



LEGAL REPORT

NITAZENES: AN EMERGING AND DEADLY NOVEL PSYCHOACTIVE SUBSTANCE

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Highlights

- In 2019, the synthetic opioid nitazenes, made in China, emerged in the illicit drug market. Far more powerful than morphine or (sometimes) even fentanyl, nitazenes have begun to cause a significant number of overdose fatalities.
- Nitazenes' prevalence is unknown because medical examiners do not ordinarily test for that drug.
- We need to respond to this new threat *now* before it becomes a new and even deadlier wave of the opioid epidemic.

Executive Summary

The recent emergence of a category of novel synthetic opioids—nitazenes—threatens to exacerbate the opioid epidemic ravaging America, to date driven by abuse of prescription opioids, heroin, and fentanyl. Far more powerful than morphine, the baseline prescription analgesic, with some versions even more powerful than fentanyl, nitazenes first appeared in the illicit street market in 2019. China is one source of nitazenes, but the drugs are relatively easy and inexpensive to synthesize, and so could soon be made in the U.S.A. There are several public health steps that should be taken to fend off or respond to this new plague, such as ensuring adequate local distribution of naloxone and improving forensic testing methods and information-sharing. Education and prevention are of paramount importance because the surest way to reduce fatal overdoses is to persuade Americans not to use dangerous illicit drugs in the first place.

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INTRODUCTION

For two-plus decades, the United States has been beset with an opioid-abuse problem² causing overdose fatalities on a Biblical scale. More than 800,000 people—an amount greater than the total deaths that our nation has suffered in all of its post-World War II conflicts³—have died from the abuse of legitimate opioids or (more commonly) the use of illicit versions of those drugs.⁴ As one physician described it, “[t]he

² “Opioids are a class of naturally derived, semi-synthetic, or synthetic drugs that target three types of opioid receptors in the brain, the mu (m), kappa (k), and delta (d) receptors. These receptors mediate a range of physiological and pharmacological effects, including analgesia. Used on a short-term basis, opioids are extremely effective for patients who suffer moderate to severe acute pain stemming from a major injury, surgery, a gunshot wound, or the end stages of terminal cancer.” Paul J. Larkin & Bertha K. Madras, *Opioids, Overdoses, and Cannabis: Is Marijuana An Effective Therapeutic Response to the Opioid Abuse Epidemic?*, 17 GEO. J.L. & PUB. POL’Y 555, 561 (2019) (footnotes omitted); U.N. OFF. ON DRUGS & CRIME, *The Challenge of New Psychoactive Substances—A Technical Update 2024*, at 43 (June 2024) [hereafter 2024 UNODC *Technical Update*] (“[A]n opioid is a generic term applied to a variety of substances including naturally occurring opiates (e.g., opium and morphine), synthetic opioids (e.g., fentanyl and tramadol), semi-synthetic opioids (e.g., heroin), as well as new psychoactive substances (NPS) with opioid effects.”). Use of illicitly made opioids, and the use of other illegal drugs (e.g., cocaine) to which opioids have been unknowingly added, poses serious individual and public health risks. See Joseph Friedman & Daniel Ciccarone, *The Public Health Risks of Counterfeit Pills*, 10 LANCET PUB. HEALTH e58 (2025) (“The principal risk for individuals, as medicine discovered late in the nineteenth century, is that opioids are highly addictive in susceptible individuals, with the added risk of an overdose. The euphoric effect of opioids overwhelms the brain’s reward centers, leading to continued opioid use and, ultimately, physical dependence or addiction. Once a person becomes addicted, quitting is a very difficult process. Unless they are aided by other medications, individuals suffering from withdrawal experience a miserable, painful period that can set in hours after taking the last dose and can last for a week or more. What is worse, someone who uses opioids for a long time, such as someone suffering from chronic back pain, can develop a tolerance to the drug, requiring ever-increasing dosages, or a more powerful opioid, to receive the same relief. Far worse still is the fact that high doses of opioids can lead to a fatal overdose because opioid receptors are abundant in the brainstem region responsible for autonomic respiration. Overactivity of the large number of mu opioid receptors in the brainstem region can suppress breathing and lower blood oxygen levels, leading to coma and death. The principal risk for a society awash with opioids, as we now have painfully learned, is a contemporary public health nightmare: the massive number of fatalities that opioid abuse can generate.” Larkin & Madras, *supra*, at 562 (footnotes omitted).

³ There have been three stages to this scourge. It began when physicians overprescribed and patients overused lawfully ordered Schedule II analgesics, such as oxycodone and hydrocodone. After the medical profession cut back on the prescription of opioids, the next stage began when people who had become dependent on opioids used the illegal opioid heroin to avoid the pangs of withdrawal from their lawfully prescribed drugs. The third, and still ongoing stage, commenced when fentanyl burst on the scene. See CNTRS. FOR DISEASE CONTROL & PREVENTION, (2025), *Overdose Prevention: Understanding the Opioid Overdose Epidemic* (2025), www.cdc.gov/overdose-prevention/about/understanding-the-opioid-overdose-epidemic.html (last accessed Feb. 23, 2026) (“From 1999-2023, approximately 806,000 people died from an opioid overdose. This includes overdose deaths involving prescription and illegal opioids.”) (footnote omitted); Larkin & Madras, *supra* note 1, at 557, 562-63, 588.

⁴ Two acts of Congress are principally relevant here. One law is the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 201(g)(1) (West 2026), which bars the distribution in interstate commerce of any “drug” unless and until it has been approved by the Commissioner of Food and Drugs. The other statute is the Controlled Substances Act of 1970, Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970, Pub. L. No. 91-513, 84 Stat. 1242 (codified as amended at 21 U.S.C. §§ 801-904 (2019)). The CSA incorporates the definition of a “drug” from the FDCA, 21 U.S.C.

proliferation of opioid use in the United States is called an epidemic, but it more resembles metastatic cancer.”⁵ Unfortunately, a newly emerging drug—nitazenes—threatens to add to the death toll produced by better known illicit opioids, like heroin, oxycotin, and fentanyl.

I. THE EMERGENCE OF NITAZENES

When science was at only a rudimentary level, humans used as medicines raw agricultural products, such as juice from the opium poppy, the cocoa leaf, and the cannabis plant.⁶ As science developed, professional and amateur chemists developed other, semi-synthetic drugs from those products, such as diacetylmorphine (heroin) and concentrated versions (*e.g.*, “shatter”) of the active ingredient in cannabis (delta-9-tetrahydrocannabinol, or THC).⁷ But twentieth-century developments in computational and synthetic chemistry have given scientists the ability to isolate the active constituents of these plants and, knowing their structure, to synthesize from readily available laboratory chemicals entirely new, more powerful forms of illicit drugs known as Novel Psychoactive Substances (NPSs) or, in the lingo, “designer drugs.”⁸ Chemists synthesize new NPSs every year.⁹ The relationship and interaction between

§ 201(g)(1), and places drugs into one of five schedules—Schedules I through V—which impose decreasingly rigorous controls on the distribution of those “controlled substances” based on three factors: whether a drug has a legitimate medical use, whether it has a high potential for abuse, and whether it can be safely used under medical supervision. 21 U.S.C. § 812(b)(1)(A)–(C). Heroin, for example, is a Schedule I drug because it fails those tests. The CSA prohibits physicians from prescribing Schedule I drugs to anyone for any use. 21 U.S.C. § 841; *see United States v. Moore*, 423 U.S. 122 (1975) (ruling that a physician can be convicted for distributing methadone, a Schedule II controlled substance, outside the boundaries of professional medical practical). By contrast, fentanyl has legitimate medical uses for surgery and as an analgesic, but it is dangerous unless prescribed by a licensed physician, so it fits into Schedule II.

⁵ David Brown, *Opioids and Paternalism*, AM. SCHOLAR 22–23 (2017).

⁶ *See* Larkin & Madras, *supra* note 1, at 575 (“The demands imposed by modern medicine and required by federal law are critically important. Until the mid-1900s, there were few chemically pure medicines available to physicians, so it was common for them to use complex natural substances, such as cannabis. The world is quite different today. Today’s medicines contain pure and stable chemicals, free of a hodgepodge of inactive and potentially harmful substances, which might contain known inert fillers, but as a regulated pharmaceutical, it enables physicians to know precisely what their patients are taking.”) (footnotes and punctuation omitted); *see also, e.g.*, MARTIN BOOTH, CANNABIS: A HISTORY (2005); LESTER GRINSPOON & JAMES B. BAKALAR, COCAINE: A DRUG AND ITS SOCIAL EVOLUTION (1976); JOHN H. HALPERN & DAVID BLISTEIN, OPIUM: HOW AN ANCIENT FLOWER SHAPED AND POISONED OUR WORLD (2019).

⁷ *See, e.g.*, ALEX BERENSON, TELL YOUR CHILDREN: THE TRUTH ABOUT MARIJUANA, MENTAL ILLNESS, AND VIOLENCE (2019); JOHN KAPLAN, THE HARDEST DRUG: HEROIN AND PUBLIC POLICY (1983); CRAIG REINARMAN & HARRY G. LEVINE, CRACK IN AMERICA: DEMON DRUGS AND SOCIAL JUSTICE (1997).

⁸ *See, e.g.*, U.N. OFF. ON DRUGS & CRIME, UNDOC LABORATORY AND SCIENTIFIC SERVICE PORTALS, *UNODC Early Warning Advisory Highlights*, 8 CURRENT NPS THREATS 1 (July 2025), <file:///Users/paullarkin/Downloads/Current+NPS+Threats+Vol.+8.pdf> (last accessed Feb. 27, 2025) [hereafter *2025 UNODC Early Warning Advisory Highlights*] (“1,396 individual New Psychoactive Substances (NPS) have been reported to the UNODC Early Warning Advisory (EWA) on NPS by 153 countries and territories worldwide.”) (punctuation altered); ROY GERONA, DESIGNER DRUGS 33 (2024).

⁹ *See 2025 UNODC Early Warning Advisory Highlights, supra* note 7, at 5 (“In 2024, a total of 101 new substances were identified for the first time.”); EUROPEAN UNION DRUG AGENCY, *European Drug*

traditional plant-based drugs and novel psychoactive substances pose growing challenges for governments and society.¹⁰

Over the past decade, more than a thousand NPSs have emerged worldwide. This rapid proliferation of “designer drugs” presents substantial challenges for drug control, forensic detection, and public health surveillance. Of even greater concern are advances in artificial intelligence (AI) in this domain. AI-enabled deep learning, quantitative structure–activity relationship modeling, molecular docking, and devising chemical synthetic routes have dramatically accelerated the potential speed at which countless potent NPS could be produced. Far surpassing conventional medicinal-chemistry approaches, modern molecular docking platforms can rapidly predict the binding affinity and potential potency of candidate NPS at receptors that are the known primary molecular targets of addictive drugs. The legal and regulatory implications of AI-generated psychoactive substances is vast. Currently, there is no law to prevent publication of models that could be misused to create NPSs. Proactive

Report 2025, New Psychoactive Substances—The Current Situation in Europe 16 (June 5, 2025) [hereafter *2025 EU Drug Report*] (“At the end of 2024, the EUDA was monitoring 1000 new psychoactive substances, 47 of which were first reported in Europe in 2024.”). There is a sizeable and expanding literature discussing NPSs. See, e.g., EUROPEAN MONITORING CENTRE FOR DRUGS & DRUG ADDICTION, *NEW PSYCHOACTIVE SUBSTANCES—THE CURRENT SITUATION IN EUROPE* (2023); EUROPEAN MONITORING CENTRE FOR DRUGS & DRUG ADDICTION, *NEW PSYCHOACTIVE SUBSTANCES: 25 YEARS OF EARLY WARNING AND RESPONSE IN EUROPE—AN UPDATE FROM THE EU EARLY WARNING SYSTEM* (2022); NOVEL PSYCHOACTIVE SUBSTANCES: POLICY, ECONOMICS, AND DRUG REGULATION 165 (Ornella Corazza & Andres Roman-Urrestarazu eds., 2017); Sara Berg, *Physicians Recognize New Psychoactive Substances as Health Threat*, AM. MEDICAL ASS’N, June 12, 2017, <https://www.ama-assn.org/delivering-care/public-health/physicians-recognize-new-psychoactive-substances-health-threat>; John J. Coleman & Robert L. DuPont, *Fentanyl as Sentinel: The Deadly Threat of Illegal Synthetic and Counterfeit Drugs*, THE HERITAGE FOUND., Backgrounder No. 3436 (2019); Michael H. Baumann, *The Changing Face of Recreational Drug Use*, CEREBRUM (Jan.-Feb. 2016), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4938259/>; Liana Fattore & Aviv M. Weinstein, Editorial, *Novel Psychoactive Substances*, 10 FRONTIERS OF PSYCHIATRY 3 (2019), <https://doi.org/10.3389/fpsyt.2019.00119>; Taylor Holborn et al., *Self-Medication with Novel Psychoactive Substances (NPS): A Systematic Review*, INT’L J. MENTAL HEALTH & ADDICTION, Nov. 29, 2023, <https://doi.org/10.1007/s11469-023-01195-8>; Dino Luethi & Matthias E. Liechti, *Designer Drugs: Mechanism of Action and Adverse Effects*, 94 ARCHIVES OF TOXICOLOGY 1085 (2020); Hawraa Sameer Sajwani, *The Dilemma of New Psychoactive Substances: A Growing Threat*, 31 SAUDI PHARMACEUTICAL J. 348 (2023); Abu Scaffi et al., *New Psychoactive Substances: A Review and Updates*, 10 THERAPEUTIC ADVANCES IN PSYCHOPHARMACOLOGY 1 (2020); Fabrizio Schifano et al., *Stimulant and Hallucinogenic Novel Psychoactive Substances: An Update*, 16 EXPERT REV. CLINICAL PHARMACOLOGY 1109 (2023); Derek K. Tracy, *Novel Psychoactive Substances: Types, Mechanisms of Action, and Effects*, 356 BRIT. MED’L J. i6848 (2017); Derek K. Tracy, *Novel Psychoactive Substances: Identifying and Managing Acute and Chronic Harmful Use*, 356 BRIT. MED’L J. i6814 (2017). See generally Paul J. Larkin, *Twenty-First Century Illicit Drugs and Their Discontents, The Challenge of Novel Psychoactive Substances*, HERITAGE FOUND., Special Report No. 282 (2024).

¹⁰ See U.N. OFF. ON DRUGS & CRIME, *The Growing Complexity of the Opioid Crisis* 2 (Oct. 2024) (“Synthetic drugs constitute one of the most significant drug problems worldwide. Along with synthetic drugs, the emergence of the new psychoactive substances (NPS) market over the last years has become a policy challenge and a major international concern. A growing interplay between these new substances and traditional illicit drug markets is being observed, and the synthetic drugs market continues to evolve rapidly.”).

regulatory responses and policies are needed to address gaps in monitoring the misuse of AI for this purpose.

NPSs can be as dangerous and addictive (or more so) as drugs that are derived entirely from botanical products, like heroin, which is synthesized from morphine produced from opium poppies.¹¹ In fact, some of the most dangerous NPSs are novel synthetic opioids (NSOs).¹² In some instances, chemists have created those drugs, like other NPSs, from patent filings and scientific articles describing two categories of drugs: (1) “ones that were originally developed as therapeutic agents but were never commercialized,” colloquially known as “failed pharmaceuticals,” and (2) others that are “falsified or unregistered/unlicensed pharmaceuticals” being “sold in countries where they are not approved for medical use.”¹³ The best-known example today is fentanyl, a synthetic opioid that has legitimate uses as a surgical anesthetic and analgesic or for the treatment of severe pain, such as what end-stage cancer can generate for its unfortunate victims.¹⁴ This drug is so potent that a miniscule amount—one

¹¹ See, e.g., GERONA, *supra* note 7, at 4; Jonathan P. Caulkins & Keith Humphreys, *New Drugs, Old Misery: The Challenge of Fentanyl, Meth, and Other Synthetic Drugs*, MANHATTAN INST., Issue Brief 1 (2023).

¹² See U.N. OFF. ON DRUGS & CRIME, *UNODC Opioid Strategy: The Growing Complexity of the Opioid Crisis* 8-9 (Oct. 2020) (identifying buprenorphine, isotonitazene, piperidyl-thiambutene, and U-47700 as examples of such drugs); Francesca Rombolà et al., *In Vitro Cytotoxic and Genotoxic Evaluation of Nitazenes, a Potent Class of New Synthetic Opioids*, 15 J. XENOBIOTICS 203, at 1 (2025) (“Over the past decade, the availability and use of New Psychoactive Substances (NPS), a class of synthetic recreational drugs designed to evade legal classification and standard detection methods, have increased significantly. Among these, New Synthetic Opioids (NSOs) have emerged as the fastest-growing and most dangerous subgroup, characterized by extreme potency and strong association with severe intoxications and fatalities.”) (endnotes omitted).

¹³ U.N. OFF. ON DRUGS & CRIME, *UNODC Opioid Strategy: The Growing Complexity of the Opioid Crisis* 8 (Oct. 2020) (noting that a study found 18 deaths in the Midwestern United States where isotonitazene was identified in biological samples”).

¹⁴ The potency of an opioid matters greatly, and not only because more potent opioids are superior painkillers. See Evan S. Schwarz et al., *Nitazenes: An Old Drug Class Causing New Problems*, 122 MO. MED. 329 (July/August 2025) (“Potency is the ability of a substance to exert a chemical effect. Put simply, substances with high potencies need smaller amounts to obtain the same effect compared to a less potent substance.”). Morphine is the baseline opioid, but some opioids, such as fentanyl, are far more powerful. “This is partially reflected in the fact that fentanyl is dosed in micrograms and morphine in milligrams when administered in the hospital.” *Id.* at 331. Fentanyl rapidly binds with brain receptors and detaches slowly and therefore can kill a user almost instantaneously, before he even can remove a hypodermic from his arm. Plus, rescue efforts with naloxone can come too late to offset synthetic opioids, or more naloxone is necessary than first responders have available. See, e.g., Laura C. Chambers et al., *Buprenorphine Dose and Time to Discontinuation Among Patients With Opioid Use Disorder in the Era of Fentanyl*, 6 JAMA NETWORK OPEN, Sept. 5, 2023, <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2809633>; Karli R. Hochstatter et al., *Characteristics and Correlates of Fentanyl Preferences Among People with Opioid Use Disorder*, 240 DRUG & ALCOHOL DEPENDENCE 109630, <https://www.sciencedirect.com/science/article/abs/pii/S0376871622003672?via%3Dihub> (noting that more than half (52 percent) of participants in a recent study preferred fentanyl alone (21.2 percent) and 30.8 percent to a heroin-fentanyl mix); Udani Samarasekera, “Even Worse Than Fentanyls”: Nitazenes in the USA, 404 LANCET 2250, 2250 (2024) (“Responding to illicit fentanyl use is challenging. Treatment standards developed for heroin users do not work as well for the synthetic opioid. Low doses of naloxone to reverse overdoses are not enough. People overdosing need more airway

measured in grains, not grams—can be fatal, an amount that would not even cover the date on a penny.¹⁵ Fentanyl is responsible for hundreds of thousands of overdose fatalities in this century.¹⁶

Fentanyl, however, is not the only NPS of concern. Another category is the compounds known as nitazenes, a new synthetic substance with opioid-like effects.¹⁷ Nitazenes are a new poison.¹⁸ Less well known, but not necessarily less dangerous, than fentanyl, nitazenes are an up-and-coming versions of those older (heroin) and

management. Approved limits for opioid agonist therapies do not work.”); Vivian W.L. Tsang et al., *Systematic Review on Intentional Non-Medical Fentanyl Use Among People Who Use Drugs*, 15 FRONTIERS IN PSYCHIATRY 1347678, Feb. 12, 2024, <https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsy.2024.1347678/full>.

¹⁵ Some analogs of fentanyl have an even more staggering potency. See Jolanta B. Zawilska, *An Expanding World of Novel Psychoactive Substances: Opioids*, 8 Frontiers of Psychiatry at 3 (2017), <https://doi.org/10.3389/fpsy.2017.00110> (“It is estimated that the clinical potency of carfentanil is 10,000 times that of morphine, 4,000 times that of heroin, and 100 times that of fentanyl[.]”).

¹⁶ See, e.g., COMMISSION ON COMBATING SYNTHETIC OPIOID TRAFFICKING, FINAL REPORT 1 (2022) [hereafter FENTANYL COMMISSION] (“Overdoses involving illegally manufactured fentanyl are now the leading cause of death for [Americans] ages 18 through 45.”); CNTRS. FOR DISEASE CONTROL & PREVENTION, *Opioids, Overdose Prevention: Fentanyl* (2025) (“Approximately 69% of all drug overdose deaths in 2023 involved synthetic opioids other than methadone (primarily reflects illegally made fentanyl).”). For other discussions of the misery fentanyl has caused this nation, see for example, BRYCE PARDO ET AL., *THE FUTURE OF FENTANYL AND OTHER SYNTHETIC OPIOIDS* (2019); SAM QUINONES, *THE LEAST OF US: TRUE TALES OF AMERICA AND HOPE IN THE TIME OF FENTANYL AND METH* (2021); BRODIE RAMIN, *THE AGE OF FENTANYL: ENDING THE OPIOID EPIDEMIC* (2020); Paul J. Larkin, *Twenty-First Century Illicit Drugs and Their Discontents: The Scourge of Illicit Fentanyl*, HERITAGE FOUND. Legal Memo. No. 313 (2022).

¹⁷ See, e.g., DIVERSION CONTROL DIV., U.S. DRUG ENFORCEMENT ADMIN., *Benzimidazole-Opioids. Other Name: Nitazenes* DEA/DC/DOE 1 (Mar. 2025) [hereafter DEA, *Nitazenes*]; 2025 UNODC *Early Warning Advisory Highlights*, *supra* note 7, at 1 (“Synthetic opioid NPS continue to be increasingly detected across the world with reports from every continent (37 countries) in 2024. Fentanyl analogues were the most dominant group with 95 different substances, followed by nitazenes with 33 individual compounds reported.”); *A Dangerous New Class of Synthetic Opioid Is Spreading*, ECONOMIST, Sept. 9, 2025, <https://www.economist.com/science-and-technology/2025/09/09/a-dangerous-new-class-of-synthetic-opioid-is-spreading> (last accessed Feb. 25, 2026) [hereafter Economist, *Dangerous Synthetic Opioid*]. Nitazenes are one of five different categories of non-fentanyl novel opioid substances (nf-NSOs). The others are diphenylethylpiperazines, cyclohexylbenzamides, cinnaylpiperazines, and benzimidazolones. Gajanan R. Jadhav & Pius S. Fasinu, *Metabolic Characterization of the New Benzimidazole Synthetic Opioids—Nitazenes*, 15 FRONTIERS IN PHARMACOLOGY 1434573, at 2 (2024). They might be part of a future wave of nf-NSOs.

¹⁸ See Carren M. Roberts et al., *Clinical Experiences with the Nitazene Class of Synthetic Opioids—A Cohort Study*, 86 ANNALS OF EMERG. MED. 475, 475 (2025) (“Nitazenes are illicit synthetic benzimidazole opioid analogs that pose an emerging concern due to the increasing number of clinical, forensic, and police seizure reports. The United Nations Office on Drugs and Crime Early Warning Advisory on New Psychoactive Substances notes a rapid increase in both unique nitazene opioids and countries where they are detected at a rate exceeding that of fentanyl. . . . In Europe, benzimidazoles have outnumbered fentanyl analogs since 2020. . . . In the United States, nitazene opioids are a public health concern with nearly 7,000 reports to the [DEA’s] National Forensic Laboratory Information System between 2019 and March 2025.”) (endnotes omitted).

more recent (fentanyl) scourges.¹⁹ In fact, “[r]ecently, the number of benzimidazole opioids [viz., nitazenes] introduced has overtaken the fentalogs.”²⁰

Nitazenes are not only sold in powdered form, but also are increasingly being added as fillers to other powdered drugs such as heroin or cocaine, or compounded into counterfeit pills, because of the additional “kick” they provide and because they are less expensive than plant-based drugs.²¹ A result is that users, particularly “opioid-naïve individuals,” are unwittingly consuming an exceptionally potent drug that puts them at serious risk of overdosing and dying.²² Unfortunately, “[m]arket conditions have . . .

¹⁹ See U.N. OFF. ON DRUGS & CRIME, 7 CURRENT NPS THREATS 2, 3 (July 2024) (noting that synthetic opioids recorded the largest number of new NPS reported to the U.N. in 2023 and that “[t]he increase in post-mortem cases compared to the previous volume of the Current NPS Threats, is primarily related to a greater number of case submissions from North America.”).

²⁰ GERONA, *supra* note 7, at 10.

²¹ See, e.g., U.N. OFF. ON DRUGS & CRIME, *UNODC Opioid Strategy: The Growing Complexity of the Opioid Crisis* 8 (Oct. 2020) (“In common with fentanyl and its analogues, non-fentanyl-related opioids may be sold as stand-alone products or used as adulterants or constituents of drugs such as heroin or falsified pain medication, and can be bought from a variety of sources including both the Internet and the Dark Web.”) (endnotes omitted); Joana R.P. Pereira et al., *Nitazenes: The Emergence of a Potent Synthetic Opioid Threat*, 30 MOLECULES 3890, at 4 (2025) (“A major concern is the unintentional consumption of nitazenes, as they are often mixed with or sold as other drugs such as heroin, fentanyl, benzodiazepines, methamphetamine, cocaine, or counterfeit medications (e.g., oxycodone, hydromorphone, Xanax, Dilaudid).”).

²² See Vincenzo Abbate et al., *Novel Synthetic Opioids*, in NOVEL PSYCHOACTIVE SUBSTANCES: CLASSIFICATION, PHARMACOLOGY, AND TOXICOLOGY 455-56 (Paul I. Dargan & David M. Wood eds., 2d ed. 2022); Pereira et al., *supra* note 20, at 4; Sune Engel Rasmussen & Ming Li, *Stronger Than Fentanyl: A Drug You’ve Never Heard of Is Killing Hundreds Every Year*, WALL ST. J., July 29, 2025, (last accessed Feb. 26, 2026) (“[Nitazenes] have been found mixed into heroin and recreational drugs, counterfeit painkillers and antianxiety medication.”); see also, e.g., Alexandra Amaducci et al., *Naloxone Use in Novel Potent Opioid and Fentanyl Overdoses in Emergency Department Patients*, 6 JAMA NETWORK OPEN 2331264, at 2 (2023) (“A subclass of synthetic opioids referred to as nitazenes contain a 2-benzylbenzimidazole structure that has μ -opioid agonism. . . . Nitazenes are structurally unrelated to fentanyl, but have been found to be up to 1000-fold more potent than morphine.”); Peter Jamison, *New Opioids, More Powerful Than Fentanyl, Are Discovered in D.C. Amid Deadly Wave of Overdoses*, WASH. POST, Nov. 29, 2021, https://www.washingtonpost.com/local/dc-politics/new-opioids-more-powerful-than-fentanyl-are-discovered-in-dc-amid-deadly-wave-of-overdoses/2021/11/29/680afb2c-4d43-11ec-94ad-bd85017d58dc_story.html (last accessed Feb. 25, 2026) (“Forensic analysts have identified a new and highly potent family of synthetic opioids in the District’s illicit drug supply, a worrisome discovery in a city already struggling with a wave of fatal overdoses that shows no signs of abating. [¶] The opioids, found on used syringes examined by scientists at the D.C. Department of Forensic Sciences in September and October, are called protonitazene and isotonitazene, respectively. Experts estimate that each is at least several times more powerful than fentanyl, the synthetic opioid that has displaced heroin in many parts of the United States and is now responsible for the majority of the country’s drug overdoses, including those in the nation’s capital.”); David Ovalle, *On the Streets, Opioids Sometimes More Potent than Fentanyl: Nitazenes*, WASH. POST., Dec. 10, 2023, www.washingtonpost.com/health/2023/12/10/nitazenes-opioid-stronger-than-fentanyl/ (last accessed Feb. 25, 2026). This problem is a particular concern in Europe. See Rasmussen & Li, *supra* (“Europe, which has skirted the kind of opioid pandemic plaguing the U.S., is now on the front line as nitazenes push into big heroin and opioid markets such as Britain and the Baltic states.”); see also, e.g., Adam Holland et al., *Nitazenes—Heralding a Second Wave for the UK Drug-Related Death Crisis?*, 9 LANCET PUB. HEALTH e71, e71 (2024) (“In the UK, nitazenes have been detected in substances sold as other opioids,

been ripe for the emergence of a new, uncontrolled class of synthetic opioid.”²³ The Taliban’s prohibition of opium production has reduced the supply of heroin, particularly in Europe, and the horrific loss of life attributable to fentanyl has focused our attention and deterrent efforts to reduce the supply of that drug. The medical and public policy literature reveals that, to keep their ill-gotten profits flowing, traffickers are distributing nitazenes in the United States, Canada, Europe, the Baltic States, Africa, Australia, Southeast Asia, and Oceania.²⁴

benzodiazepines, and cannabis products. This means many consumers are using nitazenes inadvertently, unaware of the risks they face.”) (endnotes omitted); Emma L. Keller et al., *Searching for a Needle in a Haystack—Chemical Analysis Reveals Nitazenes Found in Drug Paraphernalia Residues*, 46 DRUG & ALCOHOL REV. e70010, at 1 (2026) (“Nitazenes have been detected in a wide variety of drugs and forms including cocaine, heroin, vape liquids and counterfeit pills.”) (endnotes omitted); *id.* at 4 (“The co-detection of nitazenes with non-opioid substances such as methamphetamine and cocaine in this study is of concern. People using these substances may not be expecting opioids in their drug of choice. They are potentially at risk of overdose and may not be familiar or take precautions by considering specific harm reduction strategies, for example acquiring naloxone.”); Nicki Killeen et al., Letter, *The Emergence of Nitazenes on the Irish Heroin Market and National Preparation for Possible Future Outbreaks*, 119 ADDICTION 1657, 1657 (2024) (“Nitazenes sold as falsified medicines and as other drugs in the United Kingdom and Europe as well as the use of these substances by non-opioid using populations with no tolerance or access to naloxone, is a particular concern.”) (endnotes omitted); Univ. North Carolina (Chapel Hill) Watchlist, <https://www.opioiddata.org/unc-watchlist/#nitazenes> (last accessed Feb. 28, 2026) (“Nitazenes are the synthetic opioid most common in Europe (not fentanyl).”).

²³ *Nitazenes: Another Failure of Drug Prohibition*, [hereafter ECONOMIST, *Nitazenes*], Sept. 10, 2025, <https://www.economist.com/leaders/2025/09/10/nitazenes-another-failure-of-drug-prohibition> (last accessed Feb. 26, 2026).

²⁴ See 2025 EU Drug Report, *supra* note 8, at 14 (“Since 2019, at least 21 EU Member States have now reported the presence of a nitazene. . . . In 2023, the quantity of nitazene powders detected in Europe tripled to 10 kilograms, compared with 2022. Reports to the EU Early Warning System also suggest a recent significant increase in the availability of fake medicines containing nitazene opioids in Europe. . . . During 2023, authorities in 8 countries confiscated nearly 24 000 nitazene-containing tablets, compared to just 430 tablets in 2022. Preliminary data from 2024 support this trend, with over 50 000 tablets seized in 9 EU Member States.”); Letter from Dr. Tedros Adhanom Ghebreyesus, Director Gen’l World Health Org., to Mr. Antonio Guterres, Sec’y-Gen’l United Nations, Regarding Recommendations of the Expert Comm. on Drug Dependence 2 (Nov. 21, 2024) (recommending that four nitazenes (viz., protonitazene, metonitazene, etonitazepipne, and *N*-desethyl-isotonitazene) be added to Schedule I of the Single Convention on Narcotic Drugs (1961) for drugs that should be altogether prohibited); Isabelle Giraudon et al., *Nitazenes Represent a Growing Threat to Public Health in Europe*, 9 LANCET PUB. HEALTH e216, e216 (2024) (noting “concerns we, at the European Monitoring Centre for Drugs and Drug Addiction, have raised—that nitazenes pose a credible threat and that predicted changes in heroin availability in Europe could herald an increase in the use of synthetic opioids with possibly profound implications for public health.”) (endnotes omitted); Pereira et al., *supra* note 20, at 4; see also, e.g., EXPERT COMM. ON DRUG DEPENDENCE, WORLD HEALTH ORG., *Critical Review Report—Isotonitazene* (2020); Katri Abel-Ollo et al., *The Nitazene Epidemic in Estonia—A First Report*, 35 EUROPEAN J. PUB. HEALTH 1233 (2025); Friedman & Ciccarone, *supra* note 1; Paul N. Griffiths et al., *Opioid Problems Are Changing in Europe with Worrying Signals that Synthetic Opioids May Play a More Significant Role in the Future*, 119 ADDICTION 1334 (2024); Holland et al., *supra* note 21; Emma Partridge et al., *A Cluster of Multi-Drug Intoxications Involving Xylazine, Benzimidazole Opioids (Nitazenes) and Novel Benzodiazepines in South Australia*, 37 EMERGENCY MED. AUSTRALASIA e14512 (2025); Joseph Pergolizzi, Jr., et al., *Old Drugs and New Challenges: A Narrative Review of Nitazenes*, 15 CUREUS e40736 (2023); Rombolà et al., *supra* note 11; Schwarz et al., *supra* note 13; Marthe M. Vandeputte et al., *The Rise and Fall of Isotonitazene and Brorphine: Two Recent Stars in the Synthetic*

The goal of this Legal Report is to highlight the arrival of nitazenes as an illicit NPS that threatens users with death, sometimes unwittingly, and to warn the public that even a successful effort to vanquish illicit fentanyl will not end our need for continued vigilance to halt the distribution of NPSs. Drug traffickers profit off the misery of people who trade short-term relief from physical or psychological pain for the long-term misery or immediate death that can follow from use of dangerous drugs. Nitazenes are an example of the willingness of traffickers to use scientific advances for the degeneration of public life. Knowledge of this new threat, among other things, is critical to prevent nitazenes from becoming another scourge.

II. THE PROBLEMS CAUSED BY NITAZENES

Technically known as 2-Benzylbenzimidazole opioids, nitazenes were first synthesized by a Swiss pharmaceutical company, Chemische Industrie Basel Aktiengesellschaft (CIBA), in 1959 in an unsuccessful attempt to develop a more powerful but less addictive analgesic than morphine.²⁵ Nitazenes were far more powerful than morphine, but also far more addictive,²⁶ and had a far smaller “therapeutic window,” the range between the maximum therapeutic dose and the minimum lethal dose, which increases the risk of a fatal overdose in unlawfully purchased drugs, given their

Opioid Firmament, 46 J. ANALYTICAL TOXICOLOGY 115 (2022) [hereafter Vandeputte, *Rise and Fall of Nitazene*]; Marthe M. Vandeputte et al., *Characterization of Novel Nitazene Recreational Drugs: Insights into Their Risk Potential from In Vitro μ -Opioid Receptor Assays and In Vivo Behavioral Studies in Mice*, 210 PHARMACOLOGICAL RES. 107503 (2024) [hereafter Vandeputte, *Novel Nitazene Recreational Drugs*]; Emma Wilkinson, *Everything You Need to Know About Nitazenes*, PHARMACEUTICAL J. (Feb. 8, 2024); ECONOMIST, *Nitazenes*, *supra* note 22.

²⁵ See DEA, *Nitazenes*, *supra* note 16; GERONA, *supra* note 7, at 10-11, 84-85; Jadhav & Fasinu, *supra* note 16, at 1 (noting that NSOs are “the fastest growing group” of NPSs in North America and Europe); Vandeputte, *Rise and Fall of Nitazene* et al., *supra* note 23, at 116 (noting that CIBA’s research “showed that isotonitazene was around 500 times more potent as an analgesic than morphine.”) (endnotes omitted). Nitazenes are morphologically dissimilar from classic opioids, but, like the latter, nitazenes bind with the brain’s μ -opioid receptor—more quickly than does morphine—generating pain relief, euphoria, and, ultimately, drowsiness. Like opioids, nitazenes also suppress, and can shut down, the respiratory system, but at a lower level than morphine, given nitazenes’ greater potency. DEA, *Nitazenes*, *supra* note 16, at 1; Wilkinson, *supra* note 23. Intriguingly, fentanyl was also first synthesized in the same year by the Belgian medicinal chemist Paul Janssen and colleagues at Janssen Pharmaceutica, in pursuit of a highly potent, rapid onset, short-acting analgesic.

²⁶ “Tolerance to the analgesic and euphoric effects of opioids can develop quickly and the euphoric effects of opioids can lead to habituation and dependence. Cessation of opioid agonist use leads to a withdrawal syndrome, characterized by drug craving, dysphoria, anxiety, insomnia, irregular heart rate, loss of appetite, diarrhoea, sweating, nausea, and vomiting. The main mechanism of fatal opioid overdose is respiratory depression, leading to pathological indicators such as froth in the airways, and cerebral and pulmonary oedema. As fentanyl and its analogues have high potency compared to morphine, poor control of dose, polydrug use, and patterns of repeated use are most likely contributors to the high rates of overdose, respiratory depression, and death associated with these drugs. The clinical toxicological properties of many nitazenes have not been studied directly. There are few reports from online user forums on the acute and chronic physical and psychological effects. The adverse effects align with those commonly reported for other synthetic opioid NPS such as incoordination, dizziness, drowsiness, mental confusion, sedation, and profound intoxication.” 2024 UNODC *Technical Update*, *supra* note 1, at 49

uncertain potency.²⁷ The U.S. Food and Drug Administration (FDA) and its counterparts worldwide have never approved nitazenes as a human or veterinary medication due to their serious risk of addiction and death.²⁸ As a result, the drugs, much like vampires, zombies, mummies, toxic spores, or ghosts, lay dormant for decades before emerging in the illicit drug market in 2019 in the United States, Canada, and Europe.²⁹

Nitazenes can be used intranasally, intravenously, sublingually, or by vaping and insufflation.³⁰ Powdered nitazenes can be disguised by admixing them with drugs such as cocaine, heroin, or benzodiazepines (anti-anxiety drugs—e.g., valium).³¹ They

²⁷ See Schwarz et al., *supra* note 13, at 331 (“[Nitazenes’] greater potency, therefore, implies that it may be easier to overdose on nitazenes compared to other opioids, especially in consideration of the lack of control and precision when they are added in illicitly obtained drugs.”).

²⁸ See Laura B. Kozell et al., *Pharmacologic Characterization of Substituted Nitazenes at μ , K, and Δ Opioid Receptors Suggests High Potential for Toxicity*, 389 J. PHARMACOLOGY & EXPERIMENTAL THERAPEUTICS 219, 220 (2024) (“Taken together, there is strong evidence that structures based on a benzimidazole core have high potential for toxicity and are an emerging threat for raising mortalities, above and beyond that observed in the ongoing fentanyl crisis.”); *id.* at 224-25 (“Overdoses and deaths due to substituted nitazenes have been increasing in the United States since 2019[.] . . . Most [nitazenes] exhibited higher affinity at MOR [viz., mu opioid receptor] than fentanyl, in some cases by a factor of close to 10. Most were also more potent than fentanyl by up to a factor of 430. Efficacies at MOR were almost uniformly consistent with full or near full agonism. . . . As a class, the nitazenes appear to exceed fentanyl and fentanyl analogs with respect to their activities at MOR.”) (citations omitted); *id.* at 226 (“Given the tremendous and escalating health and societal impacts of fentanyl, a high affinity and high potency synthetic opioid, these results highlight the possibility that many nitazenes may have similar or higher potential for overdose and toxicity. . . . Notably, a number of nitazenes exhibit higher affinity, higher potency, and higher efficacy than fentanyl at opioid receptors.”); Pereira et al., *supra* note 20, at 2.

²⁹ DEA, *Nitazenes*, *supra* note 16, at 1; 2024 UNODC *Technical Update*, *supra* note 1, at 47. Today, there are dozens of different versions of nitazenes. See GERONA, *supra* note 7, at 11 (“noting that 67 NSOs were detected in Europe between 2—9 and 2020.”); U.N. OFF. ON DRUGS & CRIME, UNDOC LABORATORY AND SCIENTIFIC SERVICE PORTALS, *China: Announcement of Class Scheduling of “Nitazene” Analogues* (July 2025), <https://www.unodc.org/LSS/Announcement/Details/7e29daf9-1d49-45e6-95e7-8ce932bc94e1> (last accessed Feb. 27, 2026) (listing nitazenes reported to the U.N. Early Warning Advisory); Pereira et al., *supra* note 20, at 2; Roberts et al., *supra* note 17, at 486 (noting “more than 40 nitazene opioids”); see also Rombolà et al., *supra* note 11, at 2 (“By the end of 2024, EUDA [European Union Drug Agency] was officially monitoring a total of 22 nitazenes, 7 of which had been formally reported for the first time during that year.”) (endnotes omitted). Given their potency and other perceived financial benefits, that number almost certainly will increase over time. See Pergolizzi, Jr. et al., *supra* note 23, at 1 (“The murky legal status of these substances combined with their potent psychoactivity and relatively synthesization process is neither expensive nor unduly difficult manufacturing costs makes them valuable street drugs.”) (endnote omitted); Vandeputte et al., *Novel Nitazene Recreational Drugs*, *supra* note 23, at 3 (“Considering the historically dynamic character of the NSO market, as well as recent trends, the class of nitazenes is expected to further expand and diversify in the future[.]”) (endnotes omitted).

³⁰ See Roberts et al., *supra* note 17, at 481 (“Nitazene opioids were used both intentionally and unintentionally and consumed by multiple routes, particularly vaping of a liquid in refillable e-cigarette devices.”); Wilkinson, *supra* note 23.

³¹ DEA, *Nitazenes*, *supra* note 16, at 1 (“Toxicology analyses co-identified some of these benzimidazole-opioids with other opioids, stimulants, and benzodiazepines.”); Holland et al., *supra* note 21, at e71 (“In the UK, nitazenes have been detected in substances sold as other opioids, benzodiazepines, and

have spread widely since their 2019 arrival for several reasons: they can be produced in a laboratory without any need to grow source plants overseas, protect them during their maturation process from weather and bandits or crop eradication programs, and to transport bulky, impure source material to the U.S.; the synthesization process is neither unduly complicated nor very expensive; the structure of nitazenes can be rapidly modified to stay one step ahead of the law;³² and the final product is extremely potent, which makes it easy to transport and conceal³³—all factors that combine to threaten a likely increase in nitazene production, use, overdoses, and fatalities.³⁴

As a class, nitazenes are a heterogenous category of drugs with different potencies, but some varieties are extremely powerful analgesics, hundreds of times more powerful than morphine, with some having a greater strength than fentanyl.³⁵ Even other

cannabis products. This means many consumers are using nitazenes inadvertently, unaware of the risks they face. . . . Other European countries, particularly the Baltic states, have also reported increasing numbers of deaths related to nitazenes.”) (endnotes omitted); Alex Homer, “*His Loss Is Massive*”: *Inquests Show Spread of Deadly Synthetic Drugs*, BBC, Feb. 12, 2026, www.bbc.com/news/articles/ce3engnnp8o (last accessed Feb. 25, 2026) (“Highly potent synthetic opioid drugs called nitazenes, which experts say can be many times more potent than heroin, have been linked to hundreds of deaths in the UK. [¶] Records show some people are taking them by accident, as they are mixed in with other drugs as cheap substitutes. . . . Adam Thompson, the [National Crime Agency’s] head of drugs threat, said “[i]n most cases, organised criminals’ sole motivation for using nitazenes is greed. They buy potent nitazenes cheaply and mix them with other drugs . . . to strengthen the product being sold and make significant profits[.]’ . . . Professor Michel Kazatchkine . . . said the numbers of deaths meant the UK was ‘by far outpacing all other countries [in Europe] and it’s even outpacing Canada’.”).

³² See, e.g., Bertha K. Madras, *The Growing Problem of New Psychoactive Substances (NPS)*, in *NEUROPHARMACOLOGY OF NEW SCIENTIFIC SUBSTANCES* 13 (Michael H. Baumann et al. eds., 2017) (“Synthetic drug manufacturers rapidly adapt to shifting drug trends and legal status by modifying chemical structures to develop legions of new ‘legal’ NPS. The advent of novel compounds is announced instantaneously on social media and other Internet sites, leading to quick adoption and significant profits before the legal grey zone evaporates.”).

³³ DEA, *Nitazenes*, *supra* note 16, at 1; *supra* note 14; Pereira et al., *supra* note 20, at 2 (“Three main factors contribute to the rise of nitazenes: 1. Ease of synthesis: Nitazene analogues are relatively straightforward to synthesise, do not require controlled precursors, and can be produced in small-scale clandestine laboratories worldwide. 2. Economic appeal: Their high potency means a few grams can yield thousands of doses, making them easier to conceal and transport, which is economically advantageous for traffickers. 3. Regulatory evasion: The rapid and consistent emergence of novel nitazene analogues with slight chemical modifications enables them to circumvent existing drug laws, which are often based on specific substances, creating a regulatory lag. This trend intensified after class-wide bans on fentanyl and its analogues in the late 2010s, prompting illicit chemists to seek alternative NSOs from the historical pharmacological literature.”) (endnotes omitted); Schwarz, *supra* note 13, at 331.

³⁴ See Pereira et al., *supra* note 20, at 25 (“Nitazenes have the potential of becoming the drugs of choice in the future, resembling the shift that occurred with fentanyl. This concern is exacerbated by factors such as the economic advantages of synthetic opioids, industrialised production, and regulatory crackdowns on fentanyl in China, which incentivise the development and distribution of even more potent substances.”).

³⁵ See GERONA, *supra* note 7, at 84-85; Pereira et al., *supra* note 20, at 2; *id.* at 5 (“The potency of nitazenes is exceptionally high, with some analogues being hundreds to thousands of times stronger than morphine, and many are comparable to or even exceed the potency of fentanyl.”); Jadhav & Fasinu, *supra* note 16, at 3 (“[D]iscovery studies comparing their potency to morphine, the standard reference opioid, showed potency up to 500 times that of morphine[.]”) (citations omitted); Rasmussen &

less powerful, common, street-level nitazenes still pack a significant wallop.³⁶ Indeed, some nitazenes are 500 or more times as powerful as morphine.³⁷ That heft is attractive to “psychonauts,” people searching for “the ultimate high,” or those who have become tolerant to the euphoria of weaker opioids, even though death may be right inside that door.³⁸ The bottom line is that these drugs are a clear and certain threat to individual and societal public health.³⁹

Aggravating our problems is that a source of some of those drugs is the People’s Republic of China (PRC).⁴⁰ China is not Switzerland, let alone a member of NATO; it

Li, *supra* note 21; Schwarz et al., *supra* note 13, at 330 Tbl. 1; Marcus Stangeland et al., *Nitazenes—Review of Comparative Pharmacology and Antagonist Action*, 63 *CLINICAL TOXICOLOGY* 393, 395-96 (2025); *ECONOMIST*, *Dangerous Synthetic Opioid*, *supra* note 16 (“Once nitazenes get into the brain, they bind to gateways on the surface of neurons known as mu receptors. When activated, these can suppress the body’s pain signals. Nitazenes are more effective at activating these receptors than heroin and, in some cases, fentanyl. This means a smaller dose is needed to induce the strong analgesia and euphoria many users crave. But activation of the mu receptors can also lead to slowed breathing and, in the case of overdoses, cardiac arrest.”).

³⁶ Rasmussen & Li, *supra* note 21 (noting that other versions of nitazenes have roughly 50-250 times the strength as heroin and five times that of fentanyl).

³⁷ See Amaducci et al., *supra* note 21, at 8; Michael DePeau-Wilson, *What to Know About Nitazenes, a Class of Potent Synthetic Opioids*, *MEDPAGE TODAY*, Feb. 5, 2024, <https://www.medpagetoday.com/special-reports/features/108578>; R. Michael Krausz et al., *The Upcoming Synthetic Ultrapotent Opioid Wave as a Foreseeable Disaster*, 9 *LANCET PSYCHIATRY* 699 (2022); see also, e.g., *DRUG ENFORCEMENT ADMIN.*, *New, Dangerous Synthetic Opioid in D.C., Emerging in Tri-State Area* (June 1, 2022) *DEA*, *Nitazenes*, *supra* note 16; see also *CNTRS FOR DISEASE PREVENTION & CONTROL*, *Notes from the Field: Nitazene-Related Deaths—Tennessee, 2019-2021*, 71 *MORBIDITY & MORTALITY WEEKLY REPORT* 1196 (Sept. 16, 2022); Grant C. Glatfelter et al., *Alkoxy Chain Length Governs the Potency of 2-Benzylbenzimidazole “Nitazene” Opioids Associated with Human Overdose*, 240 *PSYCHOPHARMACOLOGY* 2573 (2023); Ryan Marino, *Nitazenes Have Entered the Drug Scene. Now What?*, *MEDPAGE TODAY*, Feb. 13, 2024, <https://www.medpagetoday.com/opinion/second-opinions/108713>; Eva Montanari et al., *Acute Intoxications and Fatalities Associated With Benzimidazole Opioid (Nitazene Analog) Use: A Systematic Review*, 44 *THERAPEUTIC DRUG MONITORING* 494 (2022).

³⁸ Samarasekera, *supra* note 13, at 2250-51 (“[Joseph] Palamar [Palamar, Associate Professor of Population Health at New York University Langone Health] said the demand for nitazenes is not high at the moment, but that could change. In the fentanyl crisis, he says, ‘At first most people who used opioids feared being exposed to fentanyl. But now many people who use opioids prefer fentanyl. This can also happen with nitazenes.’” . . . Other researchers agree, noting that regular fentanyl users seeking a more potent high could turn to nitazenes.”).

³⁹ See 2025 *EU Drug Report*, *supra* note 8, at 9 (“We cannot avoid the fact that drug issues have an impact almost everywhere. They are manifest in and exacerbate other complex policy problems, such as homelessness, the management of psychiatric disorders and youth criminality. We are also witnessing greater levels of violence and corruption driven by the drug market in some countries. Increasingly, we are observing that almost everything with psychoactive properties can appear on the drug market, often mislabelled [*sic*] or in mixtures, leaving consumers potentially unaware of what they are using, increasing health risks and creating new law-enforcement and regulatory challenges.”); *id.* at 10 (“Poisoning outbreaks can escalate rapidly, as has been seen with synthetic cannabinoids and nitazene opioids.”).

⁴⁰ *NAT’L CAPITAL POISON CNTR.*, *What are synthetic opioids?*, www.poison.org/articles/what-are-synthetic-opioids (last accessed Feb. 17, 2026) (“As of 2021, most synthetic opioids are crafted in China and Mexico, where there are limited regulations and oversight of the chemical and pharmaceutical industries. The drugs are then exported to the United States, illegally via land borders or through the

is a Communist nation and an avowed enemy of the United States. China’s aim is to surpass the United States, both militarily and economically, by 2049, the centennial anniversary of the founding of the PRC, and to dominate the world for this century and beyond, just as the United States did in in the last one.

Opioid overdose deaths weaken the United States directly and indirectly: Directly through direct economic costs (e.g., higher healthcare expenses, lost productivity, increased criminal justice costs), and indirectly through loss of human capital, family disruption, homelessness, institutional strain, demographic impacts, and erosion of community cohesion and hope. These broader social consequences can amplify the long-term effects of addiction beyond the individuals directly affected. The cost of the opioid epidemic has been estimated to be in trillions of dollars.⁴¹

Synthetic drugs are a weapon that the Chinese use for that purpose. “China excels in the manufacture of synthetic drugs and precursors.”⁴² Fentanyl is one such drug,⁴³ and China has long been responsible for shipping fentanyl or its precursors to Mexico for smuggling in processed form into this nation.⁴⁴ Nitazenes are just another tool

illicit use of international mail and shipping services. Once in the United States, the synthetic opioids enter the illicit drug market.”),

⁴¹ See WHITE HOUSE, *The Staggering Cost of the Illicit Opioid Epidemic in the United States* (Mar. 26, 2025).

⁴² JOHN A. CASSARA, CHINA-SPECIFIED UNLAWFUL ACTIVITIES: CCCP INC., TRANSACTIONAL CRIME AND MONEY LAUNDERING 16 (2023); see BEN WESTHOFF, FENTANYL, INC.: HOW ROGUE CHEMISTS ARE CREATING THE DEADLIEST WAVE OF THE OPIOID EPIDEMIC 194 (2019) (“[China’s] chemical industry, powered by global capitalism, has become a Frankenstein’s monster, powerful, destructive, and uncontrollable.”).

⁴³ According to the DEA, the handoff from Chinese companies to the Mexican Transnational Criminal Organizations (TCOs) works as follows: “The Sinaloa and Jalisco cartels and their chemical suppliers in China rely on deliberate mislabeling, multi-phase shipping maneuvers, and other evasive techniques to get fentanyl precursor chemicals into Mexico without being detected by law enforcement or stopped by international chemical regulators. Suspect vendors and darkweb marketplaces based in China use certain keywords or phrases to indicate their willingness to defy bans and restrictions, such as “discreet delivery,” “no customs issues,” or “100% guaranteed delivery or free reshipment.” In shipping notifications, vendors sometimes hide the shipment details by embedding them in photos or images that do not raise suspicions. Cargo containing these chemicals can be deliberately mislabeled or misspelled or contain the Chemical Abstracts Registry number instead of the chemical name—a number unlikely to be known by shippers, freight forwarders, or port workers. China-based chemical suppliers prefer cryptocurrency payments over other forms, and encrypted messaging and communications platforms. The Mexican cartels use international export brokers, consignees, third-party countries, and other methods to anonymize the contents and source of the chemical shipments. The cartels also use legitimate but likely complicit companies in the United States, Mexico, and India to import chemicals for subsequent diversion to clandestine fentanyl labs in Mexico.” DRUG ENFORCEMENT ADMIN., U.S. DEP’T OF JUSTICE, NATIONAL DRUG THREAT ASSESSMENT 2024, DEA-DCT-DIR-010-24, at 23 (2024). For a discussion of China’s production of processed fentanyl and its precursor chemicals, see SELECT COMM. ON THE STRATEGIC COMPETITION BETWEEN THE UNITED STATES AND THE CHINESE COMMUNIST PARTY, THE CCP’S ROLE IN THE FENTANYL CRISIS (Apr. 16, 2024).

⁴⁴ See Vanda Felbab-Brown, *Fentanyl and Geopolitics: Controlling Opioid Supply from China, in THE OPIOID CRISIS IN AMERICA: DOMESTIC AND INTERNATIONAL DIMENSIONS*, BROOKINGS INST. (July 2020); Paul J. Larkin, *Twenty-First Century Illicit Drugs and Their Discontents: The Scourge of Illicit Fentanyl*, HERITAGE FOUND., Legal Memorandum No. 313 (2022) [hereafter Larkin, *Scourge of Illicit Fentanyl*].

that China can use to weaken, and thereby surpass, the United States.⁴⁵ Only time will tell whether the PRC will continue down that path.⁴⁶

⁴⁵ See 2025 EU Drug Report, *supra* note 8, at 16 (“China’s expanded control of nitazene opioids in 2024, now covering 10 substances, may redirect the market away from dominant compounds such as metonitazene and protonitazene and towards novel derivatives or alternative opioid families.”); Abbate et al., *supra* note 21, in Dargan & Wood eds., *supra* note 21, at 453 (“Due to the ease of accessibility to precursors and other chemicals, these compounds [which includes nitazenes] are produced in clandestine laboratories primarily in Chi and sold over the internet.”) (endnote omitted); Michael Evans-Brown et al., *Legal Classification and International Systems for Monitoring and Responding to Novel Psychoactive Substances*, in Corazza & Roman-Urrestarazu eds., *supra* note 8, at 36 (“It appears that at least some of the isotonitazene on the market in Europe has been supplied from China.”); Ovalle, *supra* note 21 (“A recently unsealed federal indictment in South Florida opens a rare window into the source of nitazenes: manufacturers in China that officials say sell the drugs online and ship them to dealers in the United States. Prosecutors allege that a Deerfield Beach, Fla., man used WhatsApp and bitcoin to purchase nitazenes to mix with fentanyl or heroin, to stretch out his supplies of opioids and make an ‘ultra powerful substance.’ [¶] ‘The nitazenes can make [a drug mix] stronger than fentanyl,’ said Anthony Salisbury, the special agent in charge of the Homeland Security Investigations field office in South Florida. ‘As if we needed something stronger than fentanyl.’ . . . The South Florida case from October included indictments against a Chinese chemical sales company and an employee of that company. According to one of the indictments, the Chinese company selling nitazenes used websites, social media accounts and messaging apps to sell chemicals such as protonitazene and metonitazene to customers in the United States, Europe, Asia and South America. As part of the investigation, a U.S. Postal Inspection Service agent posing as a buyer ordered nitazenes from the company, according to the indictment.”); *id.* (“U.S. federal indictments also targeted Chinese companies allegedly selling precursor chemicals used to make fentanyl. . . . Chinese chemical and pharmaceutical companies have played a significant role in the proliferation of illicit synthetic drugs in the past decade. And although Beijing announced in November that it would curb the sale of precursor chemicals used by Mexican organized crime groups to manufacture fentanyl, experts worry that an unintended consequence could be the proliferation of other synthetic drugs such as nitazenes.”).

⁴⁶ See, e.g., Vanda Felbab-Brown, *China’s Role in the Fentanyl Crisis*, BROOKINGS INST. (Mar. 31, 2023), <https://www.brookings.edu/articles/chinas-role-in-the-fentanyl-crisis/> (“China . . . sees its counternarcotics enforcement, and more broadly its international law enforcement cooperation, as strategic tools that it can instrumentalize to achieve other objectives. Unlike the U.S. Government, which seeks to delink counternarcotics cooperation with China from the overall bilateral geostrategic relationship, China *subordinates* its counternarcotics cooperation to its geostrategic relations. As the relationship between the two countries deteriorated, China’s willingness to cooperate with the United States declined. Since 2020, China’s cooperation with U.S. counternarcotics efforts, never high, declined substantially. In August 2022, China officially announced that it suspended all counternarcotics and law enforcement cooperation with the United States.”). China also contributes to America’s drug crisis as revenge for Great Britain and America’s role in the nineteenth century Opium Wars, which forced China to accept the opium trade. See, e.g., JACK BEECHING, *THE CHINESE OPIUM WARS* (1977); ERIC JAY DOLIN, *WHEN AMERICA FIRST MET CHINA: AN EXOTIC HISTORY OF TEA, DRUGS, AND MONEY IN THE AGE OF SAIL* 31 (2013).

In 2025, China placed nitazene analogs under national control. U.N. OFF. ON DRUGS & CRIME, UNDOC LABORATORY AND SCIENTIFIC SERVICE PORTALS, *China: Announcement of Class Scheduling of “Nitazene” Analogues* (Sept. 30, 2024), <https://www.unodc.org/LSS/SubstanceGroup/Details/6aefe0ca-aafd-452c-a534-c16aa3a2e507> (last accessed Feb. 27, 2026). Perhaps that signals a decision to disconnect China’s drug policy from its overall political goals, or perhaps it suggests that China is having a domestic problem with nitazenes. That development bears attention but does not prove that China has abandoned its longstanding policy to treat its drug policy as an inseparable component of its overall foreign policy. See Felbab-Brown, *supra*, note 44.

Moreover, Chinese companies have shown a willingness to expand their variety of nitazenes.⁴⁷ The ongoing creation of new forms of nitazenes, along with the manufacture of other potentially deadly NPSs, gives Chinese companies—with the knowledge and blessing of the PRC and Chinese Communist Party—the opportunity to damage this nation on a continuing basis. Add in the toxicological challenges posed by the common occurrence of polydrug use,⁴⁸ and you can see the difficulty in responding to newly emerging, structurally modified nitazenes.

As of mid-2022, the U.S. Drug Enforcement Administration (DEA) concluded that nitazenes are sold less often than fentanyl,⁴⁹ but that practice could change over time given the nation’s intense focus on stopping illicit fentanyl’s spread⁵⁰ and because nitazenes are also relatively inexpensive and easy to synthesize.⁵¹ Europe has already

⁴⁷ See 2025 EU Drug Report, *supra* note 8, at 16 (“China’s expanded control of nitazene opioids in 2024, now covering 10 substances, may redirect the market away from dominant compounds such as metonitazene and protonitazene and towards novel derivatives or alternative opioid families.”).

⁴⁸ 2025 UNODC Early Warning Advisory Highlights, *supra* note 7, at 1 (“Polysubstance use is of significant concern with numerous toxicology cases involving the combination of multiple NPS. In 2024, 38 per cent of post-mortem cases involved two or more NPS—the proportion of deaths involving multiple substances is much higher when considering controlled drugs and pharmaceuticals”); Pereira et al., *supra* note 20, at 6, 7.

⁴⁹ In 2019, China agreed to stem the flow of illicit fentanyl into this nation, but not to halt the flow of precursor chemicals to Mexico. As the result, the Mexican TCOs synthesized fentanyl in Mexico (and, to a lesser extent, Canada) before sneaking it into the U.S. for distribution. See Vanda Felbab-Brown, *The New War on Drugs*, FOREIGN AFFS., Feb. 17, 2025. In 2025, China agreed to restrict the outflow to Mexico of illicit fentanyl’s precursor chemicals. See, e.g., Meaghan Tobin & Xinyun Wu, *China Tightens Controls on Fentanyl Precursors After Summit*, N.Y. TIMES, Nov. 10, 2025, <https://www.nytimes.com/2025/11/10/world/asia/china-fentanyl-united-states-trade.html?searchResultPosition=1> (last accessed Nov. 25, 2025).

⁵⁰ See DEA, NITAZENES, *supra* note 16; see Amaducci et al., *supra* note 21, at 2 (“The exact motivation to produce nitazenes and brorphine are unclear. The increased regulation of fentanyl and fentanyl analogues throughout the last decade may have led to a change in the chemical precursors required for clandestine laboratory production that were not yet regulated. This change in chemical precursors may have led to these newer and more potent opioids.”) (footnote omitted); Vandeputte et al. *Rise and Fall of Nitazene*, *supra* note 23, at 115 (“[W]ith fentanyl analogues and synthesis precursors being increasingly controlled, we now observe a gradual shift toward a new generation of non-fentanyl-related synthetic opioids.”).

⁵¹ See Pereira et al., *supra* note 20, at 1 (“This rise [in the presence of nitazenes] is fueled by their ease of synthesis, low production costs, and evasion of regulatory controls.”); *id.* at 6 (“One primary challenge is the inadequacy of traditional screening methods. Immunoassays, routinely used for conventional opioids, are largely ineffective for most nitazenes due to their distinct chemical structures and insufficient cross-reactivity. For example, studies confirm that commonly used fentanyl test strips fail to detect nitazenes. Although nitazene-specific test strips have recently become available, they present limitations, such as an inability to differentiate between nitazene analogues, potential issues with solubility in drug samples, and limited cross-reactivity with certain desnitazene analogues, which can give users a false sense of safety if not correctly interpreted. Furthermore, older gas chromatography–mass spectrometry methods also frequently lack the necessary sensitivity for nitazenes, often missing them in casework. . . . The extreme potency of nitazenes means they are typically present at very low concentrations in biological samples, often in the sub-ng/mL or sub-pmol/mL range, necessitating the development of highly sensitive analytical methods. Liquid chromatography–mass spectrometry-based techniques, such as liquid chromatography–triple-quadrupole mass spectrometry and liquid chromatography–time-of-flight mass spectrometry, have become the preferred approaches for

seen an increase in nitazene use,⁵² and there is no reason to presume that the United States will differ.⁵³

III. ADDRESSING NITAZENES' PROBLEMS

Traditionally, the United States has addressed drug problems from both the supply and demand sides.⁵⁴ With regard to the former: Our principal strategy has been to interdict illicit drugs before they cross our border and to use the criminal law both to deter domestic trafficking and to incapacitate anyone who disregards our controlled

screening and quantification in forensic and toxicological laboratories. These advanced systems can achieve the low limits of detection and quantification required. High-resolution mass spectrometry is particularly valuable for non-targeted screening and structural elucidation of new analogues [52–56]. Unfortunately, these instruments are very expensive to acquire and maintain, making them inaccessible to smaller laboratories and contributing to the underestimation of nitazene-related intoxications.”) (endnotes omitted); Wilkinson, *supra* note 23.

⁵² Pereira et al., *supra* note 20, at 4 (“[I]n 2023, the amount of nitazene powder seized in Europe tripled to 10 kg compared to 2022, alongside a significant increase in falsified medicines containing nitazene opioids.”).

⁵³ In an ironic development, supply-side restrictions on opium cultivation and fentanyl synthesis have contributed to the demand for nitazenes. For example, the Taliban’s ban on opium production in Afghanistan has reduced the amount of heroin available in Europe (some stockpiles still exist), while China’s restrictions on fentanyl exports have contributed to a shift towards use of other synthetic opioids and opioid-like drugs, such as nitazenes. According to Caroline Copeland, Director of the National Programme on Substance Abuse Deaths at King’s College, London, “We’ve had heroin supplies that have been adulterated by these drugs and that’s because they’re so strong and the heroin is running out.” *Id.*; see 2025 EU Drug Report, *supra* note 8, at 15 (“The Taliban’s ban on opium poppy cultivation in Afghanistan since April 2022 has significantly reduced opium production, but the extent to which this might constrain heroin supply to Europe still remains unclear as opium stocks exist within Afghanistan. Any potential supply gap could, in some countries, be filled by new synthetic opioids and other substances. However, China’s expanded control of nitazene opioids in 2024, now covering 10 substances, may redirect the market away from dominant compounds such as metonitazene and protonitazene and towards novel derivatives or alternative opioid families”); Samarasekera, *supra* note 13, at 2251 (noting that “law enforcement actions to tackle fentanyl might inadvertently boost the supply of nitazenes. Nabarun Dasgupta, who works at the Opioid Data Lab at the University of North Carolina (Chapel Hill, NC, USA), says that if the increased crackdowns on fentanyl precursors continues, ‘we would expect nitazenes to be the next thing emerging.’”); see also Friedman & Ciccarone, *supra* note 1, at e59 (“Looking globally, the Taliban’s opium ban in Afghanistan is an important factor that could accelerate the uptake of synthetic drugs in Europe and other countries with entrenched heroin markets. To fill the void of dwindling heroin supplies, local synthesis of illicit fentanyls and other synthetic drugs, or their importation from Mexico, Estonia, or China (along with pill presses), are technologically and logistically realistic outcomes.”); Griffiths et al., *supra* note 23, at 1334 (“Information from satellite monitoring and other sources suggests that actions by the Taliban have caused a dramatic reduction in poppy cultivation in 2023.”); Homer, *supra* note 30; *Nitazenes*, *supra* note 12 (“Many scientists studying nitazenes believe the explosion in recent years is a supply-side reaction to increased restrictions on other drugs. In the mid-2010s America boosted its attempts to crack down on new fentanyl analogues and their precursors and persuaded other countries to do the same; China, which is home to producers and exporters of both fentanyl and nitazenes, banned all analogues of fentanyl in early 2019, causing domestic production to plummet. In 2021 the Taliban seized control of Afghanistan, then the world’s top producer of opium (it has since fallen behind Myanmar), and outlawed the drug’s production. As opium is needed to make heroin, illicit drug producers in Europe are thought to have turned to nitazenes amid fears of an imminent drop in supply.”).

⁵⁴ See, e.g., DAVID BOYUM & PETER REUTER, AN ANALYTIC ASSESSMENT OF U.S. DRUG POLICY (2005).

substances laws. As for our demand-side strategy: Education and treatment have been our primary tactics. Sadly, however, none of those approaches has been as effective as we would like. Entirely preventing illicit drugs from being available to the public and altogether eliminating any illicit drug use are ideals that we would like to attain but lie beyond our grasp on this side of the River Styx, so we must accept something short of perfection as an attainable goal. Given the horrific number of overdose fatalities that we have witnessed over the last 30 years, however, any improvement on either the supply or demand side would be welcome. Fortunately, there are some steps that we can take now to help us out of our current predicament.⁵⁵

A. Ensure That an Adequate Quantity of Naloxone Is Widely Available

Naloxone is an antidote to the effect of opioids,⁵⁶ and, if applied shortly after someone uses the drug, can neutralize its effect and prevent an overdose from becoming a

⁵⁵ Two additional steps that have been recommended and could be undertaken are (1) developing nitazene test strips like the ones that now exist for fentanyl, and (2) test wastewater and discarded drug use equipment (e.g., hypodermics) to learn the extent of nitazene use in local populations. See Richard Bade et al., *Early Identification of the Use of Potent Benzylbenzimidazoles (Nitazenes) Through Wastewater Analysis: Two Years of Data from 22 Countries*, 120 ADDICTION 1739, 1744 (2025) (“Despite their low dose sizes, and therefore, low levels expected, our work has shown that they can be detected in wastewater. Analyses can be conducted in real-time, and data obtained within days-weeks so that findings could be relayed to relevant public health authorities. The incorporation of nitazenes into ongoing wastewater monitoring programs can provide authorities with earlier identification of emerging analogues and increased use of these compounds, enabling rapid implementation of public health interventions before the harms occur and before they become more widespread.”); Keller et al., *supra* note 21, at 1 (concluding that “chemical analysis of drug paraphernalia is feasible, noninvasive, and effective, providing early signal identification to monitor the appearance of dangerous novel psychoactive substances being consumed”); *id.* at 5-6 (“The chemical analysis of used drug paraphernalia is an underutilised approach to detect, identify, and monitor the appearance of nitazene analogues,” but requires use of “sensitive and robust analytical methods”); NPS in the illicit drug market and provides early signal detection.”) (endnotes omitted); Samarasekera, *supra* note 13, at 2250 (“Although fentanyl test strips tell users whether fentanyl is present in their purchases, they cannot detect nitazenes. No test strip currently exists for nitazenes.”); *id.* (“Some researchers think wastewater surveillance is needed in the USA to track use of synthetic opioids and warn users about nitazenes in the drug supply. They criticise the US Centers for Disease Control and Prevention (CDC) for not implementing this strategy. ‘The public health community has really failed in the United States to adopt the wastewater monitoring techniques that are well established in the EU and well established in Australia’, says Humphreys. ‘It’s an embarrassment. The CDC should feel embarrassed.’ [¶] Experts in other countries agree”). Each one raises different cost-benefit issues with no clear, indisputable answers. For instance, would the development of nitazene test strips give users an unjustified level of confidence that the drugs that they just purchased over the Internet or Dark Web do not contain one of more newly developed versions of nitazenes? That is a concern because of the ongoing development of new types of that drug. Also, people likely would question whether funds spent on wastewater testing would generate sufficient public health data to justify the expenditure of limited tax dollars, which could generate a potential public backlash against the entire education process. (John Q. Citizen: “You want to spend my hard-earned tax dollars on testing *what* for a substance that it is *illegal* to use?) Those issues need to be publicly debated before we choose either one.

⁵⁶ Naloxone works because it can “knock” opioids off the brain’s mu-opioid receptors and reverse the drug’s effects. Schwarz, *supra* note 13, at 331 (endnote omitted). Buprenorphine, which is used to treat opioid addiction by avoiding the pangs of withdrawal not only “binds more avidly to the [mu] receptor

fatality.⁵⁷ Naloxone also can be used for that purpose to offset fentanyl poisoning, although repeated doses of naloxone might be necessary to achieve that result, given fentanyl's great strength. Nitazenes share the same potency as fentanyl, requiring repeated or greater doses of naloxone to prevent a user from dying due to respiratory depression.⁵⁸ Increasing the availability of naloxone might require states to amend their laws so that a greater number of private, non-physician parties can obtain the antidote.⁵⁹

B. Improve Post-Mortem Drug Testing

Our threshold response should be to identify the extent of the problem we face. The novelty of nitazenes hinders our ability to respond.⁶⁰ Because the Commissioner of

than most opioids” and also has a “high binding affinity,” which means that its bond with a receptor allows it to inhibit the binding ability of opioids. *Id.*

⁵⁷ See 2025 UNODC *Early Warning Advisory Highlights*, *supra* note 7, at 16 (“Awareness and access to lifesaving treatments such as naloxone (an opioid antagonist which rapidly and safely reverses the effects of opioids . . .) is crucial. However, immediate medical care is critical as naloxone may not be fully effective or may require repeated dosing for some newly emerging synthetic opioid NPS.”) (endnote omitted); NANCY D. CAMPBELL, OD: NALOXONE AND THE POLITICS OF OVERDOSE (2020).

⁵⁸ See Norah Alhosan et al., *Slow Dissociation Kinetics of Fentanyls and Nitazenes Correlates with Reduced Sensitivity to Naloxone Reversal at the μ -Opioid Receptor*, 182 BR. J. PHARMACOLOGY 969, 981 (2025) (“There have been numerous reports of more naloxone, in the form of multiple or higher doses, being required to reverse overdoses involving fentanyls and nitazenes compared with heroin overdoses[.]”) (citations omitted); *id.* at 983 (“Our data confirm the view that, in overdoses involving fentanyls and nitazenes, higher doses of the antidote naloxone may be required for reversal than those normally used to reverse heroin overdose.”); Pereira et al., *supra* note 20, at 6 (“[D]ue to their high potency, slow dissociation from the MOR [μ opioid receptor] and the prolonged effects of some active metabolites, higher or repeated doses of naloxone and, in some cases, continuous infusions may be required for complete reversal.”) (endnotes omitted);

⁵⁹ Supplementary expenditures, as well as some additional education and training of first responders and emergency room physicians, might also be necessary. See Abbate et al., *supra* note 21, in Dargan & Wood eds., *supra* note 21, at 466; Pereira et al., *supra* note 20, at 8 (noting that “training on identifying nitazene intoxication, which can mimic other opioid overdoses, and to implement appropriate treatment protocols”); Mariana Gonzalez Utrilla et al., *Naloxone Dosing in the Era of Synthetic Opioids: Applying the Goldilocks Principle*, 120 ADDICTION 2165, 2170 (2025) (“The future of naloxone administration lies in personalized dosing, requiring a detailed understanding of dose titration. This shift towards more personalized dosing will necessitate enhanced training programs for both professionals and non-medically trained responders, covering not only naloxone administration but also post-reversal care and interventions.”).

⁶⁰ Unfortunately, we are likely to see other NPSs create the same problems as fentanyl and nitazene. See Alex J. Krotulski et al., *Public Alert: Increase in Fatal Overdoses Linked to Novel Synthetic Opioid N-Propionitrile Chlorphine (Cychlorphine)*, CNTR FOR FORENSIC SCI. RSCH. & EDUC. (Jan. 2026), www.cfsre.org/images/content/reports/public_alerts/Public_Alert_N-Propionitrile_Chlorphine_013026.pdf (last accessed Mar. 13, 2026) (“N-Propionitrile chlorphine belongs to an emergent subclass of novel synthetic opioids often referred to as ‘orphine analogues’ (or more simply ‘orphines’) and bears structural similarity to other benzimidazolones (e.g., broorphine, chlorphine). . . . N-Propionitrile chlorphine has been identified in 25 blood specimens from fatal overdoses tested at the CFSRE, the vast majority submitted in late-2025 and early-2026. In addition, N-propionitrile chlorphine has been tentatively identified in more than 100 toxicology cases at NMS Labs. Toxicology specimens originated from nine states across the United States, as well as three provinces in Canada. N-Propionitrile chlorphine was detected as the sole opioid in 11 of 25 cases, and alongside other opioids (e.g., fentanyl, oxycodone) and traditional stimulants (e.g., methamphetamine, cocaine). Co-detection with NPS was

Food and Drugs has never approved nitazenes as a legitimate treatment for human or veterinary medicine, we do not have studies of the long-term effects of its use in humans.⁶¹ In fact, “there is little scientific information about these drugs,”⁶² which “leaves healthcare professionals and policymakers in the blind.”⁶³ Also, because of its arrival during an opioid epidemic with fentanyl as the newest principal culprit, we do not know how often it has been a cause of overdoses and fatalities because medical examiners (MEs) do not regularly test for it,⁶⁴ and, even if they were to do so, it can be difficult to find nitazenes with standard laboratory equipment, in part because the body quickly metabolizes it.⁶⁵ Nitazenes have been ingredients of counterfeit

common (e.g., novel benzodiazepines [phenazepam], other orphine analogues [spirochlorphine], nitazene analogues, and carfentanil).”).

⁶¹ Early studies used rats for testing. See Kozell, *supra* note 27, at 220.

⁶² NAT’L CAPITAL POISON CNTR., *What are synthetic opioids?*, www.poison.org/articles/what-are-synthetic-opioids (last accessed Feb. 17, 2026); see also, e.g., U.N. OFF. ON DRUGS & CRIME, UNDOC LABORATORY AND SCIENTIFIC SERVICE PORTALS, *Nitazenes* (Sept. 30, 2024), <https://www.unodc.org/LSS/SubstanceGroup/Details/6aefe0ca-aafd-452c-a534-c16aa3a2e507> (last accessed Feb. 27, 2026) (“The clinical toxicological properties of many nitazenes have not been studied directly. There are few reports from online user forums on the acute and chronic physical and psychological effects. The adverse effects align with those commonly reported for other synthetic opioid NPS such as incoordination, dizziness, drowsiness, mental confusion, sedation, and profound intoxication.”); Abbate et al., *supra* note 21, in Dargan & Wood eds., *supra* note 21, at 462 (“The true prevalence of novel synthetic opioids is hard to determine as currently, newer modified compounds that circumvent existing drug laws are being synthesized and introduced into the drug market and necessitate the availability of reference material and rapid analytical method developments.”); Cristian Caprari et al., *The Emergence of Nitazenes: A New Chapter in the Synthetic Opioid Crisis*, 99 ARCHIVES OF TOXICOLOGY 3877, 3877 (2025) (“Since the appearance of isotonitazene in 2019, the scientific community has been challenged in the identification and characterization of new structural analogs, the study of their pharmacodynamics and pharmacokinetics, the identification of corresponding metabolites, and the development of analytical methods able to identify and quantify these compounds even at the near or sub ng/mL concentrations at which they are present in biological samples.”); Jadhav & Fasinu, *supra* note 16, at 3 (“Despite the huge public health concern that nitazenes constitutes, there is a wide knowledge gap in their metabolism and toxicokinetics.”); Montanari et al., *supra* note 36, at 475 (noting “the scarcity of reports on [nitazene]-related cases and drug co-exposures”); Roberts et al., *supra* note 17, at 475 (“Data describing the clinical course and outcome of nitazene opioid poisoning are limited.”); Stangeland et al., *supra* note 34, at 394 (“The human pharmacokinetics and toxicity are largely unknown because only limited clinical and post-mortem data are available.”) (endnotes omitted); *Nitazenes*, *supra* note 22 (“far too little is known about them.”).

⁶³ Stangeland et al., *supra* note 34, at 404.

⁶⁴ See Rasmussen & Li, *supra* note 21; Rombolà et al., *supra* note 11, at 2 (“[L]imited information is available regarding the effects of these compounds on humans and, in particular, studies on the genotoxicity of nitazenes are not yet available.”) (endnotes omitted).

⁶⁵ See Keller et al., *supra* note 21, at 5-6 (noting that “a chemical analysis of used drug paraphernalia can “detect, identify, and monitor the appearance of nitazene analogues,” but requires use of “sensitive and robust analytical methods”); Jadhav & Fasinu, *supra* note 16, at 8 (“The rapid metabolism . . . [of nitazenes] has implications for timely detection and quantification in human matrices. Due to their potent nature, it is expected that nitazenes are consumed in microgram quantities. This, in addition to rapid clearance will require a timely post-ingestion sampling and highly sensitive analytical methodology for detection and quantitation. . . . The rapid metabolism of nitazenes in hepatic matrices may also have implications for the detection of the unchanged compounds in the urine and other body matrices. This is important because most forensic analysis of drugs of abuse rely heavily on urinary

analgesic pills and antianxiety medications that are look-alikes to legitimate pharmaceuticals (even though sold illegally), and also have been admixed with powdered heroin and cocaine. MEs conducting autopsies will test for traditional opioids and fentanyl in overdose fatalities, given their prevalence, but, given nitazenes' recent arrival, they might not also test for the presence of nitazenes unless they have a particular reason to do so, given the additional testing costs involved.⁶⁶ The result is to make it difficult to identify their role in fatalities, meaning that the incidence of nitazene-induced fatalities definitely might be (perhaps considerably) higher than what has been reported.

C. Enhance Our Forensics Capabilities

Standard toxicology tests might not detect the presence of nitazenes.⁶⁷ The ongoing development of new versions will force us to enhance our forensic capabilities to be

analysis. While the detection of metabolites in the urine can be useful in determining the identities of the abused substance, the diversity, and structural similarities among the nitazenes may make this challenging.”); Stangeland et al., *supra* note 34, at 393-94 (“Routine drug testing cannot identify nitazenes, although specialized laboratories are able to detect them in biological samples.”); Samarasekera, *supra* note 13, at 2251 (“[Nabarun] Dasgupta [of the Opioid Data Lab at the University of North Carolina (Chapel Hill)] says it is difficult to detect nitazenes in post-mortem toxicology and overdose investigations. According to his colleagues in Europe, who have been dealing with nitazenes for longer and in greater volume, specialised methods for detecting nitazenes in overdose fatalities are needed because the drugs do not last long in the body and are in small concentrations. ‘So to be able to track nitazenes in the United States, there will have to be a levelling up of both equipment and skills and validated methods of detecting the nitazenes. And that would involve a massive scale up. . . . [I]t’s going to be expensive if that’s the path that happens. If it doesn’t happen, what it will look like is a lot of overdose deaths without a known or identifiable drug and that would complicate everything from criminal proceedings to health surveillance and interventions’, Dasgupta says.”).

⁶⁶ A 2020-2022 study of patient admitted to emergency department found that, of 537 patients with complete laboratory testing, two percent tested positive for only fentanyl (11) while 1.7 percent (9) tested positive for nitazenes. Amaducci et al., *supra* note 21, at 1; *see also* 2025 EU Drug Report, *supra* note 8, at 9 (“The most recent data show that drug producers continue to create new substances to avoid legal controls, with 47 new psychoactive substances notified for the first time in 2024. This is close to the annual number typically reported between 2016 and 2022.”); Kerry Breen, *What Are Nitazenes? What to Know About the Drug That Can Be 10 Times as Potent as Fentanyl*, CBS NEWS, Dec. 31, 2023, <https://www.cbsnews.com/news/nitazenes-fentanyl-substance-use-drug-supply-opioid-death-colorado/> (“I [viz., Dr. Wilson M. Compton, National Institute on Drug Abuse Deputy Director] wouldn’t be surprised if we see more and more nitazenes because they’re still under the radar to a lot of America and it takes time to implement advisories for law enforcement to all get on the same page of what they need to look for[.]”); *id.* (Claire Zagorski, a chemist and paramedic: “It really is like Whack-a-Mole. Like they just keep coming and coming and coming,’ . . . because of the way the drugs are developed. Now that stopping fentanyl is a national priority, she expects to see more nitazenes being developed by illicit manufacturers and used as authorities to catch up.”); *see also id.* at 226-43.

⁶⁷ *See* Frank T. Peters & Marcus R. Meyer, *Analytical Techniques for the Detection of Novel Psychoactive Substances and Their Metabolites*, in Dargan & Wood eds., *supra* note 21, at 225-26 (“This emergence of NPS is an ongoing challenge for analytical toxicologists in forensic as well as clinical toxicology, because most of the new drugs may cause serious toxicity or impairment but their identification is not guaranteed by established methods for several reasons. Firstly, immunoassay (IA)-based techniques targeting the classical drugs do not reliably pick up most of NPS due to low cross-reactivity. Secondly, even with more sophisticated techniques such as mass spectrometry (MS)-based screening techniques, the new drugs may be missed, either because reference mass spectra are not (yet) included

able to identify whatever new drugs are harming and killing our family members, friends, and neighbors.⁶⁸ That will require the “continuous updating of analytical methods and spectral libraries,” along with the continued adjustment and revalidation of “the equipment, protocols, regulations, and guidelines in each laboratory,” to be able to prosecute criminal trafficking cases.⁶⁹ That can prove expensive, so it will be necessary as well to decide who should undertake that responsibility—namely, the federal government or the states (and if the latter, how many).

AI can be a powerful tool in forensic science to combat the emergence of NPS, by enabling the authorities to predict and identify new compounds far more rapidly than traditional methods permit, which has been a major challenge in information sharing. Machine learning has greatly improved the speed and accuracy of detecting unknown drugs. Fortunately, the same technologies that could facilitate the design of new and potentially more potent substances can help us by aiding their detection. Thoughtful application of AI will strengthen efforts to protect public health while helping authorities keep pace with evolving drug markets.

D. Improve Information-Sharing Domestically and Internationally

Although nitazenes have become a specter of another fentanyl-like overdose epidemic in the United States, reporting on nitazenes’ role in overdose fatalities is “sparse and relies on self-reporting.”⁷⁰ Until local jurisdictions regularly test for

in the respected reference libraries, or because established methods employing selected-ion monitoring (SIM) or multiple-reaction monitoring (MRM) focusing on fragments/transitions of the classic drugs do not include fragments/transitions of NPS.”).

⁶⁸ See U.N. OFF. ON DRUGS & CRIME, *UNODC Opioid Strategy: The Growing Complexity of the Opioid Crisis* 11 (Oct. 2020) (“The ability to identify new substances goes hand in hand with a continuous need to update forensic capacities with advanced, and sometimes prohibitively costly, analytical technologies. In circumstances where access to chemical reference materials, screening tools or forensic data is insufficient, the cross-border sharing of investments in powerful, advanced analytical technologies could be considered, such as nuclear magnetic resonance spectroscopy for determining the molecular structures and purity of new substances. At the same time, investments and efforts to update the software and spectral libraries of existing laboratory and field-based forensic analytical technologies are encouraged, along with the development and validation of analytical methodologies, to ensure the ability to identify and/or verify the presence of new synthetic opioids.”).

⁶⁹ Pereira et al., *supra* note 20, at 6, 7.

⁷⁰ 2025 UNODC *Early Warning Advisory Highlights*, *supra* note 7, at 16 (“Data collection efforts need to be strengthened by considering for instance: collecting and reporting more data on causality; and more data contributors reporting non-NPS data to improve reporting on polysubstance use.”); Rasmussen & Li, *supra* note 21; *id.* (“On an early summer morning in 2023, police arrived at Anne Jacques’s door in north Wales. Her 23-year-old son had died in his sleep in his student apartment in London, they told her. [¶] Her son, Alex Harpum, was a rising opera singer and healthy. Police found Xanax tablets in his room, and evidence on his phone that he had bought pills illegally, which Jacques said he occasionally did to sleep while on medication for his attention-deficit hyperactivity disorder. [¶] Yet, the coroner established the cause of death as unexplained cardiac arrest, known as sudden adult death syndrome. Jacques, not satisfied with the explanation, researched drug contaminants and requested the coroner test for nitazenes. Seven months after her son’s death, police confirmed that his tablets had been contaminated with the potent opioid. [¶] ‘I basically had to investigate my own son’s death,’ Jacques said. ‘You feel like your child has been murdered.’ [¶] Harpum wasn’t alone. While most known overdoses affect heroin users, nitazenes have also been found in party drugs like cocaine,

nitazenes and share their test results within their own state, with other states, and with the federal government, we cannot know whether nitazenes have overtaken fentanyl as the leading cause of drug overdose fatalities. The knowledge that localities acquire regarding any potentially new epidemic must be shared with other public health agencies, hospitals, and medical schools.⁷¹ Most importantly, the results of local autopsy drug tests should also be shared with the relevant federal authorities—in particular, the U.S. Drug Enforcement Administration and the U.S. Centers for Disease Control and Prevention. We cannot overestimate the benefit of using public health and law enforcement agencies as “early warning systems” about the dangers of NPSs. Only by so doing can our nation analyze and report on whatever incidence and trends are occurring domestically.⁷²

E. Maintain Our Closed-Border Policy to Reduce the Quantity of Nitazenes Being Smuggled into the United States

Despite disavowing any intent to open our borders to any and all newcomers, the Biden administration allowed millions of aliens to enter the United States illegally across our southwest border with Mexico. An unknown number of them smuggled fentanyl into this nation, where it was distributed by domestic affiliates of the

ketamine and ecstasy, in illegal nasal sprays and vapes, and detected in benzodiazepines like Xanax and Valium. In May, two young Londoners died after taking what authorities believe was oxycodone laced with nitazenes upon returning home from a nightclub.”).

⁷¹ 2025 UNODC *Early Warning Advisory Highlights*, *supra* note 7, at 16-17 (“Ongoing monitoring of (newly emerging) NPS is crucial and early warning systems need to be established/strengthened to rapidly identify and respond to these emerging drug threats. To assist forensic drug testing and toxicology laboratories, law enforcement and healthcare providers, EWA collates NPS drug sample and toxicology case data from almost 500 different sources to ensure that information on new substances, including analytical, pharmacology and legal response data, is shared and accessible as promptly as possible.”).

⁷² See U.N. OFF. ON DRUGS & CRIME, *UNODC Opioid Strategy: The Growing Complexity of the Opioid Crisis* 11 (Oct. 2020); (“The growing complexity of the opioid crisis highlights the key role of national, regional and global early warning systems in the monitoring and early detection of new substances. Given their accelerating replacement rates, access to timely information on the emergence, prevalence and harm of new substances of abuse is critical for stakeholders to develop policy responses. However, the effectiveness of early warning systems ultimately depends on unfettered and prompt information-sharing among international, regional, country and local partners, which remains an on-going concern in several parts of the world. Breaking down barriers to information-sharing requires joint efforts from international and regional organisations and Member States alike and technical assistance with setting up national systems should be provided wherever there is a lack of capacity to identify new synthetic opioids.”). The U.S. has a drug early warning system as a function of the National Institute on Drug Abuse. See NAT’L INST. ON DRUG ABUSE, U.S. DEP’T OF HEALTH & HUMAN SERVS., *National Drug Early Warning System (NDEWS)* (Aug. 26, 2025). The European Union also has a drug Early Warning System that might provide additional discoveries. See EUROPEAN UNION DRUGS AGENCY, *Call to Action: New Synthetic Opioids: European Preparedness and Response* (Sept. 30, 2024) (last accessed Feb. 28, 2026) (“Our EU Early Warning System (EWS) has been operating at the highest level for over 25 years, with regular risk assessments of new psychoactive substances (NPS), including new synthetic opioids.”); John R.H. Archer, *Novel Detection Methods and Data Triangulation for Novel Psychoactive Substances*, in Dargan & Wood eds., *supra* note 21, at 132-33 (describing the EU Early Warning System); Michael Evans-Brown et al., *supra* note 43, in Corazza & Roman-Urrestarazu eds., *supra* note 8, at 17-26 (same).

Mexican transnational criminal organizations and might have been responsible for thousands of overdose fatalities. The Trump administration has abandoned any matter approach to immigration and has effectively limited the number of illegal entrants. While it might be difficult to calculate precisely how many lives that new policy has saved, the number surely is far from trivial. We must halt illegal entries into the United States as a supply-side component of a national effort to address our drug problems.

F. Track the Distribution of Nitazenes' Precursor Chemicals

Although nitazenes were never sold commercially, the developer filed patent applications, and scholarly articles were published on that product.⁷³ Some of those materials are available on the Internet, and it is likely that chemists have used them to synthesize nitazenes.⁷⁴ That might be helpful to law enforcement efforts to target chemists and shippers. If the literature discloses that the relevant chemical ingredients are exotic, useful only for synthesizing nitazenes and difficult to create or come by, law enforcement authorities might be able to persuade reputable manufacturers to notify them about the shipping of those ingredients. Some drugs can be synthesized in makeshift laboratories by people with only a rudimentary knowledge of the substance and practice of chemistry.⁷⁵ A result is the possibility that even overqualified and enterprising high school chemistry teachers, in New Mexico and elsewhere, might get into the nitazene synthesis and trafficking business just to make some extra bucks.⁷⁶ Limiting production in Mexico might only encourage traffickers to use the Big Square states out west to serve as a site for nitazene production.⁷⁷ Tracking precursor chemicals might be critical to keep domestic production from compensating

⁷³ See Vandeputte et al., *Novel Nitazene Recreational Drugs*, *supra* note 13, at 1 & 12 nn.5-8 (citing four papers published between 1957 and 1960 on nitazene development).

⁷⁴ See Pergolizzi, Jr. et al., *supra* note 23, at 1 (“As the Drug Enforcement Administration (DEA) and the Food and Drug Administration (FDA) have been better able to identify and schedule numerous fentanyl analogs, it appears that chemists in clandestine labs have gone back through historical pharmacology research literature for early attempts at developing synthetic opioids.”);

⁷⁵ The Wall Street Journal and New York Times published the articles cited below about the fentanyl synthesization process used by two Mexican TCOs. The articles contained photographs revealing that the process can be performed by ordinary “cooks” working in (charitably put) elementary, makeshift laboratories that no one would confuse with the facilities to be found at the campuses of Fortune 100 pharmaceutical companies. See Jon Kamp et al., *How Two Mexican Drug Cartels Came to Dominate America’s Fentanyl Supply*, WALL ST. J., Aug. 30, 2022, <https://www.wsj.com/articles/mexico-drug-cartels-fentanyl-overdosesinaloa-jalisco-11661866903> (last accessed Feb. 26, 2026); Natalie Kitroeff & Paulina Villegas, “*This Is What Makes Us Rich’: Inside a Sinaloa Cartel Fentanyl Lab*,” N.Y. TIMES, Dec. 29, 2024, www.nytimes.com/2024/12/29/world/americas/inside-fentanyl-labmexico.html (last accessed Feb. 26, 2026). Experts have said that the synthesizing nitazenes is not difficult, so the necessary facilities for “cooking” fentanyl not only might resemble the ones depicted in those photographs, but also even might serve “double duty” to make fentanyl and nitazenes.

⁷⁶ See *Breaking Bad* (AMC 2008-2013).

⁷⁷ We have seen that phenomenon before: Chinese cannabis traffickers have become the leading domestic parties in that business. See Paul J. Larkin, *China and Cannabis*, HERITAGE FOUND. Legal Memo. No. 380 (2025).

for lost foreign supply as a consequence of protecting our borders from infiltration and smuggling.⁷⁸

G. Educate the Public About Nitazenes and Reinforce Our Drug Use Prevention Efforts

Education is critical to our effort to stop our opioid epidemic and reduce its vicious toll on our fellow citizens.⁷⁹ The reason why is clear and indisputable: Illicit drugs that someone does not use cannot take his or her life.

Evidence indicates that drug use arises from a combination of biological, psychological, and environmental factors, including genetic vulnerability, reward effects, coping with distress, curiosity, family, peer and social influences, medical exposure, environmental stress, early adversity, and availability. These interacting influences explain why substance use patterns vary widely across individuals and populations. Some rationales, however, are likely most common. People suffering from what they see as a joyless, painful, hopeless existence will use drugs as a means of escaping for a brief time from being chained to their depressing circumstances. Other individuals will consume drugs to “expand their consciousness” or “horizons” for creative purposes, or simply to enjoy their (albeit short-lived) pleasant effects. And students will seek to enhance their physical and mental abilities by, for instance, staving off fatigue and sleepiness to work longer hours or an additional shift, to cram for a final exam, or to complete a term paper. In each case, users are willing to run the risks that their drug use could prove debilitating in the short term, addictive in the medium- or long-run, or sometimes (as in the case of synthetic opioids like fentanyl and nitazenes) instantly fatal because they do not intellectually understand or emotionally apprehend the risks involved, they mistakenly assume that they are not exposed to any such risk because they had obtained a drug from a “trustworthy” source, or they discount any potential downside in favor of the immediate “rush” that they seek. What worsens the dangerous situation is that, for decades now, traditional and social media have touted the benefits of an attitude that pursues immediate gratification and denigrates the value of self-sacrifice for one’s own benefit or that of others. We need to reverse that trend.

It is particularly important to reach people in their teens, 20s, and 30s, yet we know how difficult it can be to persuade people in those age groups to forego the short-term euphoria that drugs can bring. For years, the “Just Say No” and “Drug Abuse

⁷⁸ That strategy reduced domestic methamphetamine production. It declined substantially in the mid-2000s after restrictions—such as the Combat Methamphetamine Epidemic Act of 2005, Pub. L. No. 109-177, 120 Stat. 192 (codified at scattered sections of 21, 22, and 42 U.S.C.)—were placed on retail sales of pseudoephedrine, a key chemical precursor. The same type of approach might work here too.

⁷⁹ See, e.g., Samarasekera, *supra* note 13, at 2250 (“Prevention is key to stemming the opioid crisis, note experts. The Stanford–Lancet Commission recommended investing in children, especially those growing up in low-income neighbourhoods who ‘lead very stressful lives’, Humphreys says. He champions programmes that help children recognise and manage their emotions, cope with stress, bond through their schools, and ‘bond with positive social activities, be it athletic, religious, cultural, or artistic’. ‘Programmes ‘where kids can experience joy, connection, and meaning without drugs’”).

Resistance Education,” or DARE, programs, were touted as optimum drug resistance programs. Yet studies have shown that, by and large, those programs have been ineffective.⁸⁰ Nonetheless, all hope should not be lost. The evidence shows that people who do not use nicotine, alcohol, cannabis, or other illicit drugs before age 18 are highly unlikely ever to use them.⁸¹ That result is inspiring. It indicates that dissuasion is possible and can be effective.

Two possibilities—though they might be more in the nature of a football “Hail Mary” than a solid game plan—would be the following. First, persuade social media platforms to create and use algorithms that strongly disfavor content displaying or encouraging illicit drug use.⁸² The government likely could not order social media platforms to undertake those efforts, but the government could encourage them to do so and publicly identify the ones that refuse. Second, persuade some well-known, highly respected or liked public figures to take a strong stand against drug use. Taylor Swift, Denzel Washington, Aaron Judge, Tom Brady, and LeBron James come readily to mind. If we’re lucky, one or more social media platform owners and public figures will step up to try to save lives by telling people in their teens, 20s, and 30s to make the necessary sacrifice to save their own futures and those of others by not taking drugs.

CONCLUSION

Great Britain’s crime agency has said that “there never has been a more dangerous time to take drugs.”⁸³ That’s true. Heroin and fentanyl have neither disappeared nor

⁸⁰ See, e.g., Richard R. Clayton et al., *The Effectiveness of Drug Abuse Resistance Education (Project DARE): 5-Year Follow-Up Results*, 25 PREVENTATIVE MEDICINE 307, 317-18 (1996); Susan T. Ennett et al., *How Effective Is Drug Abuse Resistance Education? A Meta-Analysis of Project DARE Outcome Evaluations*, 84 AM. J. PUB. HEALTH 1394 (1994); Donald R. Lyman et al., *Project DARE: No Effects at 10-Year Follow-Up*, 67 J. CONSULTING & CLINICAL PSYCHOLOGY 590 (1999); *id.* at 593 (noting and collecting “the accumulating literature on DARE’s lack of efficacy in preventing or reducing substance use”); Steven L. West & Kerri K. O’Neal, *Project D.A.R.E. Outcome Effectiveness Revisited*, 94 AM. J. PUB. HEALTH 1027, 1028-29 (2004) (studies concluding that DARE has been ineffective). A minority of studies have argued that studies arguing that DARE might be effective but that its value depends on factors such as the quality of officers’ training and student involvement, factors that will vary widely. See, e.g., Emily R. Beamon et al., *Fidelity of D.A.R.E. Officers’ Delivery of “keepin’ it REAL” in Elementary & Middle School*, 124 PREVENTION SCI. 985, 993-95 (2023) ; William B. Hansen, et al., *D.A.R.E./keepin’ it REAL Elementary Curriculum: Substance Use Outcomes*, 18 PLOS ONE e0284457, at 11-12 (), *with, e.g.,*

⁸¹ See Robert L. DuPont et al., *Drug Use Among Youth: National Survey data Support a Common Liability of All Drug Use*, 113 PREVENTATIVE MED. 68 (2018) (relying on survey results from the 2017 National Survey on Drug Use & Health (NSDUH)). The more recent 2022 NSDUH revealed updated those results. Among youth aged 12-17 who *did not* use cannabis in the past month, only 2.6 percent used some alcohol, 1.9 percent reported binge drinking or heavy alcohol use, 4.0 percent used tobacco products or vaped nicotine, and 1.0 percent used other illicit drugs. By contrast, among youth aged 12-17 who *did* use cannabis in the past month, 20.3 percent used some alcohol, 23.6 percent reported binge drinking or heavy alcohol use, 59.1 percent used tobacco products or vaped nicotine, and 9.3 percent used other illicit drugs. See INST. FOR BEHAVIOR & HEALTH, *One Choice*, <https://www.onechoiceprevention.org/basics-be-substance-savvy> (last accessed Mar. 5, 2026).

⁸² I thank Abigail Wagner for giving me that idea.

⁸³ ECONOMIST, *Nitazenes*, *supra* note 22.

stopped coming into our nation. The development of novel synthetic opioids like nitazenes have only added to the list of potential compounds that can inflict pain and misery on their users or altogether rob them of their lives in the blink of an eye. Nitazenes threaten to become the newest addition to the sad tale of woe found in the pages of the Morbidity and Mortality Reports published by the U.S. Centers for Disease Control and Prevention.

We need to anticipate what is coming over the horizon to prepare for the next assault. Equally important, we need to avoid the feeling of opioid-abuse fatigue that would make us fatalistic about our drug prevention efforts. There are steps that we can take, summarized above, that will give us a fighting chance—the most that we can ever ask for in public health policy regarding illicit drugs—to warn the public about a new threat and limit the damage that it will cause those who fail to learn from our experience with traditional opioids.