

IDENTIFYING NEW ILLICIT DRUGS AND SOUNDING THE ALARM IN REAL TIME

BY JIM DAWSON

In October 2017, chemist and forensic toxicologist Barry Logan stood behind the podium at the National Institute of Standards and Technology's (NIST) Symposium on Synthetic Opioids and the Overdose Epidemic¹ and described a scenario that many in the audience were familiar with: Federal officers intercept a package containing an unknown white powder at a U.S. port of entry, and tests are conducted to determine if the powder is, as suspected, an illicit drug.

Is it the powerful drug fentanyl, or one of the several known fentanyl analogues being manufactured in overseas drug labs? Or is it heroin laced with fentanyl? Or could it be U-47700, an opioid developed by the Upjohn Company in the 1970s and now produced in foreign labs?

U.S. Customs and Border Protection (CBP) officers work with chemists to test for an array of known illicit drugs, yet the powder does not react to drug screening tests. It appears to be nothing more than white powder.

The agents know, however, that this may be an analogue of a known drug — a new substance created by making a slight change in a molecule of the original drug. It is still a powerful drug, but it does not react to the screening. And, because it is new, it is not on the list of illegal drugs.

But it will kill people, adding to the estimated toll of 72,000 people who die each year from drug overdoses in the United States, of which nearly 30,000 are due to overdoses of fentanyl or a fentanyl analogue.² Because of this seemingly minor alteration, a medical examiner may not be able to detect the drug in a post-mortem examination of an overdose victim and may rule the cause of death as undetermined.

Enter Logan, supported by an NIJ grant and a partnership project funded by the Centers for Disease Control and Prevention (CDC) in cooperation with the U.S. Department of Justice's Organized Crime Drug Enforcement Task Forces (OCDETF) and CBP. The project is trying to identify these novel psychoactive substances (NPS) as they arrive in the United States and quickly alert drug enforcement agencies, crime laboratories, medical examiners, and health officials — not only in the United States but also worldwide. When officers at a port of entry find a



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suspicious substance that does not react to basic drug screens and testing protocols, they can now send it to Logan, who uses sophisticated liquid chromatography-high resolution mass spectrometry (LC-HRMS) and nuclear magnetic resonance (NMR) spectroscopy to determine exactly what the substance is and what known drug it is related to.

Logan is also supported by another NIJ grant, awarded through a fiscal year 2017 NIJ Drugs and Crime program solicitation (see sidebar, “Studying the Relationship Between Drugs and Crime”). He is using that award to data mine raw electronic data acquired from liquid chromatography time-of-flight mass spectrometry (LC-TOF-MS) analysis of more than 93,000 suspected drug deaths in which the drugs were not identified, as well as 30,000 suspected cases of drug-impaired driving. By reexamining the data from medical examiners and law enforcement, Logan can engage in “toxicological time travel” in which he uses knowledge developed today about emerging drugs to examine records dating back two years. This allows him to better track drugs as they appear and disappear from the illicit drug supply, he said.

Logan is the chief scientist at NMS Labs and executive director of the Center for Forensic Science Research and Education at the Fredric Rieders Family Foundation, both located in Willow Grove, Pennsylvania. He has a long history of identifying parent drugs and their metabolites (byproducts produced when a drug is broken down in the body), and has conducted NIJ-supported research to identify designer drugs used by attendees at electronic dance music festivals in Miami and elsewhere. At the Miami festivals, Logan offered \$20 Dunkin’ Donuts cards to those who would provide urine, saliva, and blood

samples. In those studies, he found that a wide variety of NPS drugs were being used, that the mix of drugs changed each year, and that many of the attendees misidentified the drug they thought they had taken.³

“In terms of our ultimate objective,” Logan told the experts at the NIST gathering, “we’re really all working on the same thing — improvement in the quality of life and civil society — and both are certainly impacted by the opioid crisis.” Logan noted the difficulty of “rapidly responding to changes in the drug market to help educate first responders, drug use communities, and people at risk of harm.” There is a critical need to educate medical professionals so they can recognize and properly treat a person suffering from a drug overdose — be it fentanyl, an analogue substance, heroin, another new drug, or a combination of drugs, he said.

By analyzing and identifying the seized drugs and biological samples as part of the NIJ grant and his project partnerships, Logan said, he is creating an early warning system — an NPS Data Hub — that enables CDC personnel and federal and state public health and safety entities “to distribute and make that information available and actionable early in the life cycle of a substance.”⁴

The Opioid Crisis

Identifying a new drug and getting the word out quickly is becoming increasingly important, given the overwhelming scale of the problem and the speed with which new drugs are created and shipped into the United States. The CDC estimated that 72,000 drug overdose deaths occurred in 2017 (about 197 people per day); nearly 16,000 of the deaths involved heroin, and more than 29,000 involved synthetic opioids such as fentanyl and fentanyl analogues.⁵

Logan noted that most heroin currently sold on U.S. streets contains some amount of fentanyl or an analogue, and there is no way for a user to know how much is present. Fentanyl has a chemical structure that allows it to pass more easily through the blood-brain barrier; this accounts, in part, for the increasing number of opioid overdoses and deaths.

Studying the Relationship Between Drugs and Crime

In 1976, Congress directed NIJ to collaborate with the National Institute on Drug Abuse to explore the relationship between drug use and crime. By 1980, a team of four NIJ-sponsored researchers had compiled and published *Drugs and Crime: A Survey and Analysis of the Literature*.¹ This report summarized existing research on patterns of drug use and criminal behavior and the effects of drug treatment strategies on criminality, setting the stage for NIJ to launch its Drug Use Forecasting (DUF) program in 1987. DUF measured and tracked drug use among arrestees to generate reliable and current information on drug use in relation to the criminal justice system. After a decade of collecting data, NIJ refined and expanded DUF to form the Arrestee Drug Abuse Monitoring (ADAM) program, improving the quality of its annual estimates of drug use prevalence. ADAM was in operation until 2003.² The data from these two NIJ efforts proved foundational for understanding the changing landscape of drug use across regions and over time.

In addition to tracking drug use trends, NIJ has also invested significant resources in original research on how to decrease drug use. NIJ-funded studies in the 1990s showed that drug treatment could be integrated into the criminal justice system to effectively reduce criminality. Building on these findings, NIJ began to evaluate an array of drug treatment modalities for offenders, including drug courts, residential drug treatment corrections programs, intensive probation supervision, and systemwide approaches. NIJ's drugs and crime portfolio over the past decade has focused on crime reduction by studying prevention and intervention strategies for drug-related crimes, tactics for disrupting and dismantling drug markets, and technologies for improved drug detection and recognition.

More recently, NIJ research has focused on the policies, practices, and resources available to law enforcement to deter, investigate, and prosecute opioid use. As part of the U.S. Department of Justice's overall response to the opioid epidemic, NIJ's current priority is to address drug trafficking, markets, and use related to heroin and other opioids such as fentanyl and its analogues.

Notes

1. Robert P. Gandossy, Jay R. Williams, Jo Cohen, and Henrick J. Harwood, *Drugs and Crime: A Survey and Analysis of the Literature*, Washington, DC: U.S. Department of Justice, National Institute of Justice, May 1980, NCJ 159074, <https://www.ncjrs.gov/App/Publications/abstract.aspx?ID=159074>.

2. Although NIJ ended ADAM in 2003, the Office of National Drug Control Policy operated ADAM II from 2007 to 2013. Ten of the original ADAM sites were selected for geographic diversity to address questions regarding methamphetamine trends beyond the Southwest, and instrumentation was modified to add items specific to methamphetamine.

The current opioid crisis is fueled, in large part, by the enormous supply of illicit drugs that flow into this country on a daily basis. The primary source is laboratories in China where, according to a recent Government Accountability Office (GAO) report, "thousands of pharmaceutical and chemical companies operate, both legally and illegally."⁶ Federal

drug enforcement officials believe the number of Chinese labs producing illicit drugs destined for the United States to be more than 100,000.

The GAO report goes on to note, "Certain Chinese chemical exporters utilize various covert methods to ship drugs to the United States, including sending

illicit materials through a chain of forwarding systems, mislabeling narcotic shipments, and modifying chemicals so they are not controlled [listed as illegal] in the United States.”⁷

The drug shipments arrive by both traditional international mail and through express package companies such as FedEx, UPS, and DHL.⁸ In his presentation at the NIST Symposium, Logan noted that about 155,000 packages arrive per night from China at the John F. Kennedy International Airport in New York, with similar numbers inundating mail facilities at other major airports, including O’Hare International Airport in Chicago and Los Angeles International Airport. Only a fraction of the packages contain illicit drugs, but the sheer volume makes it impossible for authorities to completely screen the river of packages.

Beyond shipping fentanyl and its analogues directly into the United States, the GAO report said, Chinese traffickers also send significant amounts of fentanyl products to Mexico and Canada, where the drugs are repackaged and then smuggled into this country. The report did not put numbers on the levels of drugs coming across the northern and southern U.S. borders, saying their illicit nature makes them difficult to quantify.⁹

The financial incentive for drug dealers is clear, according to a 2017 Drug Enforcement Agency assessment: “Traffickers could purchase a kilogram of illicit fentanyl for a few thousand dollars from a Chinese supplier, create counterfeit prescription pills using illicit pill presses, and collect up to \$20 million in revenue.”¹⁰

Early Designer Drugs

The current wave of illicit drugs driving the opioid crisis is the latest and, considering the annual death count, perhaps the most severe drug crisis faced in the United States. But it is not the first illicit drug wave.

“I would characterize the rise of the opioids as another wave in the overall novel psychoactive substances arena that started with synthetic cannabinoids back

in 2008, which led to the development of other [drug] analogues in the stimulant class,” Logan said. “That is when the so-called bath salts started to take off.”

Much of the early “designer drug” phase was fueled by chemists in Chinese labs, he said, and those same chemists turned to making fentanyl analogues in response to the growing opioid crisis in the United States. “We generated our opioid crisis in this country through over-prescribing of pain pills, and once we created a demand for potent opioids then the illicit market stepped in and started to fill that demand,” Logan said. “That started in late 2013, early 2014, and then we started to see things other than heroin and fentanyl itself in our post-mortem casework.”

From 1999 to 2011, consumption of hydrocodone (one of the early prescription opioids) nearly doubled, and consumption of oxycodone (a more powerful prescription opioid) increased by nearly 500%, according to researchers writing in the journal *Annual Review of Public Health*.¹¹ The CDC added opioid overdose prevention to its list of the top five public health challenges in 2014 and, in 2015, said that the dramatic increase in opioid use led to “the worst drug overdose epidemic in [U.S.] history.”¹²

Many researchers in the field, including Logan, cite a one-paragraph letter in a 1980 issue of the *New England Journal of Medicine* as triggering what became the opioid crisis. The letter, by a doctor and colleague at the Boston University Medical Center, said that of 11,882 patients who had received at least one narcotic, there were only four instances of “reasonably well documented addiction” and the addiction was considered major in only one case.¹³

That letter, according to an article in the *2015 Annual Review of Public Health*, was embraced by pharmaceutical companies; by 1995, the American Pain Society had introduced a campaign titled “Pain as the Fifth Vital Sign,” and doctors were urged to use opioids more aggressively to treat chronic pain.¹⁴

“What that did was create the demand for opiates,” Logan said, “and once you’ve got a large population of people who are hooked or habituated or dependent

on opioids, and you take away the legal substances because they were being overprescribed, then people turned to the illicit substances as a replacement. That's what fueled the market and created the opportunity for some enterprising person to start making synthetic opioids, the fentanyl analogues."

Another notable influence in the creation of the NPS movement was a 1991 book by American chemist Alexander Shulgin titled *PIHKAL: A Chemical Love Story*. Although the book was not about opioids, it was "both a recipe book in terms of how to make psychoactive substances, as well as detailing what doses to take and what kind of effects to expect," Logan said. "So when that book was published, it opened people's eyes to the possibility of making psychoactive substances beyond what was routinely available at the time: cocaine, methamphetamine, and heroin."

A Real-Time Warning System

As the use of fentanyl and its analogues increased, the primary tool being used in forensic toxicological casework — the gas chromatography mass spectrometer — was inadequate for identifying the new drugs. "When you have to take a brand-new substance that you've never seen before and pull it apart into its chemical components and identify both its chemical composition and structure . . . well, most forensic toxicology laboratories didn't have the tools because they'd never had to do that before," Logan said.

As Logan was developing the skills and resources at his private lab to identify the emerging drugs, Assistant U.S. Attorney M.J. Menendez was assigned to work with the OCDETF. In 2014, she was the "heroin coordinator" for the office, but the drug world changed so quickly that she now describes herself as the "fentanyl, heroin, and opioid coordinator." Early in her work with the OCDETF, she realized that border agents and homeland security investigators were seeing more and more white powder that did not react to drug screening tests.

"With much of the arriving novel psychoactive substances, law enforcement officials just weren't able to identify what it was," she said. "The challenges [of] resourcing and conducting the complex testing to identify the novel substances was resulting in delays. We were taking anywhere from three months to a year or longer to analyze a substance, and that was proving to be a law enforcement impediment."

Menendez realized that the lack of identification was a significant public health impediment as well as a law enforcement issue. "If the medical examiners don't know that it's a drug they are looking for, they can't find it," she said. "So we started working with the labs for Customs and Border Protection, and they faced the same problem as most forensic labs in that they were not able to quickly identify the rapidly emerging NPS drugs, including the fentanyl analogues."

As she traveled to meetings with medical examiners and others on the front line of the drug wars, Menendez met Logan and saw his presentation on toxicological time travel. As he described retroactive data mining and talked about looking back to identify patterns of drug emergence and distribution, she realized that drug agencies needed to look forward in the fight against novel fentanyl analogues.

As Menendez met with medical examiners, coroners, and other experts, she repeatedly heard that Logan's research was creating a road map for understanding the opioid and other NPS epidemics in both toxicology and analyses of seized drugs. So Menendez called Logan and said, "You know, I know we've talked about toxicology, but I've got this issue"

Her issue was the overwhelming volume of seized drugs flowing into the United States through ports of entry, particularly drugs that could not be identified. And, beyond just identifying the new drugs, information about them had to be disseminated as quickly as possible to emergency room doctors, medical examiners and coroners, and law enforcement.

Spreading the Word on Novel Drugs

When forensic toxicologist Barry Logan identifies a new illicit drug at his laboratory in Willow Grove, Pennsylvania, he alerts virtually everyone involved in the battle against the wave of opioids flooding the United States. The information is posted on his NPS Discovery website and through a comprehensive email tree. Logan, executive director of the Center for Forensic Science Research and Education and chief scientist at NMS labs, set up the website about a year ago and has already posted detailed descriptions of more than 45 previously unidentified illicit drugs known collectively as novel psychoactive substances (NPS).

The system is optimized to effectively transmit the drug information to public health officials, emergency room doctors, toxicologists, state health offices, and local treatment communities, as well as federal, state, and local law enforcement agencies. “The goal of this was to put our arms around it and give it a name,” Logan said of the website, which is, in part, supported by NIJ.¹

The new drugs are discovered using three methods: testing of unidentified substances seized by law enforcement; toxicological data mining of electronic data from tens of thousands of suspected drug deaths in which drugs were not initially identified; and sample mining of biological fluids for traces of illicit drugs.

Logan said the website is being upgraded to make it more comprehensive; the upgraded version will include monographs for new substances and more “trend reports” on drug distribution and use patterns in the United States. The site will also be made more interactive in the near future, he said.

Note

1. NIJ provided critical funding in support of the NPS Discovery website through three of its fiscal year 2017 award programs: Research and Evaluation on Drugs and Crime; Research and Development in Forensic Science for Criminal Justice Purposes; and the Graduate Research Fellowship Program in Science, Technology, Engineering and Mathematics. For more information on the individual grant awards, go to NIJ.ojp.gov, keywords: 2017-DN-BX-0169, 2017-R2-CX-0021, and 2017-R2-CX-0002.

Menendez and Logan began working together on the OCDETF’s ports-of-entry project to rapidly identify as many of the seized, but unknown, drugs as possible. Critical to the project is disseminating the information about a new drug as soon as Logan identifies it.

Once Logan identifies a new fentanyl analogue or other new drug, he posts the identified drug, along with all of the relevant technical analytical data, on his Novel Psychoactive Substances Discovery website (see sidebar, “Spreading the Word on Novel Drugs”).¹⁵ He also disseminates the information to thousands of authorities worldwide, he said. Speed is critical.

“In the typical research cycle, if you’re funded to do a project, you set it up, you get your data, and at the end of a year or two years, you write up a report and it gets published,” he said. “By that time in the cycle of these novel psychoactive substances drugs, that is ancient history.”

Because the market changes and turns over so fast, he said, notification of a new drug has to happen very quickly. “We do that by working with the Department of Justice, and every time we get a new substance, that notification goes out to literally tens of thousands of people around the world.”

Information about the new drug “goes out in real time to people who can actually use it in the investigations of their case work,” he said. “When you think about putting research into action and being able to do that in real time — within a matter of a few weeks of the discovery of a new compound — that’s the value of this project.”

Logan said he is very aware that only a fraction of the illicit drugs being sent into the United States are being seized, “but you do anything that can be done to disrupt that supply chain.” A kilo of fentanyl that gets seized at a port of entry is 250,000 doses that never make it onto the street, he said. He concluded, “Everything that does get taken out of the supply makes a difference.”

About the Author

Jim Dawson is a forensic science writer and contractor with Leidos.

Notes

1. See American Academy of Forensic Sciences website, <https://news.aafs.org/aafs-news/nist-symposium-on-synthetic-opioids-and-the-overdose-epidemic-to-take-place-october-30-31-2017/>.
2. National Center for Health Statistics [NCHS], Centers for Disease Control and Prevention [CDC], Drug Overdose Mortality File, CDC WONDER database (cited on National Institute on Drug Abuse website, “Overdose Death Rates,” revised January 2019), <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>.
3. A.L.A. Mohr, J.K. Yeakel, M. Friscia, and B.K. Logan, “Recreational Drug Use Trends and Emerging Analytes Identified in Blood, Urine, and/or Oral Fluid from Attendees at an Electronic Dance Music Festival,” poster presentation at the American Association of Forensic Sciences annual conference, 2015.
4. National Institute of Standards and Technology, “Novel Psychoactive Substance (NPS) Data Hub,” <https://www.nist.gov/programs-projects/novel-psychoactive-substance-nps-data-hub>.

5. NCHS, “Overdose Death Rates.”
6. U.S. Government Accountability Office, *Illicit Opioids: While Greater Attention Given to Combating Synthetic Opioids, Agencies Need to Better Assess their Efforts*, GAO-18-205, March 2018, 10, <https://www.gao.gov/assets/700/690972.pdf>.
7. *Ibid.*, 10-11.
8. *Ibid.*, 11.
9. *Ibid.*, 11-12.
10. *Ibid.*, 12.
11. Andrew Kolodny et al., “The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction,” *Annual Review of Public Health* 36 (2015): 560, doi:10.1146/annurev-publhealth-031914-122957.
12. *Ibid.*
13. Jane Porter and Hershel Jick, “Addiction Rare in Patients Treated with Narcotics,” *New England Journal of Medicine* 302 (1980): 123, doi:10.1056/NEJM198001103020221 (cited in Kolodny et al., “The Prescription Opioid and Heroin Crisis,” reference 62).
14. Kolodny et al., “The Prescription Opioid and Heroin Crisis,” 562.
15. The Center for Forensic Science Research and Education, “Novel Psychoactive Substances,” NPS Discovery web page, “Novel Psychoactive Substances Discovery” page, <https://www.forensicscienceeducation.org/resources/nps-discovery..>

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NCJ 252731

Cite this article as: Jim Dawson, “Identifying New Illicit Drugs and Sounding the Alarm in Real Time,” *NIJ Journal* 281, November 2019, <https://nij.gov/topics/articles/identifying-new-illicit-drugs-and-sounding-alarm-real-time>.