentanyl injections had twice the overdose risk of heroin injections, and eight times the overdose risk of injections of common prescription opioids, such as oxycodone.[17] This increase in overdose risk is exacerbated by the fact that drugs sold as heroin or counterfeit pills may be cut with variable amounts of fentanyl, and a person may not even know that they're being exposed to this potent and dangerous opioid.[15]

References

1 Manicke, N. E. *DA043037-01 Sensitive and Rapid Screening of Synthetic Drugs by Mass Spectrometry*, <https://projectreporter.nih.gov/project_info_description.cfm?aid=9226136&icde=33955530&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pball=> (

2 Franklin, G. *et al.* A Comprehensive Approach to Address the Prescription Opioid Epidemic in Washington State: Milestones and Lessons Learned. *American Journal of Public Health* **105**, 463-469, doi:10.2105/AJPH.2014.302367 (2015).

3 Johnson, H. *et al.* Decline in drug overdose deaths after state policy changes - Florida, 2010-2012. *MMWR Morb. Mortal. Wkly. Rep.* **63**, 569-574 (2014).

4 Coffin, P. O. *DA040189-01A1 Cohort Study of Opioids, Pain and Safety in an Era of Changing Policy (COPING)*, <https://projectreporter.nih.gov/project_info_description.cfm?aid=9106796&icde=33950549&ddparam=&ddvalue=&ddsub=&cr=2&csb=default&cs=ASC&pball> (

5 Deyo, R. A. *DA031208-05 Use of Prescription Monitoring Programs to Improve Patient Care and Outcomes*, <https://projectreporter.nih.gov/project_info_description.cfm?aid=9012043&icde=33950549&ddparam=&ddvalue=&ddsub=&cr=3&csb=default&cs=ASC&pball> (

6 Perry, B. L. *DA039928-01A1 Doctor Shopping for Controlled Substances: Insights from Two-Mode Social Network Analysis*, <https://projectreporter.nih.gov/project_info_description.cfm?aid=9174102&icde=33950662&ddparam=&ddvalue=&ddsub=&cr=11&csb=default&cs=ASC&pball=> (

7 Edlund, M. J. *DA034627-03 Prescribers, Pharmacists, and the Opioid Dilemma: A Multi-Site Qualitative Study*, <https://projectreporter.nih.gov/project_info_description.cfm?aid=9058019&icde=33950549&ddparam=&ddvalue=&ddsub=&cr=4&csb=default&cs=ASC&pball=> (

8 Compton, W. M., Jones, C. M. & Baldwin, G. T. Nonmedical Prescription-Opioid Use and Heroin Use. *N Engl J Med* **374**, 1296, doi:10.1056/NEJMc1601875 (2016).

9 Muhuri, P. K., Gfroerer, J. C. & Davies, M. C. (CBHSQ [Center for Behavioral Health Statistics and Quality] Data Review, 2013).

10 Carlson, R. G., Nahhas, R. W., Martins, S. S. & Daniulaityte, R. Predictors of transition to heroin use among initially non-opioid dependent illicit pharmaceutical opioid users: A natural history study. *Drug Alcohol Depend* **160**, 127-134, doi:10.1016/j.drugalcdep.2015.12.026 (2016).

11 U. S. Department of Justice National Drug Intelligence Center. *National Drug Threat Assessment 2011*, <http://www.justice.gov/archive/ndic/pubs44/44849/44849p.pdf> (2011).

12 Cicero, T. J., Ellis, M. S., Surratt, H. L. & Kurtz, S. P. The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years. *JAMA Psychiatry* **71**, 821, doi:10.1001/jamapsychiatry.2014.366 (2014).

13 Poklis, A. Fentanyl: a review for clinical and analytical toxicologists. *J Toxicol Clin Toxicol* **33**, 439-447 (1995).

14 Mathias, R. *Rate and Duration of Drug Activity Play Major Roles in Drug Abuse, Addiction, and Treatment*, <https://archives.drugabuse.gov/NIDA_Notes/NNVol12N2/NIDASupport.html> (1997).

15 Suzuki, J. & El-Haddad, S. A review: Fentanyl and non-pharmaceutical fentanyls. *Drug Alcohol Depend* **171**, 107-116, doi:10.1016/j.drugalcdep.2016.11.033 (2017).
16 Burns, G., DeRienz, R. T., Baker, D. D., Casavant, M. & Spiller, H. A. Could chest wall rigidity be a factor in rapid death from illicit fentanyl abuse? *Clinical toxicology (Philadelphia, Pa.)* **54**, 420-423, doi:10.3109/15563650.2016.1157722 (2016).
17 Latimer, J., Ling, S., Flaherty, I., Jauncey, M. & Salmon, A. M. Risk of fentanyl overdose among clients of the Sydney Medically Supervised Injecting Centre. *Int J Drug Policy* **37**, 111-114, doi:10.1016/j.drugpo.2016.08.004 (2016).