Documentary

Foundation for WMD

Presented By:

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Families Against Fentanyl
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A PLEA FOR
WEAPON OF MASS DESTRUCTION DESIGNATION
FOR ILLICITLY MANUFACTURED FENTANYLS:
ADDRESSING A CLEAR AND PRESENT DANGER

The U.S. Government is considering designation of illegal fentanyl as a Weapon of Mass Destruction (WMD). This would enable the Department of Justice, Department of Homeland Security, Drug Enforcement Agency (DEA), Department of Defense and other relevant federal agencies to better coordinate their efforts and immediately publish the necessary administrative directives to eliminate the threat posed by these deadly substances.

Federal Statute (18 U.S. Code § 2332a) states that "any weapon that is designed or intended to cause death or serious bodily injury through the release, dissemination, or impact of toxin or poisonous chemicals, or their precursors"[1] would be defined as a WMD. Illegal fentanyl and its analogues, especially carfentanil, are such toxins, capable of causing mass deaths or biological impairment.

Illegally imported fentanyl seizures in 2018 totaled almost 5,000 lbs., which is more than 1.2 billion lethal doses and enough to kill four times the population of the U.S. In the first six months of 2019, seizures went up[2]. In August 2019, law enforcement officers took down a major trafficking conspiracy in Virginia and seized 66 pounds of illegal fentanyl; the DEA confirmed the amount intercepted was enough to kill 14 million people[3]. That same month, the Mexican Navy, in cooperation with the U.S., made a seizure of 52,000 lbs. of illegal fentanyl [4]; enough to kill 11.5 billion people. In 2019, eleven pounds of the potent analogue carfentanil was seized in Queens, NYC; enough to kill 250 million people.[5] The U.S.DEA estimates that less than 10% of all illicit drugs are being captured[6]. An EPA report in 2018 indicates that the threat of these quantities to the environment could be devastating[7].

The following list compares lethal doses of fentanyl and its more powerful analogue, carfentanil, with the highest-class nerve agent Sarin, which is currently designated as a WMD:

AGENT	**158 lb. Person: Deadly Dose**
Carfentanil[8]	**.02 mg**
Sarin[9]	**.50 mg**
Fentanyl[10]	**2 mg**

We urge all relevant federal agencies to aggressively confront this threat by naming illegal fentanyl and its analogues Weapons of Mass Destruction.

James Rauh
Families Against Fentanyl

[1] https://www.law.cornell.edu/uscode/text/18/2332a
[2] https://www.dhs.gov/news/2019/04/24/mcaleenan-through-innovation-partnership-and-prevention-dhs-confronting-opioid
[3] http://via.fox8.com/9JWuQ
[4] https://www.theepochtimes.com/mexico-seizes-52000-pounds-of-fentanyl-from-china_3059981.html
[5] https://www.usatoday.com/story/news/nation/2019/11/13/carfentanil-new-york-giovanny-arias-victor-salazar-hector-maren/4181254002/
[6] https://web.stanford.edu/class/e297c/poverty_prejudice/paradox/htele.html
[7] https://www.epa.gov/sites/production/files/2018-07/documents/fentanyl_fact_sheet_ver_7-26-18.pdf
[8] https://gandaracenter.org/?s=carfentanil
[9] https://www.encyclopedia.com/social-sciences-and-law/law/crime-and-law-enforcement/sarin-gas
[10] https://en.wikipedia.org/wiki/Fentanyl

SECTION 2: JAMES RAUH OP-ED IN CLEVELAND PLAIN DEALER – Aug. 2019

Forum

COMMENTARY

Deadly fentanyl from China killed my son

Synthetic opioids pose a national security threat

James Rauh

In honor of his late son, Tom Rauh, who died of a fentanyl overdose later traced to illicit supplies from China, James Rauh of Akron has founded the Rising Anchor Project to fighting against illegally manufactured fentanyl.
Erin Victor

AKRON — The opioid crisis became very personal for me on March 21, 2015, when my son, Tom, died from a lethal dose of Chinese-sourced fentanyl. But I also recognize that this crisis transcends the over- whelming grief shared by those of us who have been personally affected by it.

In fact, my background as a chemist and engineer — as well as recent developments in China, where I've done a considerable amount of business over the years — has convinced me that synthetic opioids now pose one of the greatest threats to our national security.

I learned a lot when the U.S. Department of Justice traced the deadly fentanyl that killed my son directly to a crime organization in China run by Fujing and Guanghua Zheng — a drug trafficking organization sanctioned this week by the U.S. Treasury Department, along with Fujing and Guang- hua Zheng and their organizations.

I learned that, every week, crime organizations within China produce and export enough fentanyl to kill millions of people. I also discovered that virtually all of the world's supplies of synthetic opioids come from these organizations, and that the Chinese government has done virtually nothing to eliminate this threat.

This is especially troubling when you consider the chemical properties of these dangerous substances. Essentially, fentanyl, carfentanil and other synthetic opioids are nerve agents in powder form — in other words, weapons of mass destruction. And the weaponization of fentanyl is not a far-fetched concept for sci-fi novels. For example, fentanyl-based aerosol has been used by Russia to subdue Chechen rebels.

As a powder, fentanyl can easily be disbursed in air, water or food. This is a major national security issue, and we shouldn't just be concerned about rogue nations or terrorist organizations.

Today, even a lone psychopath with limited resources could kill thousands using a simple fentanyl-based weapon. Coordinated deployment with the right dispersal technology could be catastrophic.

Unfortunately, syntheticopioids are cheap and easy to find. In a clandestine operation run by the Department of Justice, more than 50 web-based vendors offered the investigators shipments of fentanyl and other synthetic opioids at astoundingly low costs. For example, one kilogram of fentanyl — enough to kill 500,000 people — can be purchased for $3,000-$5,000. For a similar price, one can purchase enough carfentanil (a fentanyl analogue) to kill 50 million people.

By its own estimation, according to the U.S. indictment, the Zheng family could produce 10,000 kilograms of fentanyl every month — an operation that the Chinese government could easily trace and eliminate.

As Assistant U.S. Attorney Matt Cronin noted in a recent episode of "60 Minutes," if China wanted to shut down the illicit opioid industry, it could do it in one day.

Meanwhile, China continues to strengthen its military capabilities and footprint. In response, the U.S., Great Britain, France and Germany have stepped up their naval presence in waters adjacent to China.

Historians might be reminded of China's disastrous "Opium Wars" with Britain and France, which dominated the drug trade in the mid-19th century. But the tables are now turned, with China controlling the flow of far-more-powerful synthetic opioids around the world and possibly exploring ways to weaponize these dangerous substances. A mountain of evidence has already shown that the Chinese government has no intention of prosecuting the Zheng family and, in fact, is a complicit partner in the organization's activities.

Is the Chinese government currently using the opioid trade to destabilize the United States and our global partners?

One thing is certain: The casualties continue to mount — and the best way to save lives is to make trade with China contingent upon its government ceasing production and distribution of these deadly poisons.

In honor of his late son, James Rauh founded the Rising Anchor Project(risinganchor.com), a community dedicated to fighting against illicitly manufactured fentanyl. Earlier this year, he appeared on an episode of "60 Minutes" on CBS-TV that focused on the Zheng crime family in China.

SECTION 3: GOVERNMENT INVOLVEMENT

A. James McDonnell, Assistant Secretary WMD Memo – Feb. 2019

FOR OFFICIAL USE ONLY

February 22, 2019

INFORMATION

MEMORANDUM FOR THE SECRETARY

FROM: James F. McDonnell
Assistant Secretary for Countering Weapons of Mass Destruction

SUBJECT: **Use of counter-WMD authorities to combat fentanyl**

Purpose: Discuss plans to use appropriate CWMD authorities against fentanyl. Under this construct, fentanyl would be considered a WMD material when certain criteria are met (e.g. quantity and configuration).

Key Issues:

- Fentanyl's high toxicity and increasing availability are attractive to threat actors seeking nonconventional materials for a chemical weapons attack. In July 2018, the FBI Weapons of Mass Destruction Directorate assessed that "...fentanyl is very likely a viable option for a chemical weapon attack by extremists or criminals."
  - As little as two to three milligrams of fentanyl can induce respiratory depression, respiratory arrest, and possibly death. And some fentanyl analogues, such as carfentanil, are orders of magnitude more potent.
- In the policy arena, the federal interagency has long regarded fentanyl as a chemical weapons threat. However, most CWMD planning efforts and programs do not currently focus on fentanyl as a target material for detection and interdiction (see Background).
- The recent authorization of the DHS CWMD Office through P.L. 115-387, Countering Weapons of Mass Destruction Act of 2018, provides an opportunity to apply DHS CWMD assets and capabilities to the fentanyl problem through the lens of WMD.
  - The CWMD Office can assist in countering fentanyl and its analogues through: managing and developing requirements for technology development, supporting the deployment of sensors (i.e. detection technology), and providing analytical expertise to the operating components.
- CWMD, as a support component, already provides direct support to DHS front line operating Components for WMD detection and prevention. The development and deployment of new capabilities that include fentanyl as a target substance would be a minor adjustment to current activities.
  - As an example, although Office of Health Affairs and Domestic Nuclear Detection Office, as DHS legacy organizations, had not previously planned specifically for countering the Hydrogen Sulfide threat, the newly organized CWMD Office (limited to 872 authorities) was immediately able to develop and field countermeasures and training and deploy detection equipment in twenty urban areas.
- CWMD Office efforts will focus on quantities and configurations that could be used as mass casualty weapons. However, many activities, such as support to fentanyl interdiction and

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detection efforts, would tangentially benefit broader DHS and interagency counter-opioid efforts.

- Additionally, DHS/CWMD is in a position to help coordinate and leverage efforts from across DHS and the broader federal CWMD enterprise toward the fentanyl problem set. Relevant activities include using tools from the CWMD community for supply chain interruption, to include interdiction and targeting as is currently done for other WMD materials.

Background:

- Over the past several years, the federal WMD policy community has periodically discussed the chemical weapons threat from fentanyl and other pharmaceutical-based agents.
  - Senior USG officials have made public statements at the Organization for the Prohibition of Chemical Weapons emphasizing that no country should be developing, producing, stockpiling, or using these agents even in a law enforcement scenario.
  - In parallel, the Department of Defense (DOD) has been developing materiel capabilities against these non-traditional agents within its Chemical and Biological Defense Program.
  - However, certain operational CWMD entities at DOD and elsewhere have been slow to act due to concern of getting pulled into the counter-narcotics mission.
- Within the past couple years, there has been a reinvigorated interest in addressing fentanyl and its analogues as WMD materials due to the ongoing opioid crisis.
- In April 2018, you signed a Material Threat Determination for Pharmaceutical-Based Agents (including fentanyl), indicating that these chemical agents pose a material threat to the U.S. population. This was the first step toward enabling Project BioShield funding and acquisition for medical or other security countermeasures that enhance preparedness for this threat.
- Recently, senior leaders in DOD, such as the Commander of U.S. Southern Command (USSOUTHCOM), have proposed formally designating fentanyl as a WMD material. Over the past two months, DHS/CWMD has had informal discussions on the topic with USSOUTHCOM, the Defense Threat Reduction Agency, U.S. Special Operations Command, USCG, CBP, and ICE.
  - These conversations revealed a general consensus that fentanyl, in certain configurations, has properties that make it a chemical with the potential for mass casualty effects.

Next Steps:

- CWMD will brief DHS operating components on counter-WMD efforts related to fentanyl, and discuss how best to incorporate these efforts into existing DHS interdiction, counter-opioid, and other operational activities.
- DHS/CWMD will host an interagency planning event (including DHS components) to perform a DOD-style "opportunity analysis" model on the fentanyl supply chain including from bulk manufacturing overseas to smuggling through pathways into the U.S.

Attachment(s): Classified slides are available upon request.

SECTION 3: GOVERNMENT INVOLVEMENT

B. DHS is Considering Classifying Fentanyl as WMD – Apr. 2019

WAIT WHAT

Exclusive: DHS is considering classifying fentanyl as a 'weapon of mass destruction'

NEWS

Paul Szoldra April 15, 2019 at 08:31 AM

The Department of Homeland Security is considering designating the painkiller drug fentanyl as a weapon of mass destruction "when certain criteria are met," according to an internal memo obtained by Task & Purpose.

Dated Feb. 22, 2019 under the subject line "Use of counter-WMD authorities to combat fentanyl," the information memorandum prepared for then-Secretary Kirstjen Nielsen from James F. McDonnell, DHS assistant secretary for countering weapons of mass destruction, offered background on the drug and how some elements of the U.S. government see fentanyl as a potential "mass casualty weapon."

"Fentanyl's high toxicity and increasing availability are attractive to threat actors seeking nonconventional materials for a chemical weapons attack," wrote McDonnell, a longtime Homeland Security executive appointed by President Donald Trump to lead the Countering Weapons of Mass Destruction (CWMD) Office in May 2018.

"In July 2018, the FBI Weapons of Mass Destruction Directorate assessed that fentanyl is very likely a viable option for a chemical weapon attack by extremists or criminals," he wrote.

The Department of Justice did not respond to a request for comment from Task & Purpose. The Department of Homeland Security also declined to answer any questions from Task & Purpose regarding the memo.

In 2017, President Trump declared the opioid crisis a public health emergency amid tens of thousands of American deaths traced to fentanyl overdose in recent years.

Roughly 50 to 100 times more powerful than morphine, fentanyl is a synthetic opioid that is medically-prescribed to treat severe pain under such names as Sublimaze and Actiq, according to the National Institute on Drug Abuse.

The illegal version — usually sourced from China or Mexico — is sometimes manufactured and sold as powder, put in small candies and eye droppers, or mixed into other illicit drugs to increase their potency, which has led to a significant increase in overdoses for unknowing drug users.

SECTION 3: GOVERNMENT INVOLVEMENT

C. Attorney General Sessions Indictment Announcement – Aug. 2018

THE UNITED STATES DEPARTMENT of JUSTICE

JUSTICE NEWS

Department of Justice
Office of Public Affairs

FOR IMMEDIATE RELEASE
Wednesday, August 22, 2018

Two Chinese Nationals Charged with Operating Global Opioid and Drug Manufacturing Conspiracy Resulting in Deaths

While in Cleveland, Ohio, Attorney General Jeff Sessions today announced the unsealing of a 43-count indictment in federal court in Cleveland, which charges two Chinese citizens with operating a conspiracy that manufactured and shipped deadly fentanyl analogues and 250 other drugs to at least 25 countries and 37 states. The indictment also alleges the drugs sold by the group directly led to the fatal overdoses of two people in Akron, Ohio.

Fujing Zheng, aka Gordon Jin, 35, and his father Guanghua Zheng, 62, both of whom reside in Shanghai, China, are charged with conspiracy to manufacture and distribute controlled substances, conspiracy to import controlled substances into the United States, operating a continued criminal enterprise, money laundering and other crimes. The charges carry a potential sentence of life imprisonment because the drugs involved resulted in death, and the defendants' conduct qualifies for an enhancement under the kingpin statute.

The indictment was announced by Attorney General Jeff Sessions, Assistant Attorney General Brian A. Benczkowski for the Justice Department's Criminal Division, U.S. Attorney Justin Herdman for the Northern District of Ohio, Acting Administrator Uttam Dhillon of the U.S. Drug Enforcement Administration (DEA), Special Agent in Charge Timothy Plancon of DEA's Detroit Field Office, Special Agent in Charge Steve Francis of U.S. Immigration and Customs Enforcement's Homeland Security Investigations (HSI) for Michigan and Ohio and Special Agent in Charge Ryan Korner of IRS Criminal Investigation (CI) Cincinnati Field Office.

"Fentanyl and its analogues are the number one killer drug in America today, and most of them come from China," said Attorney General Sessions. "That's why the Department of Justice under President Donald Trump has taken historic new steps against the threat of Chinese fentanyl. In October, we announced the first-ever indictments of Chinese nationals for fentanyl trafficking; 32 defendants have been charged in those cases. Today we are announcing an indictment of the leaders of the Zheng drug trafficking organization based in China, who the indictment alleges sold drugs that have killed at least two Ohioans. I want to thank U.S. Attorney Herdman and his fabulous Assistant U.S. Attorneys, our Criminal Division, DEA, FBI, Homeland Security Investigations, and IRS Criminal Investigation special agents and our Postal Inspectors for all of their hard work on this case. By cutting off fentanyl and its analogues at the source, we can save American lives."

"As detailed in this indictment, the trail from at least two dead bodies in Akron, Ohio, leads to the Zhengs," said U.S. Attorney Herdman. "This group has shipped deadly fentanyl analogues and other drugs around the globe for a decade. Law enforcement will follow the evidence wherever it leads, including overseas, to stop the flow of drugs that have caused so much heartbreak and destruction in Ohio."

“DEA will relentlessly pursue anyone shipping deadly fentanyl analogues to the United States wherever they may be and bring them to justice,” said DEA Acting Administrator Dhillon. “These Chinese drug traffickers are directly responsible for the deaths of U.S. citizens and we will hold them accountable in a U.S. court of law.”

“This case clearly shows that our collaborative efforts with law enforcement at every level continue to have an impact,” said HSI Special Agent in Charge Francis. “These efforts exhibit the combined resources of American law enforcement agencies’ resolve to ending this deadly epidemic.”

“Today’s indictments, which include charges related to the defendants’ smuggling drug profits in and out of the United States, are a victory for the American public and a defeat to drug traffickers everywhere,” said IRS-CI Special Agent in Charge Korner. “The special agents of IRS Criminal Investigation continue in their mission to disrupt the flow of ill-gotten gains that are the life-blood for these criminals.”

According to the indictment:

The Zhengs and others used numerous companies, including Global United Biotechnology, Golden Chemicals, Golden RC, Cambridge Chemicals, Wonda Science, and others, to manufacture and distribute hundreds of controlled substances, including fentanyl analogues such as carfentanil, acetyl fentanyl, furanyl fentanyl, and others. They created and maintained numerous websites to advertise and sell illegal drugs in more than 35 languages.

From 2008 to the present, the Zheng drug trafficking organization (Zheng DTO) engaged in this conspiracy from its base of operations in Shanghai. The organization claimed to ship “over 16 tonnes of chemicals every month” from its “own laboratory” and to “synthesize nearly any chemical on a bespoke basis in any quantity.”

The Zheng DTO touted its ability to create custom-ordered drugs and avoid detection from customs and law enforcement when shipping the drugs. The Zheng DTO explained in emails and online that it had “special ways” to “go through customs safely” in “USA, Russia, Europe,” and other locations around the world. If customs still managed to seize the parcels, the DTO promised it would “re-ship free.”

The Zheng DTO used co-conspirators in other countries, including the United States, to receive, repackage, and redistribute the drug shipments, thereby hiding their Chinese origin. For example, it used companies run by Massachusetts-based co-conspirator Bin Wang to smuggle drugs past customs agents in China and the United States. Wang then shipped the drugs to customers across the country.

Wang has pleaded guilty to his role in the conspiracy and is scheduled to be sentenced Nov. 13.

The Zheng DTO has sent millions of lethal doses of fentanyl analogues and other drugs linked to overdoses in the United States and around the world.

On Feb. 15, 2015, Akron, Ohio resident, Leroy Steele, emailed the Zheng DTO saying he “would like to purchase Acetyl fentanyl.” The Zheng DTO explained in its correspondence with Steele that it was “a professional acetyl fentanyl manufacturer in China” and that “a lot of U.S. and Europe customers purchase largely from us monthly.” The acetyl fentanyl that the Zheng DTO distributed to Steele resulted in the overdose deaths in Ohio of Thomas Rauh, 37, and Carrie Dobbins, 23, on or about March 21 and 28, 2015.

Steele was subsequently convicted of drug offenses and is currently serving a 20-year prison sentence.

Excerpt From: https://www.justice.gov/opa/pr/two-chinese-nationals-charged-operating-global-opioid-and-drug-manufacturing-conspiracy

Despite the deadly consequences of its actions, the Zheng DTO continued manufacturing and distributing drugs. In 2015, it advertised that it delivered "to all 50 USA states" and "worldwide to Australia, Europe, Asia and Africa."

When China would ban a synthetic narcotic, the Zheng DTO would use its chemical expertise to create an analogue of the drug with a slightly different chemical structure but the same or even more potent effect. In this manner, the DTO entirely bypassed China's restrictions on international narcotics sales.

Last month, the Zheng DTO agreed to manufacture adulterated cancer medication, creating counterfeit pills that replaced the active cancer-fighting ingredient with dangerous synthetic drugs. It also created and shipped counterfeit Adderall pills that were adulterated with deadly bath salts.

The Zheng DTO laundered its drug proceeds by using digital currency such as Bitcoin, transmitted drug proceeds into and out of bank accounts in China and Hong Kong, and bypassed currency restrictions and reporting requirements.

If convicted, the defendant's sentence will be determined by the Court after review of factors unique to this case, including the defendant's prior criminal record, if any, the defendant's role in the offense and the characteristics of the violation. In all cases, the sentence will not exceed the statutory maximum and in most cases it will be less than the maximum.

This investigation was conducted by the DEA, HSI, and IRS-CI. The following agencies assisted in the investigation: U.S. Postal Inspection Service, FBI, Organized Crime and Drug Enforcement Task Force, Special Operations Division, the Medway Drug Task Force, Akron Police Department, federal law enforcement on assignment at the U.S. Embassy in Beijing and federal law enforcement in the following districts: District of Massachusetts, Middle District of Florida, District of Colorado, District of Missouri, District of Minnesota and Western District of Texas. The Criminal Division's Office of International Affairs provided assistance. The Chinese Ministry of Public Security provided assistance during the course of the investigation.

Assistant U.S. Attorney Matthew J. Cronin of the Northern District of Ohio and Justice Department Criminal Division Trial Attorneys Adrienne Rose of the Narcotic and Dangerous Drug Section and Deputy Unit Chief Stephen Sola of the Money Laundering and Asset Recovery Section, are prosecuting the case.

An indictment is only a charge and is not evidence of guilt. A defendant is entitled to a fair trial in which it will be the government's burden to prove guilt beyond a reasonable doubt.

Attachment(s):
Download Zheng ECF filed indictment

Topic(s):
Drug Trafficking
Opioids

Component(s):
Criminal Division
Office of the Attorney General

Press Release Number:
18 - 1085

Updated August 31, 2018

SECTION 4: WEAPONS OF MASS DESTRUCTION

A. Michael Morell CIA Former Acting Director Article – Sept. 2017

The Opioid Crisis Becomes a National Security Threat

SEPTEMBER 3, 2017 | MICHAEL J. MORELL

U.S. President Donald Trump is expected to officially declare the American opioid epidemic a public health emergency Thursday, as part of an effort to combat a crisis that is killing an estimated 142 Americans a day. Reports, however, indicate he will not go as far as classifying it a national emergency, meaning no new funding will be allotted. But, as former Acting Director of the CIA and Cipher Brief Expert Michael Morell wrote last month, the threat the opioid crisis poses extends beyond public health: it is a national security threat. In light of the President's announcement Thursday, The Cipher Brief revisits Morell's analysis today.

On October 23, 2002, dozens of armed Chechen terrorists seized a Moscow theater and took some 850 people hostage. Because of the layout of the theater, the number of extremists, and the large amount of explosives in their possession, a SWAT-type raid was out of the question.

When two of the hostages were murdered almost three days into the crisis, the Russian government chose to pump an incapacitating agent into the theater via the air vents. But the agent was too toxic, and while all the extremists were killed, so too were some 130 of the hostages. The Russians have never publicly identified the particular chemical agent used, but it is widely believed to have been carfentanil.

Fast forward to June 2016, when authorities in Vancouver, Canada seized one kilogram of carfentanil. The agent was sent via mail from China to an address in Canada, and it was hidden in a package that was declared on a customs form to be printer accessories. It was the largest seizure of carfentanil to date.

Carfentanil, a synthetic opioid, is highly toxic. The drug is 10,000 times stronger than morphine and 5,000 times more potent than heroin. Only 20 micrograms, roughly the size of a grain of salt, can be fatal. The seizure in Vancouver was enough to kill 50 million people – every man, women, and child in Canada.

Carfentanil was developed in the 1970s as a tranquilizer for large animals – elephants and hippos. Dr. Rob Hilsenroth, the executive director of the American Association of Zoo Veterinarians said last year that carfentanil is so powerful that zoo officials wear protective gear "just a little bit short of a hazmat suit" when sedating animals because even one drop in a person's eye or nose can be fatal.

The extreme lethality of carfentanil has led most countries to classify it as a chemical weapon. It is banned from the battlefield under the Chemical Weapons Convention. Andrew Weber, President Barack Obama's Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Program, said it plainly and simply last year: "It's a weapon."

So, what is a chemical weapon doing on the streets of Canada – and the U.S.? Over the past year, drug dealers have learned that they can cut carfentanil into the heroin they sell to increase the "high" and to increase profits, as heroin is 15 times more expensive than carfentanil. In a public warning last fall, the Drug Enforcement Administration said "carfentanil is surfacing in more and more communities" and that it "has been linked to a significant number of overdose deaths in various parts of the country."

The drug is largely produced in China by thousands of small chemical firms and shipped either through Mexico and Canada to the United States or directly through the mail system, often after an order is placed online. It is also produced by drug cartels in Mexico (with key ingredients imported from China). China, working with the United States, is now regulating carfentanil production and export, but the large number of producers there means the problem has only been reduced, not resolved.

There are signs that the production of carfentanil could be moving here as well, particularly after the Chinese government's crack down. Some of equipment used to make carfentanil in China has been found in the United States. And the key ingredient to fentanyl – a less potent cousin of carfentanil – has also been discovered in the U.S., suggesting that fentanyl is being manufactured here. In May, federal agents in Massachusetts seized 50 kilograms of a key chemical used to make fentanyl.

The public discussion about – and the government focus on – carfentanil is all about the dangerous role it plays in the contemporary drug epidemic – with good reason. Drug overdoses, with a growing number caused by carfentanil, are now the leading cause of death from injury in the United States,

surpassing motor vehicle accidents, suicides, and homicides. Some police and paramedics have themselves overdosed after coming into contact with carfentanil.

But the drug also constitutes a significant threat to national security. It is a weapon of mass destruction.

Indeed, carfentanil is the perfect terrorist weapon. It is readily available in large quantities. It comes in several forms – including tablets, powder, and spray. It can be absorbed through the skin or through inhalation. It acts quickly. And, it is deadly. Peter Ostrovsky, a senior official of the Immigration and Customs Service, said last fall, "Could it be weaponized? Yeah, it could be weaponized." In short, a single terrorist attack using carfentanil could kill thousands of Americans.

And, there has been little focus on the drug as a terrorist weapon. In the Director of National Intelligence's 2017 Worldwide Threat hearings, the issue of synthetic opioids was treated as part of the international drug problem, not as a terrorism risk. No one from either the Obama or Trump administrations has spoken publicly about the threat. The same is true for Congress. There has been little to no work by think tanks or the media on the terrorism risks.

This needs to change. There needs to be an NSC-directed policy and strategy on getting our arms around the national security risks of carfentanil – including increasing the focus of the Intelligence Community as well as the law enforcement and homeland security communities. There needs to be a focus by Congress, in part, to oversee the work of the Executive Branch. There needs to be work done at the state and local level that is integrated with what is happening at the federal level. There is a great deal to do.

Both al Qaeda and ISIS have said they are interested in acquiring weapons of mass destruction and that they would use them if they acquired them. Osama bin Laden called it a religious duty to do so. ISIS has used chemical weapons on the battlefield in Iraq and Syria. And now such a weapon is easily available to them. It would be a terrible tragedy if foreign terrorists were to use the consequences of our own domestic drug problem against us – particularly when it is so easy to see what might be coming.

Excerpt From: https://www.thecipherbrief.com/column_article/opioid-crisis-becomes-national-security-threat

SECTION 4: WEAPONS OF MASS DESTRUCTION

B. Steven L. Shafer, MD Carfentanil as WMD Editorial – Jan. 2019

Can J Anesth/J Can Anesth (2019) 66:351–355
Exerpt From: https://doi.org/10.1007/s12630-019-01295-x

EDITORIALS

Carfentanil: a weapon of mass destruction

Steven L. Shafer, MD

Received: 12 December 2018 / Accepted: 12 December 2018 / Published online: 14 January 2019

Which would you choose as a weapon of mass destruction: a thermonuclear bomb or carfentanil?

Carfentanil[1,2]—it's not even close.

North Korea recently tested a thermonuclear bomb with a mass of approximately 300 kg[3] and an estimated yield of 250 kilotons.[4] If exploded over a major urban center, a thermonuclear bomb of this weight would kill approximately 2 million people[5]—i.e., about 10,000 people per kilogram of bomb mass. Fortunately, thermonuclear bombs are incredibly difficult to make. Delivered by intercontinental ballistic missiles, they invite likely obliteration of any country insane enough to launch a nuclear attack.

Now consider carfentanil. Carfentanil is about twice as potent as sufentanil,[6] and 20-fold more potent than fentanyl.[7] I confirmed potency of carfentanil with Dr. James Frost (James Frost, personal communication, September 14, 2018), who used [^{11}C]-carfentanil as an opioid ligand in human positron emitted tomography (PET) studies over the past three decades.[8-11] These PET studies initially used 0.1 $\mu g \cdot kg^{-1}$, but the investigators reduced the dose because of mild ventilatory depression. They found that 0.02 $\mu g \cdot kg^{-1}$ produced almost no discernable effect. This is compatible with a 20-fold potency relative to fentanyl where 2 $\mu g \cdot kg^{-1}$ of fentanyl would cause mild ventilatory depression, and 0.4 $\mu g \cdot kg^{-1}$ would have virtually no discernable effect. These updated carfentanil calculations contrast with what is frequently (and thus erroneously) stated as being 100-fold more potent than fentanyl.[12,13] Consistent with the early reports by Janssen[6] and Mather,[7] three decades of human PET studies with [^{11}C]-carfentanil studies suggest this was an exaggeration.

Nevertheless, an opioid 20-fold more potent than fentanyl represents a significant threat. If 1,000 μg of fentanyl would be a lethal dose in the absence of ventilatory support (anybody disagree?), an equivalent lethal dose of carfentanil would be just 50 μg. As documented by Leen and Juurlink in this issue of the *Journal*,[14] "the Royal Canadian Mounted Police seized 1 kg of carfentanil." One kilogram of carfentanil represents 20 million fatal 50 μg doses, enough to kill half the population of Canada. On a per kilogram basis, carfentanil is arguably 2000-fold deadlier than a thermonuclear bomb.

The Figure shows the death rates from synthetic opioids (primarily fentanyl) in the United States from 1999–2017.[15] I modeled the data as a linear increase from 1999–2010, with a superimposed logarithmic increase from 2010 onwards (black line). Logarithmic growth ends badly, as suggested by the extrapolation (red line) from 2017–2022. The model suggests synthetic opioid overdoses will double approximately every 14 months, reaching over a million deaths/year by 2022. This probably won't happen, because drug dealers will die of opioid overdose, the population of potential users will shrink, and society will find better ways of preventing addiction. Nevertheless, the trends show the grim potential for synthetic opioid overdoses.

Carfentanil has arrived, appearing throughout the United States,[16-19] Europe,[20,21] and Canada.[22] The Figure is based primarily on fentanyl deaths. Synthetic opioid deaths are likely to accelerate with carfentanil, which must be diluted 100 million-fold to create a sellable 10 μg dose. How many drug dealers have the pharmaceutical grade equipment to aliquot carfentanil with enough accuracy to not eventually kill their customers?

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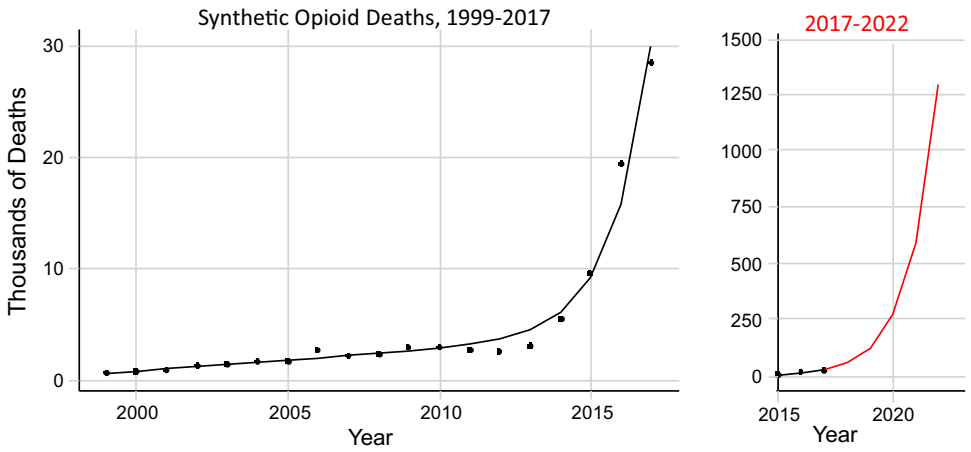

Figure The graph to the left shows synthetic opioid deaths in the United States from 1999–2017, based on data from the Centers for Disease Control.[15] The black line represents a superimposed additive fit of the data and superimposed exponential fit starting in 2010. The graph to the right shows the model extrapolation (red line) from 2017–2022

Le graphique de gauche présente le nombre de décès par opioïde de synthèse aux États-Unis de 1999 à 2017 d'après les données des Centers for Disease Control.[15] La ligne noire représente la superposition de l'addition des données et de l'ajustement exponentiel à partir de 2010. Le graphique de droite présente l'extrapolation du modèle (ligne rouge) pour les années 2017 à 2022

Trying to block the supply of carfentanil is a fool's errand. Paul Janssen clearly explained the synthesis of carfentanil, which is no more difficult than synthesizing fentanyl.[23] Decades ago I lost a close friend to fentanyl he synthesized in his desk drawer. This isn't rocket science. Domestic production will likely replace imported sources. Thousands of doses can be mailed in overnight express envelopes. Policing has failed miserably to stop the supply of heroin and fentanyl. Despite the success of the Royal Canadian Mounted Police busting dealers with staggering amounts of carfentanil,[24] there is no chance a police-focused approach will successfully interdict carfentanil supply.

To eliminate the threat to users, and to our society, we must eliminate the demand. This isn't news to anybody. What is different today is the urgency. Look back at the Figure. We can't wait a year or two. The opioid of mass destruction is here today.

We must understand the causes of substance use disorder.[25,26] We must provide individuals at risk with the social, medical, psychiatric, and spiritual support to address the root causes that place them at risk of opioid use. We need to treat opioid abuse disorder as a disease, which means providing the research and therapeutic investment we make in every other significant threat to public health (i.e., cancer, heart disease, diabetes). We need to think outside the box. Maybe we need to decriminalize drug use, so we can get addicts into treatment. Going further, maybe we should we create centres for supervised injection of pharmaceutical grade opioids, perhaps even offered in exchange for addicts agreeing to inpatient detoxification, thus treating their disorder while drying up the market for fentanyl and carfentanil?

Every life is an endless conveyor belt of stress, challenge, and pain. We must provide those at risk with tools to cope with life's challenges without resorting to opioids. Everyone needs support. Everyone needs security. Everyone needs something to live for. This will be expensive. This will never be "solved."

To policy makers who would rather buy military hardware, I'm sorry to share bad news, but opioid addiction, turbocharged with carfentanil, represents an existential threat. We must defeat it by combining sustained resources with steadfast dedication and political resolve.

The risk from nuclear weapons is no different. Nukes pose an ongoing, existential threat to our society. Recognizing this, we have committed vast sustained resources and political resolve to reduce the risk of nuclear annihilation. Carfentanil is arguably more dangerous than nuclear weapons. It has arrived; the death toll is rising; and pound for pound, it is orders of magnitude more dangerous than a thermonuclear bomb.

The time to act is now.

SECTION 4: WEAPONS OF MASS DESTRUCTION

C. Reuters WMD Jonathan Landay Statement – Aug. 2019

Fentanyl—Weapon of Mass Destruction

Jonathan Landay of Reuters reported August 2nd this year that there were 28,000 synthetic opioid-related overdose deaths in 2017, mostly from fentanyl related substances of which, he said, there are 1,400 known analogues. Nearly all the fentanyl related to those deaths was manufactured in and distributed into the United States from China. Though China promised in May of this year to put a stop to that manufacture and distribution and has passed legislation making such manufacture and distribution illegal, it has not enforced its laws and the manufacture and distribution continues. Federal statutes make anyone who uses, threatens, or attempts or conspires to use a weapon of mass destruction a crime punishable by life imprisonment and if death results, by death (See 18 U.S. Code §2332a). Fentanyl and its analogues (particularly carfentanil) are such weapons as defined in the statutes: They are toxins consisting of synthetic molecules capable of causing death or other biological malfunction in humans.

It is long past the time when those involved in their distribution should be charged under those federal statutes and, if death results, should face the death penalty. And, if China, a signatory to the Chemical Weapons Convention, does not immediately enforce its own laws and shut down the points of manufacture and distribution of these weapons of mass destruction into the United States, it should be considered a nation state conspiring to use weapons of mass destruction to injure and kill our citizens.

(See Landay, J. (2019, August 2). Trump accuses China's Xi of failing to halt fentanyl exports to US. Reuters. Retrieved from https://www.reuters.com/article/us-usa-china-fentanyl/trump-accuses-chinas-xi-of-failing-to-halt-fentanyl-exports-to-u-s-idUSKCN1US1WI)

SECTION 5: RELEVANT FENTANYL NEWS ARTICLES

A. Queens, NYC – Nov. 2019

Drug 100 times stronger than fentanyl becomes new concern

Posted: Nov 13, 2019 8:18 PM EST Updated: Nov 13, 2019 10:14 PM EST

A new synthetic drug that is 100 times stronger than fentanyl is causing concern as the battle against the deadly opioid crisis continues.

Carfentanil is a tranquilizer used for large mammals, and it's 10,000 times more potent than morphine. It has already proved deadly in Maryland and New Hampshire.

Just last week, the Queens DA announced the largest seizure of its kind of carfentanil. Officials say they seized 11 pounds of the drug when they busted a trafficking operation that stretched from California to New York. They also seized cocaine, fentanyl and heroin.

Steve Chassman, who is with the Long Island Council on Alcoholism and Drug Dependence, says officials have not yet seen the presence of carfentanil on Long Island.

"Eleven pounds of carfentanil, given the lethality of that opioid, could potentially take out all five boroughs and the population in it," says Chassman.

SECTION 5: RELEVANT FENTANYL NEWS ARTICLES

B. Dayton, OH – Oct. 2019

Fentanyl seized in drug bust equates to chemical warfare and a weapon of mass destruction, Ohio AG says

By **Allen Kim**, CNN
Updated 1:41 PM ET, Thu October 31, 2019

(CNN) Authorities have seized 20 kilograms of suspected fentanyl in a huge drug bust in Dayton, Ohio.

That is enough of the synthetic opioid "to kill the entire population of Ohio, many times over," said Homeland Security Investigations Special Agent in Charge Vance Callender.

"The quantity of fentanyl in this case amounts to chemical warfare and a weapon of mass destruction," Ohio Attorney General Dave Yost said in a statement.

"I applaud the work of our task force and our law enforcement partners -- this is an enormous amount of deadly drugs that will no longer be on our streets."

Agents also seized 1,500 grams of suspected methamphetamine, 500 grams of suspected heroin, three firearms and over $30,000 during last week's operation.

"These illegal drugs ruin lives, destroy families, fuels violence, drives up property crime, and wrecks neighborhoods. Anyone associated with it -- especially those who sell and traffic it -- are doing violence to people and causing harm in our communities," Montgomery County Sheriff Rob Streck said in a statement.

Montgomery County Coroner Dr. Kent Harshbarger said that fentanyl and methamphetamine are responsible for the "vast majority of overdose deaths" in the area, and believes that getting these drugs off the streets "will save lives."

A recent report from the US Centers for Disease Control and Prevention's National Center for Health Statistics found that fentanyl is the drug most commonly identified in fatal overdoses.

The multimillion-dollar seizure "clearly shows the enormity of the opioid problem in this area," FBI Acting Special Agent in Charge Joseph M. Deters said.

"Law enforcement will continue to work aggressively to address the illegal drug supply, but there is also a continuing need to address demand as well."

Three suspects have been arrested in connection with the investigation. They are facing charges of possession with intent to distribute 400 or more grams of fentanyl and felon in possession of a firearm.

CNN's Rebekah Riess contributed to this story.

SECTION 5: RELEVANT FENTANYL NEWS ARTICLES

C. U.S./Mexico Border – Aug. 2019

A display of fentanyl and meth seized by U.S. Customs and Border Protection officers at the Nogales Port of Entry at a press conference in Arizona on Jan. 31, 2019. (Mamta Popat/Arizona Daily Star via AP)

CHINA-US NEWS

Mexico Seizes 52,000 Pounds of Fentanyl From China

BY CHRISS STREET

August 29, 2019 Updated: August 29, 2019

The Mexican Navy in the Port of Cardenas discovered 52,000 pounds of fentanyl powder in a mismarked container from a Danish ship arriving from Shanghai, China.

The cargo manifest for the 40-foot ocean container stated that the powder content was 23,368 kilograms of inorganic calcium chloride, commonly used as an electrolyte in sports drinks, beverages, bottled water and as a non-sodium flavoring for pickles.

The Navy of Mexico intercepted the unloaded 40-foot container on Aug. 24, which originated from Shanghai, China and was bound for the Sinaloa Cartel home-base in Culiacan, 300 miles north of the port. According to local media, the Navy alerted customs authorities from the

nearby City of Lazaro Cardenas. Samples collected from plain bulk-bags were taken to a laboratory that confirmed the powder was fentanyl.

Mexican Customs seized 931 sacks of the substance weighing about 25.75 tons. The total weight of the fentanyl powder seizure is preliminary, with authorities still evaluating the purity of fentanyl seized. But if the seizure is confirmed as pharmaceutical-grade fentanyl, it could be pressed into tens of millions of tablets.

Fentanyl synthetic-opioid was hailed as a wonder drug 50 years ago when it was approved as a more effective treatment than drip morphine for cancer patients' pain. With four types of opioid receptors throughout the human body, pharmacological fentanyl is more effective attaching faster to all the receptors than the highest purity of illicit street-heroin.

Drug cartels favor fentanyl or fentanyl precursors imported from China because it can be diluted with fillers and marketed by street-dealers as cocaine, heroin or meth. Fentanyl can also be pressed into pills and sold on the street as oxycodone.

The National Institute on Drug Abuse warns that pharmaceutical-grade fentanyl is 50 to 100 times more potent than morphine. Fentanyl is extremely dangerous to handle because as little as 0.25 milligrams absorbed through the skin can be lethal.

According to the non-partisan U.S. Congressional Research Service dated Aug. 15, Mexico's transnational crime groups expanded their control of the opioids market, with U.S. overdose deaths rising to a record 72,000 in 2017.

The Port of Lazaro Cardenas fentanyl seizure follows the U.S. Drug Enforcement Administration (DEA) Aug. 15 announcement of cumulative year 2019 seizures of 1,138,288 illicitly created fentanyl pills by its Phoenix DEA Field Office in cooperation with Arizona law enforcement agencies. That is nearly triple the 380,000 fentanyl pills seized in year 2018, and over 56 times the 20,000 fentanyl pills seized in year 2016.

Former Sinaloa Cartel crime boss Joaquin Guzman Loera ("El Chapo") was extradited to the United States in January 2017. He was earlier convicted in Mexico for trafficking cocaine, heroin and fentanyl. But he successfully escaped from two Mexican prisons.

Guzman was sentenced by a U.S. district judge in July 2019 to a life term in a maximum-security U.S. prison, with the addition of 30 years, and ordered to pay $12.6 billion in forfeiture for being the principal leader of the Sinaloa Cartel and for 26 drug-related charges, including a murder conspiracy.

Breitbart News' Texas news bureau reported last week that the Mexican army, federal police, and investigative personnel with the attorney general's (FGR) office raided a Sinaloa Drug Cartel lab at a residence in the northwest section of Culiacan.

The two fentanyl cooks arrested were identified as Cuban nationals with street names of Abel "N" aka "El Cubano" and Carmen "N," Abel's wife. Investigators confiscated 2,500 pills and a press to mass-produce blue M-30s, sold illicitly as "Mexican Oxy."

Chriss Street is an expert in macroeconomics, technology, and national security. He has served as CEO of several companies and is an active writer with more than 1,500 publications. He also regularly provides strategy lectures to graduate students at top Southern California universities.

SECTION 5: RELEVANT FENTANYL NEWS ARTICLES

D. Phoenix, AZ – Jan. 2019

THE ASSOCIATED PRESS

The Latest: Border officials report biggest fentanyl bust

January 31, 2019

PHOENIX (AP) — The Latest on a record fentanyl seizure at the U.S.-Mexico border in Arizona (all times local):

11:30 a.m.

U.S. Customs and Border Protection officials say they have made their biggest fentanyl bust ever, capturing nearly 254 pounds (114 kilograms) of the deadly synthetic opioid in Arizona.

The Nogales CBP Port Director Michael Humphries said Thursday that the drug was seized Saturday from a tractor-trailer carrying produce from Mexico after it was stopped for inspection at the border crossing.

Agents also seized an additional 2.2 pounds (1 kilogram) of fentanyl pills and a large cache of methamphetamine.

The Mexican man driving the truck was arrested.

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9:15 a.m.

U.S. Customs and Border Protection officials in Arizona say they've made their biggest fentanyl bust ever.

The agency says it will provide details Thursday during a late morning news conference at the Mariposa border crossing in Nogales, Arizona.

Authorities say illicit fentanyl in recent years has become the biggest source of fatal overdoses in the United States.

Mexican traffickers are increasingly smuggling the drug into the United States, mostly hidden in northbound passenger vehicles crossing at ports of entry in the Nogales and San Diego areas.

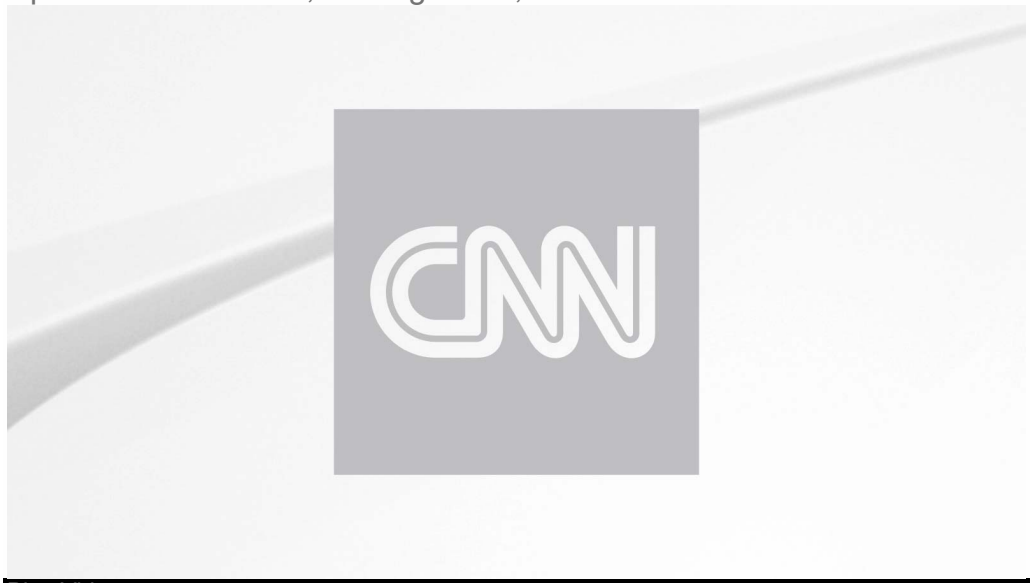
Law enforcement says the illicit version of the painkiller is now seen mostly as a white powder that can mixed with heroin for an extra kick and as blue pills that are counterfeits of prescription drugs like oxycodone.

SECTION 5: RELEVANT FENTANYL NEWS ARTICLES

E. Newport News, VA – Aug. 2019

Law enforcement seize enough fentanyl to kill 14 million people

By Lauren del Valle
Updated 4:18 PM ET, Fri August 30, 2019



Play Video
Why are opioids so addictive? 00:55

(CNN) Authorities arrested 35 people and seized enough fentanyl to kill roughly 14 million people in a three-state drug bust announced on Thursday by the US Justice Department.

The alleged drug trafficking ring is an example of fentanyl coming to the US from China, said US Attorney G. Zachary Terwilliger of the Eastern District of Virginia.

"The illicit fentanyl that's coming in, the vast majority is from China and a lot of it is coming in through the mails," he said at a press conference announcing the arrests.

At least one suspect ordered fentanyl from a vendor in Shanghai that was successfully mailed through US Postal Service to Newport News, Virginia, according to the indictment.

"The last thing we want is for the US Postal Service to become the nation's largest drug dealer and there are people way above my pay grade working on that, but absolutely it's about putting pressure on the Chinese," Terwilliger said.

A grand jury charged 39 co-conspirators with 106 counts for their involvement in an alleged drug trafficking conspiracy that began in March 2016, according to the indictment. The alleged suspects range

in age from 19 to 63 years old. One individual charged had been deported in 2014 and reentered the US illegally.

Officers seized 24 firearms, 30 kilograms of heroin, 5 kilograms of cocaine and more than $700,000 in cash along with 30 kilograms of fentanyl, according to a press release from the US attorney's office.

More than 120 law enforcement officers from 30 law enforcement agencies in Virginia, North Carolina and Texas executed the three-day targeted arrest operation dubbed Operation Cookout.

"We're not talking about $5 and $600 deals, we're talking hundreds of thousands of dollars, you know, $20,000 in the trunk of somebody's car in a gym bag behind a local restaurant," Terwilliger said.

The alleged co-conspirators purchased and received narcotics from suppliers in Mexico, California, and New York, then smuggled the narcotics to locations in the Hampton Roads area of Virginia, according to authorities.

The suspects transported the drugs using hidden traps in privately owned vehicles, semi-trailers, trucks, and recreational vehicles, authorities said.

The suspects attempted to thwart law enforcement surveillance using Facebook, and encrypted communications apps like FaceTime and WhatsApp, according to the indictment. Some suspects switched phones regularly and used prepaid cell phones that did not need a subscriber's name.

Four suspects named in the indictment remain at large: Jennifer Bing, Parris McMillan, Mark David and Travis Walters, Terwilliger said.

Excerpt From: https://www.cnn.com/2019/08/30/us/virginia-fentanyl-drug-bust/index.html

SECTION 5: RELEVANT FENTANYL NEWS ARTICLES

F. Orange Co., CA – Oct. 2019

18 pounds of fentanyl seized in Southern California — enough to make 4 million lethal doses

OCTOBER 20, 2019 / 3:53 PM / CBS/AP

Santa Ana, California — Southern California authorities say 18 pounds of fentanyl have been seized in Orange County. It's enough of the synthetic opioid to create four million lethal doses and has an estimated street value of more than $1.25 million. The Orange County Register reports the seizure last week yielded almost half the amount of fentanyl seized by authorities in the county during all of 2018 — a sign the drug is quickly growing into a substantial public threat.

Sheriff's officials say investigators served a search warrant and arrested Rudolph Garcia, 60, on multiple drug charges. It wasn't known if Garcia has an attorney.

Investigators also seized a semi-automatic handgun, heroin, methamphetamine and $71,000 in cash.

According to the California Department of Public Health, deaths in Orange County attributed to fentanyl have risen from 14 five years ago to 93 in 2018.

"The threat this extremely potent drug poses to our community is increasing exponentially, not subsiding," said Sheriff Don Barnes in a statement.

In 2017, there were 47,000 opioid deaths — that's more Americans than were killed in vehicle accidents or by firearms. Fentanyl is like rocket fuel in the sharp rise of the crisis. It is a painkiller invented in the 1960s and used to relieve the agony of advanced cancer. It is 50 times more potent than heroin.

Fentanyl has been linked to the deaths of musicians Mac Miller and Prince — and took the life of Angels pitcher Tyler Skaggs.

The total economic cost of the crisis, declared a federal public health emergency in 2017, reached at least $631 billion from 2015 to 2018, an analysis from the Society

of Actuaries (SOA) found. That is more than the gross domestic product of such countries as Belgium, Sweden and Taiwan.

Three drug distributors — AmerisourceBergen, Cardinal Health and McKesson Corporation — and two manufacturers — Johnson & Johnson and Teva — have reportedly offered a total of $50 billion to settle more than 2,000 lawsuits filed by towns, cities, counties and tribal governments and avoid going to trial.

Megan Cerullo contributed to this report.

First published on October 20, 2019 / 3:53 PM

SECTION 6: FACTS AND BACKGROUND

A. China Is Using Fentanyl as ‘Chemical Warfare,’ Experts Say – Sep. 2019

Firefighters help an overdose victim in Rockford, Illinois, on July 14, 2017. (Scott Olson/Getty Images)

CHINA

China Is Using Fentanyl as 'Chemical Warfare,' Experts Say

BY BOWEN XIAO

September 4, 2019 Updated: September 25, 2019

Behind the deadly opioid epidemic ravaging communities across the United States lies a carefully planned strategy by a hostile foreign power that experts describe as a "form of chemical warfare."

It involves the production and trafficking of fentanyl, a synthetic opioid that caused the deaths of more than 32,000 Americans in 2018 alone, and fentanyl-related substances.

China is the "largest source" of illicit fentanyl in the United States, a November 2018 report by the U.S.-China Economic and Security Review Commission stated. That same commission said that since its 2017 report, they found no "substantive curtailment" of fentanyl flows from China to the United States. They also noted that in "large part, these flows persist due to weak regulations governing pharmaceutical and chemical production in China."

President Donald Trump has continued to increase his crackdown on fentanyl—he recently ordered all U.S. carriers to "search for and refuse" international mail deliveries of

the synthetic opioid pain reliever. Trump specifically named FedEx, Amazon, UPS, and the U.S. Postal Service (USPS).
Jeff Nyquist, an author and researcher of Chinese and Russian strategy, said China is using fentanyl as a "very effective tool."

"You could call it a form of chemical warfare," Nyquist told The Epoch Times. "It opens up a number of opportunities for the penetration of the country, both in terms of laundering money and in terms of blackmail against those who participate in the trade and become corrupt like law enforcement, intelligence, and government officials."
China also uses the money generated by the importing of fentanyl to effectively "influence political parties," according to Nyquist.
"It opens doors for Chinese influence operations, Chinese People's Liberation Army, and intelligence services, so that they can get control of certain parts of the U.S.," he said.
In August, Trump called out Chinese leader Xi Jinping, accusing him of not doing enough to stop the flow of fentanyl, which enters the United States mostly via international mail.

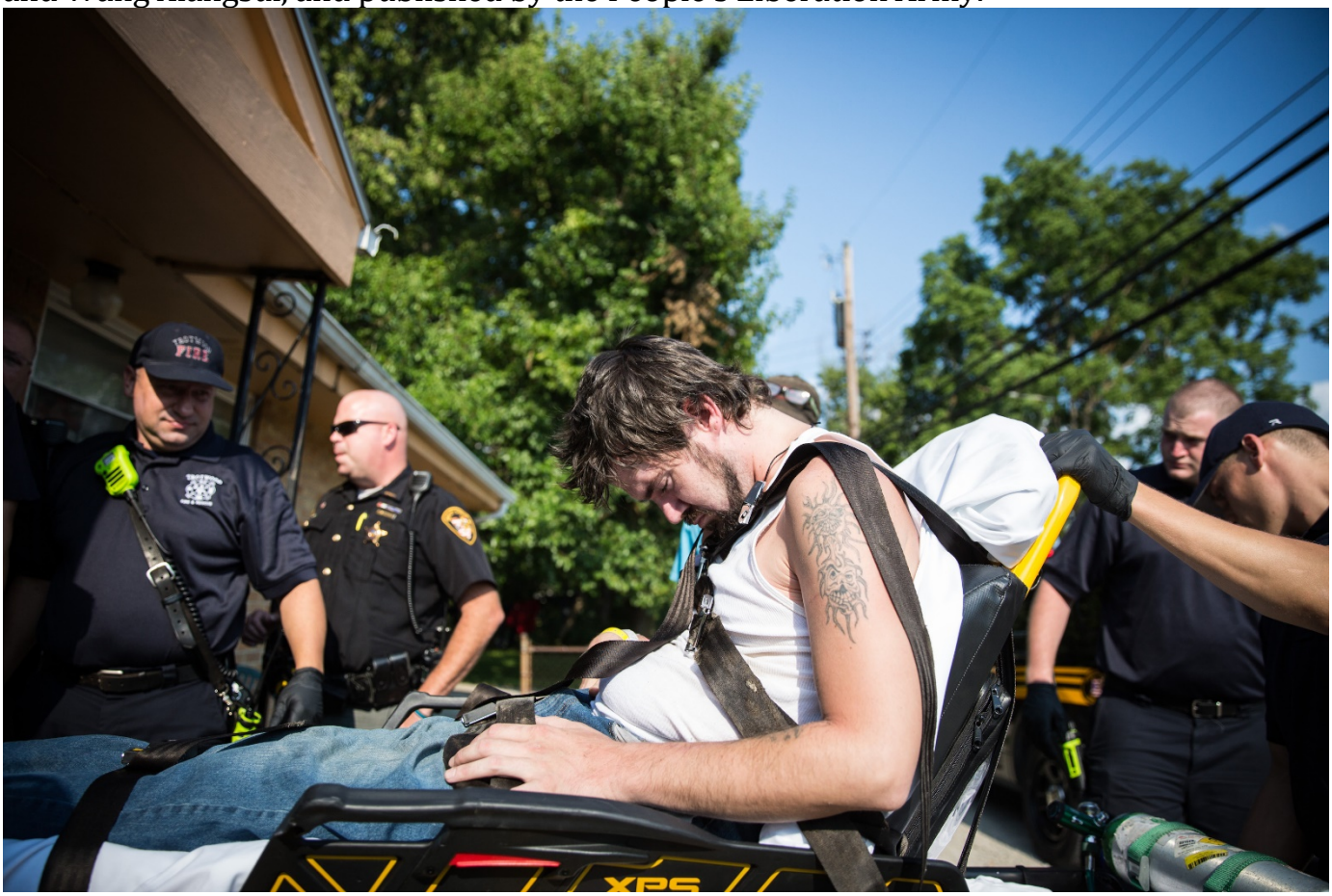
Liu Yuejin, vice commissioner of the China National Narcotics Control Commission, disputed Trump's criticism, telling reporters on Sept. 3 that they had started going after illicit fentanyl production, according to state-controlled media. China also denies that most of the illicit fentanyl entering the United States originates in China.
"President Xi said this would stop—it didn't," Trump said on Twitter on Aug. 23.
Overdose deaths from synthetic opioids such as fentanyl surged from around 29,000 in 2017 to more than 32,000 in 2018, according to data from the Centers for Disease Control and Prevention (CDC).
Not all opioid-related deaths in the United States can be blamed on China's fentanyl export policies, as some come from prescription overdoses, according to Dr. Robert J. Bunker, an adjunct research professor at the U.S. Army War College Strategic Studies Institute.

But Bunker told The Epoch Times that China is still "greatly contributing" to America's opioid epidemic. Bunker described how Beijing is using the trafficking of dangerous drugs to achieve its greater Communist Party goals.

"Contributing to a major health crisis in the U.S., while simultaneously profiting from it would in my mind give long-term CCP plans to establish an authoritarian Chinese global system as a challenge to Western liberal democracy," he said via email.

“[It’s] a win-win situation for the regime,” he continued. “In fact producing and sending fentanyl to the U.S., which could be considered a low-risk policy of ‘drug warfare,’ is very much in line with the means and methods advocated in the 1999 work ‘Unrestricted Warfare.’”

The book mentioned by Bunker is authored by two of China’s air force colonels, Qiao Liang, and Wang Xiangsui, and published by the People’s Liberation Army.



Local police, fire department, and deputy sheriffs help a man who is overdosing in the Drexel neighborhood of Dayton, Ohio, on Aug. 3, 2017. It’s unclear what he overdosed on. (Benjamin Chasteen/The Epoch Times)

Recent cases of fentanyl-related overdose and deaths are linked to “illegally made fentanyl,” the CDC has said. Fentanyl is 50 times more potent than heroin and 100 times more potent than morphine.

Fentanyl has been approved for treating severe pain for conditions such as late-stage cancer. It is prescribed by doctors typically through transdermal patches or lozenges. Fentanyl should only be prescribed by doctors who are experienced in treating pain in cancer patients, according to Medline Plus, an online site by the United States National Library of Medicine. It may become addictive, especially with prolonged use.

A USPS spokesman told The Epoch Times they are "aggressively working" to add in provisions from the STOP Act. The Synthetics Trafficking and Overdose Prevention legislation, signed in 2018 by Trump, aims to curb the flow of opioids sent through the mail while increasing coordination between USPS and the U.S. Customs and Border Protection (CBP).

USPS has notified China's postal operations that if any of their shipments don't contain Advance Electronic Data (AED), they "may be returned at any time," the spokesman said via email. CBP is also notifying air and ocean carriers to confirm that 100 percent of their postal shipment containers have AED before loading them onto their conveyance.

Recent Seizures

In August, law enforcement seized 30 kilograms (around 66 pounds) of fentanyl, among other narcotics as part of a major arrest operation over the course of three days. As a result, officers arrested 35 suspects for "conspiracy to distribute and possess with intent to distribute large amounts of heroin, fentanyl, cocaine, and cocaine base."
G. Zachary Terwilliger, U.S. Attorney for the Eastern District of Virginia, said in a statement that the amount of fentanyl seized was enough to "kill over 14 million people." One of the suspects in Virginia had ordered the fentanyl from a vendor in Shanghai and was receiving it at his residence through USPS, according to the indictment.

"The last thing we want is for the U.S. Postal Service to become the nation's largest drug dealer, and there are people way above my pay grade working on that, but absolutely, it's about putting pressure on the Chinese," Terwilliger said.

CBP Enforcement Statistics reveal that fiscal year seizures of illicit fentanyl spiked from about one kilogram (2.2 pounds) in 2013 to nearly 1,000 kilograms (2,200 pounds) in 2018. The number of law enforcement fentanyl seizures in the United States also vaulted from about 1,000 in 2013 to more than 59,000 in 2017.
Also, in August, the Mexican navy found 52,000 pounds of fentanyl powder in a container from a Danish ship that was coming from Shanghai. The navy intercepted the unloaded 40-foot container on Aug. 24, at the Port of Cardenas.

“There is clear evidence that fentanyl or fentanyl precursors, chemicals used to make fentanyl is coming from China,” Dr. Andrew Kolodny, co-director of Opioid Policy Research at the Heller School for Social Policy and Management, told The Epoch Times.

A fatal dose of fentanyl displayed next to a penny. (DEA)

Two commonly used fentanyl precursors are chemicals called NPP and 4-ANPP. In early 2017, journalist Ben Westhoff started researching the chemicals, finding many advertisements for them all over the internet from different companies. He later determined a majority of those companies were under a Chinese chemical company called Yuancheng, according to an excerpt from his upcoming book “Fentanyl, Inc.: How Rogue Chemists Are Creating the Deadliest Wave of the Opioid Epidemic,” an excerpt of which was published in The Atlantic.

Fentanyl Analogs

One of the concerns related to the production of illicit opioids is the creation of fentanyl analogs, products that are similar to fentanyl and also simple to make.

"You can very easily manipulate the molecule and create a new fentanyl-like product that hasn't been banned, that's not technically illegal," Kolodny told The Epoch Times. "Some of the manufacturers, the folks creating the drugs, are aware of that."

"We saw this with other synthetic drugs that are abused in the U.S., when law enforcement make the drug illegal or when they ban the molecule," he said. "In some cases, fentanyl analogs are even stronger than fentanyl. There's an analog called carfentanil, which is even more potent than fentanyl."

Carfentanil has a quantitative potency "approximately 10,000 times that of morphine and 100 times that of fentanyl," according to the National Center for Biotechnology Information.

Just one microgram is needed for carfentanil to affect a human. The drug is "one of the most potent opioids known" and is marketed under the trade name Wildnil "as a general anesthetic agent for large animals."

"Sometimes, it's hard for law enforcement to keep up with the chemist," Kolodny added.

A bill dubbed the SOFA Act or the "Stopping Overdoses of Fentanyl Analogues Act," has yet to pass Congress. The act was introduced in May by Republican senators and would give law enforcement "enhanced tools to combat the opioid epidemic and close a loophole in current law that makes it difficult to prosecute crimes involving some synthetic opioids."

Kolodny said pharmaceutical industries have been lobbying to stop any legislation meant to restrict fentanyl analogs "because these are products they are trying to bring to market."

In August, an Oklahoma judge ordered Johnson & Johnson to pay $572.1 million to the state for deceitfully marketing addictive opioids. The sum was less than what investors had expected, according to Reuters, which resulted in shares of the multinational corporation rising in value.

"We should be doing everything we can to keep fentanyl out of the country," Kolodny said. "We should be doing everything we can to ban fentanyl analogs."

Billion-Dollar Grants

As part of the Trump administration's latest efforts to combat the opioid crisis, the U.S. Department of Health and Human Services (HHS) on Sept. 4 announced nearly $2 billion in funding to states.

The funding would expand access to treatment and also support near-real-time data on the drug overdose crisis, according to a release.
In announcing the move, White House counsel Kellyanne Conway told reporters in a conference call that their administration is trying to interject the word "fentanyl" into the "everyday lexicon" as part of their efforts to increase awareness.

Data suggests that of the approximately 2 million Americans suffering from opioid use disorder, approximately 1.27 million of them are now receiving medication-assisted treatment, according to the HHS.

"Central to our effort to stop the flood of fentanyl and other illicit drugs is our unprecedented support for law enforcement and their interdiction efforts," she said.

Conway then brought up the DHS seizures of fentanyl in 2018, which totaled an equivalent of 1.2 billion lethal doses.

"Ladies and gentlemen, that is enough to have killed every American four times," she told reporters.

Just weeks ago, the White House released a series of private-sector advisories aimed to help businesses protect themselves and their supply chains from inadvertently trafficking fentanyl and synthetic opioids.
The four advisories aim to stem the production and sale of illicit fentanyl, fentanyl analogs, and other synthetic opioids. The advisories focus on the manufacturing, marketing, movement, and monetary aspects of illicit fentanyl.
In March 2018, the Interior Department created a task force aimed to specifically combat the crisis on tribal lands. Since then, the department has arrested more than 422 individuals and seized 4,000 pounds of illegal drugs worth $12 million on the street, including more than 35,000 fentanyl pills.

Conway, on the conference call, described the epidemic of pain relievers as an "opioid and fentanyl crisis."

SECTION 6: FACTS AND BACKGROUND

B. Opinion: Treat the fentanyl crisis like a poisoning outbreak – Sep. 2019

OPINION

Opinion: Treat the fentanyl crisis like a poisoning outbreak

Drug dealers add fentanyl, which is up to 100 times more potent than morphine, to heroin and counterfeit prescription medicines because it is much cheaper than heroin.
(Cliff Owen / Associated Press)

By BRYCE PARDO, JONATHAN P. CAULKINS AND BEAU KILMER
SEP. 1, 2019

The U.S. Centers for Disease Control and Prevention recently released drug overdose statistics for 2018, and they are shocking. Of the estimated 47,000 deaths from opioids last year, roughly two-thirds involved potent synthetic opioids, most of them fentanyl.

America's fentanyl problem is far deadlier than past crises with other illegal drugs. It also has a fundamentally different character. For most victims, fentanyl was not their drug of choice. Rather, they were poisoned by dealers who mixed it into baggies of heroin or pressed into fake-opioid tablets.

https://www.latimes.com/opinion/story/2019-08-30/fentanyl-opioids-overdose-deaths-treatment-sales

What is happening with fentanyl is unlike the trajectory of previous drug epidemics. Those typically involved "contagious" spread of initial use — primarily among those who may have been ignorant of the drug's risks. This was the case with prescription opioids, which were prescribed aggressively for chronic pain. Some individuals who sought pain treatment now have an opioid use disorder. So do others who got the pills from neighbors or friends for recreational use.

In the case of fentanyl, it is largely the suppliers — not users — who have embraced the drug because it is an ideal cost-cutting substitute. Synthetic opioids are produced in labs, so they are much cheaper than heroin — perhaps as much as 99% cheaper per dose after adjusting for potency. It's also easy to acquire. Anyone with an internet connection can purchase synthetic opioids that are most frequently made in China and delivered through the mail or by parcel service. Some Mexican crime syndicates trafficking heroin are also adding fentanyl to their portfolios.

Dealers add fentanyl, which is up to 100 times more potent than morphine, to heroin and counterfeit tablets made to look like genuine prescription medications. Adding a few milligrams gives a powerful kick; a few more turn deadly.

In short, most of the people exposed to — and dying from — fentanyl didn't think they were buying it and didn't want to use it. Rather than increasing the number of users, fentanyl is driving up the death rate.

This distinction is important: It means our traditional methods for responding to drug epidemics won't reverse the death toll. Usually government agencies focus on preventing experimentation, reducing accessibility of drugs, and treating individuals to suppress demand. These efforts remain valuable, but they won't immediately curb overdose deaths in places that are drowning in fentanyl.

It is better to conceptualize the fentanyl problem like a poisoning outbreak. The poison is out there — but how can exposure to it be minimized? How can its spread to other regions be contained?

Efforts to disrupt online purchases, for instance, might look very different than traditional drug interdiction efforts. It could include hacking or seizing websites that sell the drugs. Law enforcement might set up fake websites that offer fentanyl but never deliver it. The failure of some sites to fulfill orders might lead to distrust of web-based sales generally.

Eliminating the supply entirely seems impossible. But delaying fentanyl's expansion in the western United States by even a few years could save thousands of lives. Today, fentanyl deaths are concentrated in Appalachia, New England and parts of the Midwest. In 2017, if the

rest of the country had had a per capita rate of synthetic opioid-related deaths that was just half of New England's, some 9,000 more Americans would have died from synthetic opioids that year.

Policymakers should be expanding access to naloxone, the overdose reversal medication, but must also look beyond that. Some innovative approaches used in other countries include supervising consumption of illegal drugs so overdoses don't become fatal and providing heroin-assisted treatment for those who have not benefited from other therapies.

Yet, these still may not be enough. Vancouver, Canada, has embraced harm reduction interventions and still has a synthetic opioid-involved overdose death rate comparable to some of the hardest-hit places in the United States. This does not mean such interventions haven't saved lives. But it does suggest that it will take more than this to solve this problem.

New ideas — be they public policies, technologies or law enforcement strategies — are desperately needed. Continuing to treat fentanyl just like previous drug epidemics will likely be insufficient and may condemn thousands more to early deaths.

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SECTION 6: FACTS AND BACKGROUND

C. Council of Economic Advisors Full Cost of Opioid Crisis –Oct. 2019

The Full Cost of the Opioid Crisis: $2.5 Trillion Over Four Years

October 28, 2019

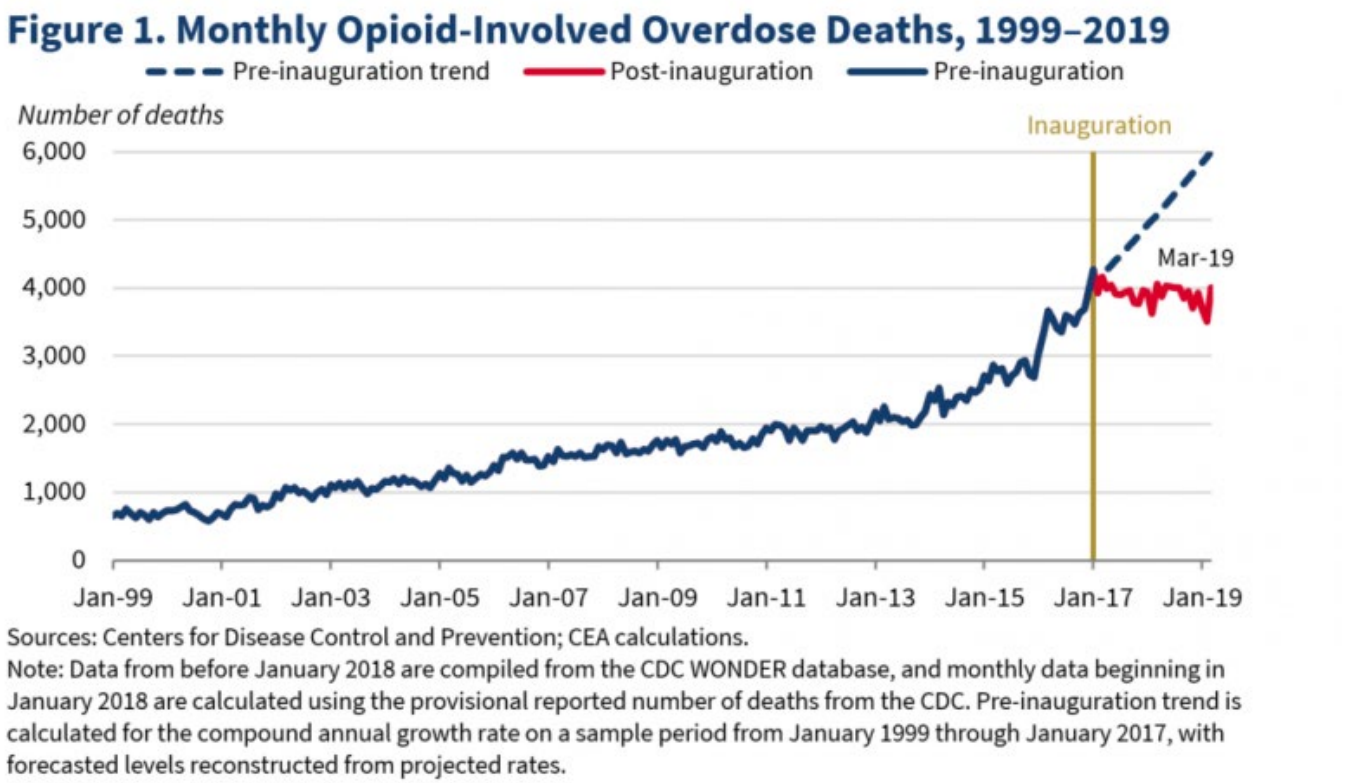
Council of Economic Advisers

October 26 marked National Prescription Drug Take Back Day, which provided Americans an opportunity to prevent drug misuse and theft by ridding their homes of potentially dangerous expired, unused, and unwanted prescription drugs. One of the most tangible examples of the dangers of misusing prescription drugs comes from the opioid crisis, which the Council of Economic Advisers (CEA) estimates cost $696 billion in 2018—or 3.4 percent of GDP—and more than $2.5 trillion for the four-year period from 2015 to 2018. These massive costs point to the nationwide economic destruction from America's very human "crisis next door."

In 2017, CEA published a report that measured the full cost of the opioid crisis by considering the value of lost lives, as well as increases in healthcare and substance abuse treatment costs, increases in criminal justice costs, and reductions in productivity. The updated estimates for 2018 were calculated using a similar methodology as the 2017 report.

CEA's cost estimates are more than three times higher than the findings from a recent Society of Actuaries study, because CEA accounts for the value of a statistical life (VSL). VSLs are commonly used by regulators for benefit-cost analyses and regulatory impact analyses. CEA prefers this comprehensive measure because the opioid crisis not only increases costs and lowers productivity throughout the economy, it also prematurely ends lives, which have value beyond their effect on economic output. (For more information on calculating VSL, see Section 2 of CEA's 2017 report.)

Overdose deaths involving opioids are coming down during the Trump Administration, reversing the upward trend that has persisted since at least 1999. As displayed in Figure 1, monthly opioid-involved overdose deaths stopped their steep upward nationwide growth starting in January 2017.



Sources: Centers for Disease Control and Prevention; CEA calculations.
Note: Data from before January 2018 are compiled from the CDC WONDER database, and monthly data beginning in January 2018 are calculated using the provisional reported number of deaths from the CDC. Pre-inauguration trend is calculated for the compound annual growth rate on a sample period from January 1999 through January 2017, with forecasted levels reconstructed from projected rates.

Compared to the previous trend for monthly opioid-related overdose deaths, CEA estimates that almost 30,000 lives were saved from January 2017 through March 2019 (the latest available provisional data). Had this trend continued its upward trajectory, CEA estimates that the cost of the opioid crisis would have been $326 billion higher between January 2017 and March 2019.

Just as the start and growth of the opioid crisis had many causes, ending the crisis requires many solutions. Increased funding for treatment, enhanced education about the dangers of opioids, and improved security to stop the flow of illicit drugs are all necessary tools to fight the crisis. Thankfully, last year Congress passed and President Trump signed the SUPPORT Act, which is the largest legislative package addressing a single drug crisis in U.S. history.

In fiscal years 2018 and 2019, $6 billion in new funding was secured to fight opioid abuse, including to expand access to medication-assisted treatment. According to estimates from the Department of Health and Human Services (HHS), from 2016 to 2019, the number of Americans receiving medication-assisted treatment rose 38 percent, from approximately 921,000 to 1.27 million.

Aided by better education for healthcare providers and patients, there has been a nearly one-third decline in the total amount of opioids prescribed since President Trump took office through June 2019, according to HHS estimates. Importantly, nearly 60 percent fewer young adults between the ages of 18 and 25 began using heroin in 2018 than in 2016.

Another necessary component to solving the opioid crisis is securing the border to limit deadly drugs from flowing into the United States. U.S. Customs and Border Protection (CBP) nationwide seizures of fentanyl are up 265 percent over the last three fiscal years. And CBP seized enough fentanyl in fiscal year 2019 to support 10,000 fentanyl users for more than 200 years, based on typical usage. In a promising sign that these

Excerpt From: https://www.whitehouse.gov/articles/full-cost-opioid-crisis-2-5-trillion-four-years/

coordinated efforts are working, as of March 2019, preliminary data show year-over-year drug overdose deaths in Pennsylvania and Ohio—two of the states hit hardest by the crisis—were down from their peak levels by more than 23 percent.

Even with the decrease in opioid-related deaths under President Trump, the $696 billion cost in 2018 shows that this crisis is far from over. To help the public and policymakers understand the economic causes and costs of the opioid crisis, CEA will continue publishing reports on this critically important policy priority.

(For further reading about the economic causes of the opioid crisis, see CEA's 2019 report The Role of Opioid Prices in the Evolving Opioid Crisis.)

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D. A.R. Thomas & R.M. Schwartz Publication At Risk Populations – Aug. 2019

Journal of Transportation Security
Excerpt From: https://doi.org/10.1007/s12198-019-00202-1

At-risk populations to unintentional and intentional fentanyl and fentanyl+ exposure

Andrew R. Thomas[1,2] · Robert M. Schwartz[1]

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Abstract

Rising exposure to **Fentanyl** and **Fentanyl+** is causing both intentional and unintentional effects. Besides the increasing number of overdoses and deaths from these toxic substances, there are risks for many others such as first responders in law enforcement, fire services, the medical sector. as well as those in transportation, and the public-at-large. **Fentanyl** and its derivatives (labeled here as **Fentanyl+**) can be over 20 times more profitable than heroin. The powder is cheap and easy to obtain on the Dark Web; and, is shipped via the United States Postal Service, or other delivery firms, almost undetected from China where it is produced. Mexico is also becoming a major producer and distributor of **Fentanyl** and its derivatives. In November 2017, the National Institute for Occupational Safety and Health – a division of the Centers for Disease Control- developed recommendations to address a wide area release of **Fentanyl+** as a weapon of terrorism. This paper seeks to articulate the threat posed by rising **Fentanyl** and **Fentanyl+** usage; and, identifies the potential at-risk populations from intentional and unintentional exposure to these dangerous chemicals.

Keywords Fentanyl · Fentanyl analogs · Fentanyl derivatives · Opioids · First responders · Supply chain risk. At risk populations · Supply chain security · Chemical weapons · Terrorism · Transportation security

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Introduction

This paper seeks to articulate the threat posed by rising **Fentanyl** and **Fentanyl+** usage; and, identifies the potential at-risk populations from intentional and unintentional exposure to these dangerous drugs. Real concerns about exposure to **Fentanyl** and its derivatives are spreading across multiple populations, as usage of these toxic substances spreads beyond producers, distributors, and consumers. The widespread introduction of highly addictive prescription pain pills like OxyContin in the late 1990's surged quickly across the USA. As the abuse of pain pills eventually metastasized into heroin for many users, death and destruction followed. In 1999, over 10,000 Americans died each year from a drug overdose. By 2016, that number had topped more than 64,000: something greater than all the names on the Vietnam Memorial in Washington D.C.[1]

The nature of the threat

According to Hoffer, the first goal of risk reduction of a potential threat is the need to clearly identify the nature of the threat. Then, once this is accomplished, priorities can be set; and, then, efforts designed to mitigate vulnerabilities can be undertaken.[2] Moreover, as threats to safety and security continuously emerge, planners must embrace the concept that the threat environment is evolving.[3] Continuously assessing the nature of threats in an environment is key to obtaining the maximum benefits from risk reduction.[4]

How did we get here?

Fentanyl and **Fentanyl+** (which include all analogs and derivatives of Fentanyl) are increasingly involved in opioid overdose deaths. Further, new variants of **Fentanyl+** continue to be identified. For example, Carfentanil, the most potent fentanyl analog detected so far in the United States, is intended for sedation of large animals and is estimated to have 10,000 times the potency of morphine.[5] Frank and Pollack[6] state that Fentanyl is being used by suppliers to "cut" heroin due to its low cost ($3500/kg compared to wholesale heroin at $65,000/kg) and potency when mixed with heroin or

[1] Erik Hoffer "The Context of Supply Chain Security" in Global Supply Chain Security Andrew R. Thomas Editor (Springer, 2016) p. 4
[2] Ibid.
[3] Frances L. Edwards and Daniel Goodrich "Supply Chain Security and the Need for Continuous Assessment" in Supply Chain Security: International Practices and Innovations in Moving Goods Safely and Efficiently Vol. 2 Andrew R. Thomas Editor (ABC CLIO, 2010) p.2.
[4] Ibid.
[5] Fogarty MF, Papsun DM, Logan BK. Analysis of fentanyl and 18 novel fentanyl analogs and metabolites by LC–MS-MS, and report of fatalities associated with methoxyacetylfentanyl and cyclopropylfentanyl. J Anal Toxicol 2018. Epub May 18, 2018.
[6] Frank, RG and Pollack, HA. Addressing the Fentanyl Threat to Public Health. N Engl J Med 2017; 376:605–607. https://www.nejm.org/doi/full/10.1056/NEJMp1615145 Accessed January 15, 2019

other street drug to maximize profits. They discuss that many users are unaware they are taking this drug and- with drug dealers having a lack of technical knowledge mixing drugs- it leads to a high overdose potential.

Understanding the scale of the challenge is not easy. The Centers for Disease Control funds 32 states and the District of Columbia (DC) to abstract detailed data on opioid overdose deaths from death certificates and medical examiner and coroner reports through the State Unintentional Drug Overdose Reporting System (SUDORS).[7] Twelve states began reporting in August 2017, and 20 states and DC will begin reporting in August 2018. CDC analyzed trends in overdose deaths testing positive for Carfentanil and other fentanyl analogs during July 2016–June 2017 in 10 SUDORS states (Kentucky, Maine, Massachusetts, New Hampshire, New Mexico, Ohio, Oklahoma, Rhode Island, West Virginia, and Wisconsin).[8] States abstract data on all substances (both opiods and nonopioids) that contributed to death, as well as all substances for which the decedent tested positive.

According to the SUDORS database, during July 2016–June 2017, among 11,045 opioid overdose deaths, 2275 (20.6%) decedents tested positive for generic **Fentanyl+**, and 1236 (11.2%) tested positive for Carfentanil. Fourteen different fentanyl analogs were detected.[9] Among overdose deaths with **Fentanyl**, the analogs were determined by medical examiners or coroners to have contributed to the death in >95% of deaths.

During the first half of 2017, the number of deaths by **Fentanyl+** detected (1511) nearly doubled, compared with the number during the second half of 2016 (764); deaths with Carfentanil detected increased 94%, from 421 to 815. The proportions of deaths with any **Fentanyl+** or with Carfentanil detected nearly doubled during this period.

The emergence of the threat in recent years has been mirrored in rapid changes to CDC policy. In 2015, CDC issued a nationwide public health advisory about increases in fentanyl-related overdose deaths in multiple states.[10] A year later, in 2016, the CDC

[7] SUDORS estimates of opioid-involved overdose deaths might differ from those of the National Vital Statistics System because SUDORS uses preliminary death certificate data and collects additional information from medical examiner and coroner reports, which are abstracted within 8 months of death. In SUDORS, an opioid-involved overdose death either was identified through review of the medical examiner/coroner report or had International Classification of Disease, Tenth Revision (ICD-10) underlying cause-of-death codes X40–44 (unintentional) or Y10–Y14 (undetermined) and multiple cause-of-death codes of T40.0, T40.1, T40.2, T40.3, T40.4, or T40.6 on the death certificate. Data for this report were downloaded on April 25, 2018, and might differ from reports using earlier data.

[8] Data for the period from July 2016 through June 2017 were collected only by the 12 states that began reporting in August 2017 (Kentucky, Maine, Massachusetts, Missouri, New Hampshire, New Mexico, Ohio, Oklahoma, Pennsylvania, Rhode Island, West Virginia, and Wisconsin). At the time of reporting, data for Missouri and Pennsylvania were not complete and were therefore excluded.

[9] Fentanyl analogs detected in at least one death: 3-methylfentanyl, 4-fluorobutyrfentanyl, 4-fluorofentanyl, 4-fluoroisobutyrfentanyl, acetylfentanyl, acrylfentanyl, butyrylfentanyl, Carfentanil, cyclopropylfentanyl, cyclopentylfentanyl, furanylethylfentanyl, furanylfentanyl, isobutyrylfentanyl, and tetrahydrofuranylfentanyl. Decedents might have tested positive for more than one analog, as well as for other opioid and nonopioid substances. Multiple substances could have been used separately or mixed together, either with or without the decedents' knowledge.

[10] CDC. Increases in fentanyl drug confiscations and fentanyl-related overdose fatalities. HAN no. 384. Atlanta, GA: US Department of Health and Human Services, CDC; 2015. https://emergency.cdc.gov/han/han00384.asp accessed August 8, 2018

issued an update to that advisory to warn about increasing availability of fentanyl and fentanyl-related substances being pressed into counterfeit pills, and the potential for broad distribution across the United States.[11] In response to findings in SUDORS data, in 2018, CDC issued a second update highlighting the emerging prevalence of fentanyl analogs contributing to opioid overdose deaths.[12]

Dangers beyond producers, distributors, and consumers

The nature of **Fentanyl** and **Fentanyl +** make these drugs a broader immediate threat to the greater society; not just to those groups and individuals that produce, distribute, and consume them. Beyond the already tragic consequences to those who use these drugs, there is emerging and broader threat to tens of millions of Americans from the increased use of **Fentanyl** and **Fentanyl +** by others.

Fentanyl is broadly categorized as an Incapacitating Agent by the Center for Disease Control.[13] These types of agents can alter states of consciousness along with making thinking less clear. There are similarities to morphine and heroin. Yet, according to the CDC, **Fentanyl** is estimated to be 80 times (8000%) more potent than OxyContin; and, hundreds of times (20,000 + %) stronger than heroin.[14]

The class is known as "rapid-acting synthetic opioids", commonly used for pain relief for those with chronic pain or after surgery. According to the U.S. Drug Enforcement Administration, these are Schedule II prescription drugs, which have a "high potential for abuse, with use potentially leading to severe psychological or physical dependence." While not approved for medical use, they can be very dangerous and potentially fatal as it "acts quickly to depress the central nervous system and respiratory function." Other drugs in the **Fentanyl** analogs that are included in the **Fentanyl +** category are acetylfentanyl, butyrfentanyl, Carfentanil, alfentanil, sufentanil, and remidfentanil.[15]

Its chemical formula is $C_{22}H_{28}N_2O$. **Fentanyl** appears as a crystal or crystalline powder. It has several means of dissemination, which include aerosol (indoor and outdoor air), water, food, and agricultural contamination. There are various methods of exposure to the body such as inhalation, oral exposure or ingestion, or skin contact."[16]

Fentanyl + is similar to **Fentanyl** in its properties and the means of dissemination. It is, however, much more powerful. For reference, exposure to two milligrams of pure **Fentanyl**, which is about the size of about four grains of table salt, is enough to kill an

[11] CDC. Influx of fentanyl-laced counterfeit pills and toxic fentanyl-related compounds further increases risk of fentanyl-related overdose and fatalities. HAN no. 395. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. https://emergency.cdc.gov/han/han00395.asp accessed August 8, 2018

[12] CDC. Rising numbers of deaths involving fentanyl and fentanyl analogs deaths, including Carfentanil, and increased usage and mixing with non-opioids. HAN no. 413. Atlanta, GA: US Department of Health and Human Services, CDC; 2018. https://emergency.cdc.gov/han/han00413.asp

[13] Centers for Disease Control and Prevention, Emergency Preparedness and Response. "Incapacitating Agents", https://emergency.cdc.gov/agent/incapacitating/index.asp accessed June 24, 2018

[14] Ibid.

[15] Centers for Disease Control and Prevention, NIOSH, "Fentanyl", https://www.cdc.gov/niosh/topics/fentanyl/default.html accessed June 24, 2018

[16] Centers for Disease Control and Prevention, NIOSH, "Fentanyl: Incapacitating Agent", https://www.cdc.gov/niosh/ershdb/emergencyresponsecard_29750022.html accessed June 24, 2018

average adult. One milligram of **Fentanyl**+− or roughly the size of two grains of salt-would end an adult's life.

Training is critical to assist in the preparedness, response, and mitigation of potential exposure to these highly toxic substances. Knowledge is a key to help make responders safer in dangerous environments. Some of the items required include recognition of the suspected drugs, when to use Personal Protective Equipment (PPE), and adjusting PPE requirements based on field conditions. Other training items include knowledge of various means of exposure, recognizing symptoms, and when to call for medical assistance[6].

An interview with an officer in a suburban Washington, D.C. county sheriff's department mentioned items for preparedness such as education and training to recognize **Fentanyl** basics (how to recognize the substance, treat individuals), know that when dealing with heroin it is probably **Fentanyl** or a derivative. Naloxone administration knowledge is required and all patrol cars are equipped with this drug.

The range of preparedness for exposure to **Fentanyl** and **Fentanyl**+ are a daily hazard for first responders simply doing their normal jobs and activities. Deadly exposure can occur through inhalation, ingestion, mucous membranes, or via an open cut. Contact on the skin is another form. According to the CDC, there are no established occupational exposure limits for these drugs.[17]

Emergency Medical Services are regularly called to deal with a patient that has a suspected overdose. **Fentanyl** or **Fentanyl**+ could be near the individual, on their clothing, or their person, creating the potential for exposure for the first responders. These risks could also apply to firefighters. Firefighters face the vulnerability of going into a burning structure with the presence of these drugs on the scene of a vehicle incident. Hazardous material teams could also be potentially exposed to these chemicals.

Every day responsibilities of law enforcement officers expose them to **Fentanyl** or **Fentanyl**+ substances. These could be from traffic stops, vehicle accidents, apprehending a suspect, a drug raid, or an overdose call. In addition, forensic personnel from investigations to handling evidence could be subject to exposure. Besides human law enforcement officers, there are risks to working dogs such as K-9 officers (this risk is also to their handlers).

There are some common-sense safe operating procedures that responders should follow for their safety. According to NIOSH[6], responders should be cautious around locations with **Fentanyl** or **Fentanyl**+. No food, beverage, smoking, or bathroom use should be in these areas. Mucus membranes such as eyes, mouth, and noses should not be touched after potential contact with suspected substances. Hand washing with soap and water should be completed as soon as possible to avoid potential contamination. "Do not use hand sanitizers or bleach solutions to clean contaminated skin." Another method to reduce contamination is to avoid anything that could aerosolize the drugs.

Besides education and training, the first line of defense is Naloxone or commonly known as *Narcan* or *Evzio*. Naloxone's purpose is to rapidly reverse an overdose from an opioid. For those suffering an overdose, their breathing is either reduced or stopped.

[17] Centers for Disease Control and Prevention, NIOSH, "Preventing Occupational Exposure to Emergency Responders", https://www.cdc.gov/niosh/topics/fentanyl/risk.html, Accessed July 1, 2018

Naloxone restores normal respiration by binding to the opioid receptors and blocks the effects of the opioid drug.[18]

There are three main methods of administering Naloxone. These methods are injectable (Naloxone), auto-injectable (Evzio), and a Prepackaged Nasal Spray (Narcan). Trained responders along with medical professionals such as paramedics and emergency room doctors usually administer injectables. Depending on the state, others can use the auto-injectable or nasal spray. Even though Naloxone is a prescription drug, some states and pharmacies allow the distribution without a prescription.

Once a person has been treated with Naloxone, the individual should be observed until professional medical responders arrive on the scene. Medical personnel should observe the patient for a minimum of two hours after the last dose to be sure respiration is normal with no stopping or slowing of breathing.

Normal latex gloves are not sufficient and officers carry the thicker blue gloves. Law enforcement works with the fire departments and HazMat teams for the larger quantities of the drug. Forensic collection has officers gowned up in PPEs and respirators. Evidence is now with a HEPA filter drug-processing table that is contained and filtered in the stations.[19] Keys to mitigation are training and knowledge. Every vehicle contains Narcan, gloves, and masks. There is one person per shift and per squad that is designated for collecting evidence wearing the proper PPEs.

Healthcare personnel could be exposed in their workplace dealing with patients, personal items of patients such as clothing, and even those with incidental contact such as signing paperwork. As with the responders, exposure could come from a powder, liquid, or tablet and personnel need to be aware of the symptoms. EMS workers should give advance notice to those at facilities for proper coordination and safety. There are other common-sense practices described by NIOSH.[20]

The United States Surgeon General advised more individuals to carry Naloxone for those at risk. Besides responders, this includes friends, family, and those who are addicted to opioids.[21] This message was in a public health advisory distributed April 2018. Their slogan is "Be Prepared. Get Naloxone. Save a Life."[22]

Weaponizing fentanyl or fentanyl+

In November 2017, the National Institute for Occupational Safety and Health – a division of the Centers for Disease Control- developed recommendations to address a

[18] National Institutes of Health, National Institute on Drug Abuse, "Opioid Overdose Reversal with Naloxone (Narcan, Evzio)" https://www.drugabuse.gov/related-topics/opioid-overdose-reversal-naloxone-narcan-evzio Accessed January 29, 2019

[19] Holter, Lt. J., Charles County Sheriff's Department, Interview, July 1, 2018

[20] Centers for Disease Control and Prevention, NIOSH, "Preventing Occupational Exposure to Healthcare Personnel in Hospital and Clinic Settings" https://www.cdc.gov/niosh/topics/fentanyl/healthcareprevention.html, Accessed July 1, 2018

[21] U.S. Surgeon General, Department of Health and Human Services, "Opioid Overdose Protection" https://www.surgeongeneral.gov/priorities/opioid-overdose-prevention/index.html Accessed August 8, 2018.

[22] U.S. Surgeon General, Department of Health and Human Services, "https://www.surgeongeneral.gov/priorities/opioid-overdose-prevention/naloxone-advisory.html Accessed August 9, 2018.

wide area release of **Fentanyl +** as a weapon of terrorism.[23] The threat of an intentional, anthropogenic event weaponizing **Fentanyl** or **Fentanyl +** is a distinct possibility. A suspected incident of exposure to responders occurred in Harris County Houston, Texas in late June 2018. It was reported that around 12 vehicles from the Sheriff's Office had paper flyers on the windshield that were laced with **Fentanyl**. A sergeant was hospitalized with exposure to the drug even after receiving two doses of Naloxone on the scene.[24] **Fentanyl +** derivative was used by the Russian military in a Moscow theater in 2002 where terrorists were holding hostages (127 of the hostages perished). With the ease of dissemination, the general population faces the rising possibility of these chemicals being used as a weapon of mass destruction.

At-risk populations

As more and more ***Fentanyl*** and ***Fentanyl +*** are being produced, transported, distributed and consumed, the risk of exposure to ever larger and more numerous populations grows exponentially. Table 1 attempts to illustrate and identify the at-risk populations to unintentional and intentional ***Fentanyl*** and ***Fentanyl +*** exposure.

Given what we know today about exposure to **Fentanyl** and **Fentanyl+**, there appears to be (6) distinctive at-risk populations. They include:

First Responders with NALOXONE- these are individuals who, as part of their job, will quickly respond to a suspected **Fentanyl** or **Fentanyl +** situation; and, would likely be equipped with NALOXLONE or similar solutions.

First Responders without NALOXONE – these are individuals who- by the nature of their profession- are likely to encounter a **Fentanyl** or **Fentanyl +** situation with little or no training on how to respond; and, with little chance of NALOXONE or similar solutions being available to them.

Direct Interactors with NALOXONE- these are individuals who are prepared for a **Fentanyl** or **Fentanyl +** incident; and, would likely have NALOXONE or similar solutions available on the scene.

Direct Interactors without NALOXONE – these are individuals because of the nature of their job are likely to directly encounter a **Fentanyl** or **Fentanyl +** situation; possess little or no understanding of what to do; and, would likely have no NALOXONE or similar solutions available.

Indirect Interactors without NALOXONE – these are individuals or groups that possess little no or understanding of **Fentanyl** or **Fentanyl +** and yet can be exposed to it and unknowingly suffer the effects. They are highly unlikely to have NALOXONE or similar solutions available.

General Populations at Risk – these are individuals or large groups in particular settings who would be exposed to an intentional dispersion of **Fentanyl +** .

[23] In November 2017, the National Institute for Occupational Safety and Health – a division of the Centers for Disease Control- developed recommendations to address a wide area release of **Fentanyl +** as a weapon of terrorism. They can be found here https://www.cdc.gov/niosh/ershdb/emergencyresponsecard_29750022.html

[24] Jordan, Jay R. Houston Chronicle, "Fentanyl-laced flyers placed on Harris County sheriff's fleet vehicles in East Houston" https://www.chron.com/news/houston-texas/houston/article/Fentanyl-flyers-Harris-County-sheriff-vehicles-13027828.php, Accessed June 26, 2018.

Table 1 At-risk populations to fentanyl or fentanyl+ exposure

First responders likely w/ naloxone	First responders likely w/out naloxone	Direct interactors likely w/out naloxone
• Police • Fire / EMS • Private ambulance services • Medical transport • Emergency room personnel • Teachers • School nurses • Prison staff	• Airline flight crews • Public transport personnel (buses, trains) • Supply chain personnel • Hotel / motel staff • Librarians • Restaurant staff • Good Samaritans	• Children's services • Parole / Probation Officers • Coroner's office • Cargo inspectors
Direct interactors likely w/out naloxone (Con't.)		Indirect interactors likely w/out naloxone: transport
• Utility workers • Home health care • Home food delivery • Home inspectors • Hotel / motel staff • Good Samaritans	First responders and interactors	• Cargo transport (air, truck, rail) • Cargo handling (warehouse) • Cargo delivery (UPS, FedEx, USPS)
Indirect interactors likely w/out naloxone: transport (con.t)	Indirect interactors likely w/out naloxone: cleaning services	General populations at risk to an intentional dispersion of fentanyl+
• Tow-truck drivers • Rental car agencies • Car hire services (Uber, Lyft, taxi)	• Public restrooms • Hotel / motel • Homes • Airlines • Public transport • Rental cars	• Mass transit • Commercial aviation • Mass gatherings

While first responders are generally considered the primary constituencies facing the greatest threat from **Fentanyl** and **Fentanyl+** exposure, ever-larger numbers of at risk populations are emerging as the situation around the country worsens. Distressingly, many of these populations do not possess the same knowledge, training, and resources to deal with possible exposure that first responders do. Yet, as consumption patterns continue, more and more of the non-using population is coming into direct or indirect contact with these deadly substances.

Unintentional and intentional dispersion within transport networks

The unintentional dispersion of **Fentanyl** and **Fentanyl+** within the transportation sector is one of the most likely scenarios for a cascading mass casualty event. For example, a package unknowingly containing **Fentanyl** or **Fentanyl+** is opened causing exposure to personnel. In Fiscal Year (FY) 2017, the U.S. Immigration and Customs Enforcement (ICE) seized nearly 2400 pounds of **Fentanyl** and **Fentanyl+** that was being shipped into the country.[25] All of it was found on traditional transport networks. According to ICE, the primary source of these drugs is China. Mass

[25] U.S. Department of Homeland Security https://www.ice.gov/features/opioid-crisis Accessed August 18, 2018

quantities of **Fentanyl** and **Fentanyl+** are being produced in China and brought illegally to the United States- often through Mexico- via supply chain routes such as the US postal service, other service delivery firms, as well as ocean shipping containers and air cargo. Land routes such as border crossing between the U.S. and Mexico are also frequently used. ICE admits that even given their best efforts, only a small fraction of the drugs shipped in to the U.S. from abroad are ever identified and seized.[26] The sheer volume of drugs being shipped raises the likelihood of exposure to personnel working within the transport sector.

Mass transit, supply chain networks, and commercial air transport are some of the highest risk areas where the intentional dispersion of **Fentanyl** and **Fentanyl+** can result in large casualty incidents. As an Incapacitating Agent, Fentanyl can be disbursed easily to large number of individuals in various forms such as an aerosol, contaminate food and water supplies, and agricultural product.

In 2018, during routine surveillance at the Amtrak train station in Omaha, Nebraska, a special agent with the Drug Enforcement Administration noticed a black suitcase, without an ID tag, tucked in the far back of the self-storage luggage area. Inside were 15 vacuum-sealed bundles of white powder of **Fentanyl+**. Each weighed 1.2 k, or roughly 2.7 pounds. It had an estimated street value of $15 million. At the time, the U.S. Attorney's office called it the largest fentanyl seizure in Nebraska- and one of the largest in the nation.[27]

Also in 2018, U.S. Customs and Border Protection agents in Philadelphia discovered 110 pounds of **Fentanyl+** inside barrels of iron oxide being shipped from China with a street value of about $1.7 million, according to the agency. The cargo was flown into Chicago and then shipped by "truck in-bond" through to Philadelphia.[28]

As consumption continues to rise, travelers who have overdosed and contain residue on their person raise the threat level for personnel and fellow travelers as they continue on their journeys. The risks of mass casualty events on mass transit systems, commercial airlines, and other networks become greater. Moreover, concerns over a chemical weapons via transportation networks attack remain viable.

A need for further research and countermeasures

This paper has laid out in broad strokes the nature of the threat and just some of challenges emerging from **Fentanyl** and **Fentanyl+** exposure. Further research is needed to assist each at risk population so that it can recognize and manage this emerging threat. In addition, as exposure levels rise potentially within each of these

[26] Ibid.

[27] Lincoln Star Journal, "California man sentenced for 15 k of fentanyl seized at Omaha train station", June 15, 2018, https://journalstar.com/news/local/911/california-man-sentenced-for-kilos-of-fentanyl-seized-at-omaha/article_d791a8c4-fc80-51a1-8697-d8cb3a7caf91.html#1, accessed January 28, 2019

[28] Chris Palmer, "Feds say 110 pounds of fentanyl valued at $1.7 M seized in Philly", *Philadelphia Inquirer*, July 2, 2018, http://www.philly.com/philly/news/crime/fentanyl-seizure-philadelphia-customs-border-protection-110-pounds-opioid-epidemic-china-20180702.html
accessed January 28, 2019

at-risk populations, the scope of the problem will require new technologies and countermeasures. While Naloxone and other solutions remains the first line of defense in almost every circumstance, the changing nature of the threat mandates development and deployment of other countermeasures.

SECTION 6: FACTS AND BACKGROUND

E. EPA Fentanyl Fact Sheet – May 2018

The Fentanyl Fact Sheet was developed for U.S. Environmental Protection Agency (EPA) Federal On-Scene Coordinators (OSC) who may respond with, or provide technical advice to, local first responders who may encounter environmental contamination from fentanyl class compounds (fentanyl analogs). This fact sheet provides information regarding characteristics of fentanyl and fentanyl analogs; the physical properties of fentanyl, fentanyl citrate, carfentanil, 3-methylfentanyl and α-methylfentanyl; potential exposure pathways; provisional advisory levels (PAL) and industry occupational exposure limits (OEL); opioid relative potency, equianalgesic dose and estimated lethal dose; personal safety; personal protective equipment (PPE); field detection; sampling; analysis; decontamination/cleanup; personnel decontamination; waste management; and technical references. EPA does not assume responsibility for errors, misinterpretation of technical information, injury or illness as a result of use or misuse of this fact sheet. Technical content may change without prior notice. Non-EPA personnel are encouraged to develop health and safety guidance for their own personnel. Mention of trade names or services does not convey official EPA approval or endorsement. ***For additional information regarding this fact sheet, contact the EPA Chemical, Biological, Radiological and Nuclear (CBRN) Consequence Management Advisory Division (CMAD) via the EPA Emergency Operations Center (HQ-EOC) at 202-564-3850 (24-hr access).***

CHARACTERISTICS OF FENTANYL AND FENTANYL ANALOGS

Classification: A synthetic opioid; Schedule II, Controlled Substances Act.

Fentanyl, Salts and Analogs: Fentanyl, Fentanyl citrate, Carfentanil, 3-Methylfentanyl, α-Methylfentanyl and numerous others.

Synonyms: 1-Phenethyl-4-(N-phenylpropionamido)piperidine; 1-Phenethyl-4-(phenylpropionylamino)piperidine; 1-Phenethyl-4-N-propionylanilinopiperidine; DEA# 9801; Fentanest; Fentanil; Fentanila (Spanish); Fentanylum (Latin); Leptanal; N-(1-Phenethyl-4-piperidinyl)-N-phenylpropionamide hydrochloride; N-(1-phenethyl-4-piperidyl)-, hydrochloride; N-(1-Phenethyl-4-piperidyl)propionanilide; N-Phenethyl-4-(N-propionylanilino)piperidine; N-Phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]propanamide hydrochloride; N-Phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]propanamide; Pentanyl; Phentanyl; Propanamide, N-phenyl-N-(1-(2-phenylethyl)-4-piperidinyl); R4263; Sentonil.[1]

Description: Odorless, solid/crystalline powder.[2] Can be white or colored powder, or brown and pebbly.[3] Fentanyl is a member of a class of drugs known as fentanyl analogs, which are rapid-acting opioid (synthetic opiate) drugs that alleviate pain without causing loss of consciousness at therapeutic levels. Fentanyl analogs are also abused due to the euphoric effects they produce.[4] The U.S. Drug Enforcement Administration (DEA) has identified 15 common fentanyl derivatives, which are referred to in this document as fentanyl analogs. Fentanyl is a free standing base. As a result, the active forms of fentanyl often exist as fentanyl salts, e.g., fentanyl citrate. Fentanyl analogs may be dissolved in a polar organic solvent such as alcohol. With the exception of fentanyl salts, most fentanyl analogs show limited solubility in water. The fentanyl analogs may be present in solution, as powders, and in several other forms, e.g., pills and on blot paper.

Persistence: While there have been few studies investigating the environmental persistence of fentanyl, fentanyl is considered persistent on surfaces and in water under normal environmental conditions. Persistence will depend upon release, environmental conditions, and the types of surface(s) and materials affected.

PHYSICAL PROPERTIES OF FENTANYL, FENTANYL CITRATE, CARFENTANIL, 3-METHYLFENTANYL, α-METHYLFENTANYL

(Physical properties are listed at/near standard temperature and pressure unless otherwise indicated)

FENTANYL[5]	CAS: 437-38-7		
Molecular Weight:	336.5 g/mole	**Formula:**	$C_{22}H_{28}N_2O$
Boiling Point:	870.8°F / 466°C	**Soluble:**	Insoluble to slightly soluble in water; soluble in alcohols [6, 7]
Melting/Freezing Point:	181-183°F / 83-84°C	**Aqueous Solubility:**	Low, 200 milligrams per liter (mg/L) at 25°C
Flash Point:	367°F/186°C	**Density:**	1.087 grams per cubic centimeter (g/cm^3)
FENTANYL CITRATE[8]	CAS: 990-73-8		
Molecular Weight:	528.6 g/mole	**Formula:**	$C_{22}H_{28}N_2O{\cdot}C_6H_8O_7$
Boiling Point:	870.8°F / 466°C	**Soluble:**	Soluble in water; soluble in alcohols[9]
Melting/Freezing Point:	307-313°F / 153-156°C	**Aqueous Solubility:**	Moderate, 1 g/40 milliliter (mL)
Flash Point:	367°F/186°C	**Density:**	Not available (NA)
CARFENTANIL[10]	CAS: 59708-52-0		
Molecular Weight:	394.5 g/mole	**Formula:**	$C_{24}H_{30}N_2O_3$
Boiling Point:	946.4°F / 508°C	**Soluble:**	Water and alcohols
Melting/Freezing Point:	501.8°F / 261±30°C	**Aqueous Solubility:**	Low, 4.21 mg/L at 25°C
Flash Point:	502°F / 261°C	**Density:**	1.142 g/cm^3
3-METHYLFENTANYL[11]	CAS: 42045-86-3		
Molecular Weight:	350.5 g/mole	**Formula:**	$C_{23}H_{30}N_2O$
Boiling Point:	883.4°F / 473°C	**Soluble:**	Water and alcohols
Melting/Freezing Point:	NA	**Aqueous Solubility:**	Low, 0.015 mg/mL at 25°C
Flash Point:	367°F / 186±19°C	**Density:**	1.064 g/cm^3
α-METHYLFENTANYL[12]	CAS: 79704-88-4		
Molecular Weight:	350.5 g/mole	**Formula:**	$C_{23}H_{30}N_2O$
Boiling Point:	885.2°F / 474±38°C	**Soluble:**	Water and alcohols
Melting/Freezing Point:	NA	**Aqueous Solubility:**	Low, 1.295 mg/mL at 25°C
Flash Point:	367°F / 185.1±19.1 °C	**Density:**	1.082 g/cm^3

POTENTIAL EXPOSURE PATHWAYS

Exposures by incidental ingestion and inhalation are most probable; however, other exposure routes should be considered.

- **Illicit Drugs:** Illicit drug operations present multiple exposure pathways. Responders may encounter packaged powder, loose powder, pill mills, aqueous liquids and hardened (described as concrete-like) fentanyl analogs. Bulk fentanyl is mixed with other narcotics because it is a cheap filler material.[13] Makeshift laboratories are found in apartments, houses, garages and storage facilities. These operations are known as cutting houses, and are commonly associated with heroin. As a result, responders should assume that heroin repackaging operations have fentanyl analogs present. Due to fentanyl's much higher potency as compared to heroin, extra care must be taken to eliminate/limit any inhalation or dermal contact with fentanyl. Illicitly synthesized fentanyl analogs are referred to as non-pharmaceutical fentanyls (NPF).[14] Responders may also find other chemicals including: N-bomb (glitter) LSD; U4770; 4-chloro-N-[1-[2-(4-nitrophenyl)ethyl]-2-piperidinylidene]-benzenesulfonamide (referred to as W-18); propionyl chloride; sodium borohydride; 4-piperidone hydrochloride; phenethyl bromide; phenethyl tosylate; and N-phenethyl-4-piperidone (NPP) or 4-anilino-N-phenethyl-4-piperidine (ANPP). NPP and ANPP are immediate precursors of fentanyl. The DEA restricts the purchase of NPP and is expected to do the same with ANPP. W-18 is used as a substitute for fentanyl or mixed with batches of fentanyl.[15] Responders should plan for the possible presence of these compounds when responding to incidents in illicit fentanyl manufacturing labs.
- **Open Areas:** While fentanyl is a solid powder at room temperature, it poses an inhalation or incidental ingestion exposure threat if sufficient powder becomes airborne. Fentanyl can also be dissolved in solvents and fentanyl citrate is soluble in water, which allows exposure in aerosol form. The literature indicates that police officers showed symptoms of opiate exposure after police activities created fentanyl dust/aerosol or when they worked in dusty areas.
- **Water/Water Systems:** Fentanyl in liquid solution creates a possible dermal exposure pathway and is commonly used in many medicinal forms of fentanyl. Literature reviews indicate that aqueous fentanyl may be found as an illicit drug in intravenous form, nasal sprays, eye drops, and vape pen liquids. While fentanyl could enter natural waters or a water system, neither is a likely exposure pathway.
- **Indoor Facility:** Fentanyl could potentially be dispersed as solid particulates or liquid spray (aerosol) inside a building or facility; HVAC systems may be affected. Fentanyl particulates are heavier (less buoyant) than air and will accumulate on lower levels and in utility corridors and/or deposit on surfaces inside a building.
- **Food:** While food is an unlikely exposure pathway, fentanyl can be released as a fine dust or aerosol that may contaminate food.
- **Other:** Fentanyl is sold commercially under several brand names and in various forms: lozenge (Actiq®); under the tongue (sublingual) tablet (Abstral®); a film applied to the inner lining of the cheek or lip (Onsolis®); a tablet that goes between the gum and cheek (Fentora®); nasal spray (Lazanda®); sublingual spray (Subsys®); and a transdermal skin patch (Duragesic®).[16] Use caution when handling these items because accidental exposures have occurred. These products may also be found at illicit drug operations where users cut up the patches to smoke, squeeze the fentanyl out of them, or crush them for illicit pill manufacturing operations.

PROVISIONAL ADVISORY LEVELS (PAL)[17] & INDUSTRY OCCUPATIONAL EXPOSURE LIMITS (OEL)

Advisory: Inhalation, dermal, and ocular exposure guidelines (IDLH, AEGLs, TLVs)* have not been established for fentanyl and fentanyl analogs. *Until appropriate Occupational Safety and Health Administration (OSHA) / National Institute of Occupational Safety and Health (NIOSH) exposure limits are developed, this fact sheet recommends that safety officers use alternative exposure values, such as the PALs** and industry derived OELs listed below. The OELs have not been vetted by the appropriate regulatory agencies and are subject to change without notice as new data become available. Please use with caution.* ***Note:*** *Dermal occupational exposure limits have not been established; however, skin contact is a potential exposure route based on limited dermal absorption rate data.*[18, 19, 20, 21]

Fentanyl: Inhalation	**µg/m³**	**Fentanyl: Ingestion**	**mg/L**
24 Hour (≤ 24-hr exposure) PAL 2 (serious, possibly irreversible health effects)	0.0037	24 Hour PAL 1 (mild, transient, reversible health effects)	0.03
24 Hour PAL 3 (lethal effects)	0.011	24 Hour PAL 2	0.23
Industry OEL 8-hr TWA[22]	0.1	30 Day (>24 hr, ≤30 days) PAL 1	0.03
		30 Day PAL 2	0.23
		90 Day (>30 days, ≤90 days) PAL 1	0.03
		90 Day PAL 2	0.23
Fentanyl Citrate: Inhalation	**µg/m³**	**Fentanyl Citrate: Ingestion**	**mg/L**
USP Short-Term Exposure Limit (15 min)[23]	2.0	Effect levels do not exist	NA
Mallinckrodt Short-Term Exposure Guidelines (15 min)[24]	2.0		
USP 8-hr TWA	0.1		
Mallinckrodt Occupational Exposure Guideline: 8-hr TWA	0.7		
Carfentanil: Inhalation	**µg/m³**	**Carfentanil: Ingestion**	**mg/L**
Cambrex, Inc. OEL 8-hr TWA[25]	0.04	24 Hour PAL 2	0.007
		24 Hour PAL 3	1.1
3-Methylfentanyl: Inhalation	**µg/m³**	**3-Methylfentanyl: Ingestion**	***mg/L***
Effect levels do not exist	NA	24 Hour PAL 2	0.007
		24 Hour PAL 3	1.1
α-Methylfentanyl: Inhalation	**µg/m³**	**α-Methylfentanyl: Ingestion**	***mg/L***
Effect levels do not exist	NA	24 Hour PAL 2	0.007
		24 Hour PAL 3	1.1

* IDLH: immediately dangerous to life or health; AEGL: acute exposure guideline level; TLV: threshold limit value

** PALs: Please see EPA's technical brief for more information on PALs limitations and usage: https://cfpub.epa.gov/si/si_public_file_download.cfm?p_download_id=531760

SECTION 6: FACTS AND BACKGROUND

F. United States Government Fentanyl Advisory –Aug. 2019

August 21, 2019

Advisory to the Chemical Manufacturing Industry on Illicit Activity and Methods Related to the Manufacturing of Fentanyl and Synthetic Opioids

Drug Trafficking Organizations (DTOs) purchase illicit fentanyl, fentanyl analogues, and other synthetic opioids, primarily from Chinese fentanyl suppliers, and prepare these drugs for individual use and redistribution. DTOs may increasingly seek these drugs from other sources and/or expand their acquisition of the precursors and equipment needed for clandestine synthesis.

This advisory should be shared with Chief Executive Officers, Chief Operations Officers, Chief Risk Officers, Legal Departments, Chief Compliance Officers, the Chemical/Laboratory Equipment Industry, and the Pharmaceutical Industry.

Introduction

The opioid crisis is a serious epidemic that requires a multidisciplinary approach including aggressive investigation and prosecution, in addition to collaboration with private sector partners in the fields of technology, health care, prevention, treatment, and education. Federal, state, local, tribal, and territorial partners must work together with the private sector to leverage resources in the fight against this deadly threat. The private sector can play a key role in combatting the opioid epidemic by working with law enforcement to identify the ways in which criminals are exploiting legal platforms for illicit means and referring criminal activity to law enforcement.

This advisory[1] is intended to broaden the public and private sectors' awareness of unique manufacturing characteristics of synthetic opioids, so that all stakeholders can partner in combatting the scourge of fentanyl and other synthetic opioids entering the United States and minimize their impact on our nation. This advisory provides private sector partners information to identify the various stages of illicit fentanyl manufacturing and redistribution; refer this activity to law enforcement partners when identified; and end trafficker acquisition and transfer of the tools needed to prepare these drugs for individual use. This advisory is intended to enhance awareness so as to disrupt the devastating trade in fentanyl and illicit synthetic opioids.

[1]This advisory is also part of a larger, United States government Fentanyl advisory covering the movement, manufacturing, marketing, and monetary aspects of the trafficking of fentanyl and other synthetic opioids. The comprehensive *21st Century Drug Trafficking: Advisories on Fentanyl and Other Synthetic Opioids* can be found here https://www.whitehouse.gov/briefings-statements/white-house-announces-actions-crack-trafficking-fentanyl-synthetic-opioids-better-position-private-sector-protect-homeland/

There are two, largely separate supply chains for fentanyl, fentanyl analogues,[2] and other synthetic opioids in the United States: the licit international and domestic supply chain, which has significant government oversight and safeguards, and the illicit supply chain. Available information suggests that most fentanyl and fentanyl-related substances abused in the United States are illicitly synthesized abroad and trafficked into the United States via international mail, express consignment, or across the Southwest Border. The extent to which fentanyl originating overseas is synthesized in clandestine laboratories versus synthesized off-hours in facilities that legally manufacture pharmaceuticals in their own countries is unknown. Diversion of pharmaceutical fentanyl in the United States occurs on a small scale, with the diverted fentanyl intended for personal use and low-level street sales.

Within the United States, traffickers typically acquire synthetic opioids and process them for street sales by cutting with diluents; mixing with other drugs such as cocaine, heroin, or methamphetamine; or pressing into pill form with binders and diluents. Pills containing synthetic opioids are often sold under the guise of prescription opioids.

Typologies

The predominant source of illicit fentanyl in the United States is manufactured in international clandestine synthesis laboratories. To date, the vast majority of precursors and finished illicit fentanyl in the Western Hemisphere has originated from China. Sources of illicit fentanyl fueling the opioid epidemic include (i) International or domestic clandestine laboratory synthesis and (ii) on a very limited scale International and domestic diversion. The licit and illicit use of the equipment necessary to prepare these highly potent drugs for individual use presents additional law enforcement challenges; these challenges are discussed in section (iii), Redistribution: pill presses/tableting machines, encapsulating machines, and binding agents.

[2] While fentanyl analogues have a similar chemical structure to fentanyl, small structural changes result in a seemingly endless number of variations of the drug with similar effects and of potentially unknown potency.

[1] This advisory is also part of a larger, United States government Fentanyl advisory covering the movement, manufacturing, marketing, and monetary aspects of the trafficking of fentanyl and other synthetic opioids. The comprehensive *21st Century Drug Trafficking: Advisories on Fentanyl and Other Synthetic Opioids* can be found here https://www.whitehouse.gov/briefings-statements/white-house-announces-actions-crack-trafficking-fentanyl-synthetic-opioids-better-position-private-sector-protect-homeland/

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G. Naval Postgraduate School Prof. Dr. John Arquilla: Perils of the Gray Zone – 2018

The Chinese People's Liberation Army Navy is establishing a network of enhanced reefs enabling China to exert control over the South China Sea. (SatelliteImage©2018DigitalGlobe)

Perils of the Gray Zone
Paradigms Lost, Paradoxes Regained

By John Arquilla

In the long years since the 9/11 attacks on America, the wide-ranging "war on terror" has morphed into terror's war on the world. Terrorist incidents have increased seven-fold, with the casualties caused by such attacks more than quintupling.[1] Just as troubling, since the start of the current decade the overall number of wars under way has increased nearly a third—from 31 to 41.[2] There is much overlap between the worst of these conflicts and the number of terrorist incidents, with Iraq, Afghanistan, Syria, and Yemen heading the list in recent years. Paradoxically, the first two of the countries listed have seen extended, very expensive, yet problematic American invasions and occupations. The American military footprint has been light in Syria and Yemen, but these wars have also proved vexing.

If these challenges were not enough, plaguing the lower end of the spectrum of conflict as they do, there are serious threats at the levels of the mid-range and major powers as well. Roguish regional states like Iran and North Korea each pose grave problems. The Islamist regime in Tehran oversees an arc of strategic involvement in wars ranging from Syria to the southern Arabian Peninsula; supports the vibrant, violent Hezbollah organization; and cultivates covert nodes, cells, and networks throughout the world.[3] As for North Korea, Kim Jong Un's vision is focused primarily on continuing his family's totalitarian dynasty. But a key aspect of his strategy includes the development of a robust nuclear deterrent, something seen as highly threatening in capitals ranging from Washington to Beijing.

Mention of Beijing is a reminder of the rise of China, and of its increasingly bumptious policies and actions—from reef enhancement to edgy sea patrols—in the East and South China Seas. The cyber domain is yet another area in which China's behavior can only be described as highly aggressive, given the skill and systematic predations of its corps of hackers—whether they are part of Chinese officialdom or somehow just working at the behest of Beijing. Their ability to make off with vast amounts of intellectual property has resulted in their enjoying a greatly disproportionate share of what then Director, National Security Agency and Commander, U.S. Cyber Command General Keith Alexander called—while he was still in uniform—"the greatest transfer of wealth in history."[4] Needless to say, Russian and/or Russian-backed hackers have enjoyed a healthy share of these spoils as well.

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However, the Russian challenge goes well beyond cybercrime, to include serious acts of political warfare—specifically, of late, attempts to influence democratic elections—across many countries, not least the United States. The Russians have also reasserted their growing power in more muscular though hardly conventional ways as well. Not only in their self-defined "near abroad"—reference should be made here to the bloodless annexation of Crimea and covert combat support to separatist rebels in Donetsk—but also in Moscow's sharp military intervention in the bloody Syrian civil war. Thus, if we are not seeing a recrudescence of the Cold War, without doubt a kind of "cool war" has indeed set in.[5]

Given all the global turmoil, and the seeming inability of American power—even when enhanced by allies—to cope effectively with the wide range of these challenges, it is small wonder that strategists have been casting about in search of fresh paradigms and more innovative concepts of operations. For it is abundantly clear that "overwhelming force"—the foundation of the grand strategic doctrine that bears General Colin Powell's name—will not suffice against hidden networks, or nations that choose covert, unconventional action as their preferred modus operandi.

In an era featuring few stand-up fights, there is a premium on doctrinal innovation. Yet even while the various aggressors of the world seem to have truly grasped the need for and mastered the process of creativity, the United States and its allies have become mired in older habits of mind, manifesting an all-but-nostalgic longing for the return of traditional conventional warfare. The American defense budget is quite revealing of this mindset, with more than 90 percent of expenditures aimed at shoring up or expanding on conventional combat capabilities. Even the most generous views of support for U.S.

Rehearsal of the parade in honor of Victory Day in Donetsk.

Special Operations Command (USSOCOM), for example—including direct and "enabling" funding—have historically reflected little more than 3 percent of the overall budget allocated to it, along with but 4 percent of monies dedicated to overseas contingency operations.[6] In terms of personnel, USSOCOM's estimated 70,000 service members constitute just 5 percent of the total active duty force.

However, there have been voices raised in recent years, pointing to the costly, problematic interventions in Afghanistan and Iraq, the rise in global terrorist networks, and the evidence that mid-level and major powers are flexing their muscles in a mostly unconventional manner—hardly ever distinguishable as familiar traditional warfare. The effort to categorize this challenge has coalesced around a notion of gray zone conflict, a concept defined by strategist Hal Brands as an "activity that is coercive and aggressive in nature, but that is deliberately designed to remain below the threshold of conventional military conflict."[7] A recent report by the International Security Advisory Board—a Federal Advisory Committee established to provide the Department of State independent insight, advice, and innovation—describes the gray zone more narrowly as

> *the use of techniques to achieve a nation's goals and frustrate those of its rivals by employing instruments of power—often asymmetric and ambiguous in character—that are not direct use of acknowledged regular military forces.*[8]

Whatever the differences in definition between these views—and those arising from myriad other gray zone studies—the emphasis on this zone being unconventional comes through loud and clear.

This prompts two questions: "why do we need the gray zone concept?" and "has the focus on today's so-called gray zone resulted in a dangerous diversion of attention away from the accumulated body of knowledge about unconventional aspects of conflict developed over the past two hundred years?" The problems posed by irregular warfare in the 19th century, from Carl von Clausewitz's notions of *kleiner Krieg* in the Napoleonic era to C.E. Callwell's "small wars" during the heyday of colonialism, were deeply studied by these two, and many others.[9] As to the anti-colonial guerrilla wars of the 20th century, these were closely examined by insurgents and counterinsurgents alike. Mao Zedong, Che Guevara, and Vo Nguyen Giap were undoubtedly the best guerrilla memoirists, respectively, of Chinese, Cuban, and Vietnamese insurgent movements. The counterinsurgent perspective on the past century has perhaps been best exposited in remarkable works by David Galula, Otto Heilbrunn, and Lewis Gann.[10] These are but a few of the highest peaks in a whole mountain range of studies of irregular warfare. In light of this existing literature, why is the gray zone concept needed?

As to the second question, about diversion of attention away from accumulated knowledge of the subject of conflict "other than traditional conventional warfare," it seems that here too there is much cause for concern. Brands puts the matter succinctly, noting that "exaggerating the newness of the [gray zone] phenomenon risks muddling rather than sharpening our comprehension."[11]

Paradigms Lost

Beyond impairing our understanding of the current landscape of conflict, failure to recall and rely upon relevant security paradigms of the past—in favor of simply ginning up a new term for longstanding practices—has led to a sharp loss of earlier knowledge and insight, consequences of which have surely played a significant role in the unsatisfying course of events described in the opening section of this article. It is with deep concern about the severe price paid by forgetting the substance and power of earlier security paradigms—an inattentiveness that plays

right into our enemies' hands—that I provide the following reminders.

Perhaps the most important insight to recall and reflect on speaks to the very rise of an age of irregular warfare. This was predicted by political scientist Kenneth Waltz more than sixty years ago, when he observed that "mutual fear of big weapons may produce, instead of peace, a spate of smaller wars."[12] Journalist Robert Taber affirmed this view a decade later in his classic *War of the Flea*, which foretold the future dominance of insurgency and terror on the conflict spectrum. As Taber viewed the matter, a traditional military simply had "too much to defend, too small, ubiquitous and agile an enemy to come to grips with."[13] This insight resonated with bright jihadis, especially Abu Mus'ab al-Suri, the deepest strategic thinker that al-Qaeda produced. He used Taber's work in his teachings during the 1990s, when al-Qaeda ran a "university of terror" in Afghanistan.[14] Waltz and Taber had hardly been heeded in the United States, and much too conventional means were applied in Vietnam. A predictable debacle ensued, yet American thought still turned back to conventional war with development of an AirLand Battle doctrine after the communist overrun of South Vietnam in 1975. And it would take more than 30 years—after 9/11 and in the middle of the insurgency in Iraq—before a new counterinsurgency manual was published.[15]

With regard to the notion of a blurriness between peace and war—a key aspect of the justification for the gray zone concept—it is hardly new. Forty years ago Eliot Cohen was writing insightfully about "the blurring of war and peace . . . the struggle to mobilize the populace . . ." and a "new era of warfare [differing] sharply from that which preceded it."[16] As to notions of covert action as means by which to effect regime change and pursue other political objectives, this portion of the gray zone was illuminated, studied, and critiqued long ago. Given that the United States was an eager participant in this realm, it is hard to see why a new construct for this form of action is necessary. Indeed, a look back at the heyday of covert action, and its often problematic results—in Iran, Guatemala, Cuba, Chile, Angola, and Nicaragua, to name just a few places where Americans plied this craft—might curb the future appetite for this dark mode of statecraft.[17] Conversely, given the high failure rate of covert actions, excessive fear of others using them might be eased.

In addition to covert action—a phenomenon closely associated with the world of intelligence and counterintelligence—the defined gray zone implicitly relates also to aspects of warfighting that extend well-beyond the aforementioned guerrilla operations. These modes of conflict are generally reflected by instances in which a nation chooses to counter or confront a potential adversary by investing in off-design technologies and highly innovative concepts of operations, rather than by imitating the structure and doctrine of the opposing forces. The best current example of such an approach can be found in Beijing's strategy in the East and South China Seas. Instead of relying on aircraft carriers—though the Chinese People's Liberation Army Navy now has two of them—Beijing is establishing a network of enhanced reefs, one with potential to exert control over these narrow seas with supersonic anti-ship missiles, brilliant mines, and attack aircraft based on or otherwise using them. By these varied means, Beijing is taking a highly asymmetric approach to dealing with American carrier-based power projection capabilities.

This notion of asymmetric warfare, pioneered more than 40 years ago by Andrew J.R. Mack, is one of those well-developed paradigms in danger of being lost as soldiers and statesmen flock to the gray zone. For Mack, the asymmetry was not only to be found in the concept of field operations but also in the combatants' relative motivations. Key studies that have built upon his thinking, and advanced fresh ideas, have addressed both the

operational and the motivational dimensions.[18] In the world today, these factors are much on display at all levels. Clearly, the Taliban see their campaign in Afghanistan as a total war for control of the state, while the U.S.-led coalition operates with a limited conflict in mind, seeking to "hold the line" with the minimum level of human and material resources expended. At the level of the major powers, Russia has a high level of commitment to holding the Crimea, and to supporting ethnic Russians in Donetsk, while NATO is clearly less determined to see any redress of the situation in favor of Ukraine. As to the United States and Britain, signatories to the 1994 Budapest Memorandum on Security Assurances, which guaranteed Ukraine's territorial integrity, both major powers seem to be suffering from selective or strategic amnesia.[19]

As to terrorism, it seems that the gray zone concept is limited in its ability to help us grasp the strategic implications of the shift in this phenomenon from its origins as a form of symbolic violence with some form of extortion in mind to a mode of conflict in its own right. On this point, though, it is clear that much earlier thinking on terrorism as an emerging form of warfare remains highly relevant. Indeed, the Baron von der Heydte—a German paratroop commander during World War II and an international legal scholar after—was among the first to see, in the wake of the Six-Day War in 1967, that terrorism was becoming a form of "war out of the dark" in which "the decision is sought, and ultimately achieved, in a very large number of small, individual operations."[20] To say the least, the Baron was prescient. As was Claire Sterling, who observed back in the 1980s that terrorism was growing via networked forms of organization—and would continue to do so.[21] The challenge in the great post–9/11 war among nations and terrorist networks is to understand the characteristics, including the strengths and vulnerabilities, of networks. The gray zone concept does little to achieve this. Sterling's ideas do, and can form the basis for a counter-network paradigm. Just as the Baron von der Heydte's formulations provide a foundation for viewing the nature of the current era of conflict.

Thus it seems clear that there are times when, in the words of Winston Churchill, "the farther back you can look, the farther ahead you will see." This is such an era, an age of irregular warfare, terror, covert action, and other asymmetric modes of conflict. To confront and master these challenges, older, deeper, more developed concepts are likely to serve better than just freshly-minted terms. For example, Lewis Gann observed not only how often guerrillas have been defeated, but also the key elements upon which victory or defeat pivot in these wars. Beyond well-known factors like denying havens and inhibiting external support, Gann emphasized the largely psychological nature of guerrilla wars, railed against having counterinsurgent forces with "big administrative tails," and suggested cost-effective ways to improve the ability to gain information critical to finding the hidden.[22] Recent scholarship has powerfully affirmed Gann's views—especially about the frequency with which and conditions under which guerrillas can be and have been defeated.[23]

Otto Heilbrunn should also be mentioned. Almost 50 years ago, he provided an outstanding analysis of the conditions favoring victory by the counterinsurgents over irregulars and, conversely, conditions associated with the likelihood of seeing an insurgent victory. Briefly, Heilbrunn identified three types of insurgencies: terrorist wars (e.g. Palestine); small-unit guerrilla wars (e.g. Malaya, Kenya, Greece, and Algeria); and large-unit insurgencies (e.g. Tito, Mao, and Giap). He went on to argue that terrorist wars generally lead to stalemates—a point he made so long ago, yet which resonates quite powerfully today. Small-unit guerrila wars have been won, more often than not, by the counterinsurgents; whereas guerrillas have won all large-unit conflicts.[24] Heilbrunn's typology

of irregular wars and his analysis of them remain highly relevant, yet his work—and that of others who grappled with these challenges—will all too likely be forgotten or lost in the gray zone. Another example of the risk run by relabeling a longstanding phenomenon.

Paradoxes Regained

As important as it is to take a retrospective view and search out still-valuable paradigms before they become totally lost or simply ignored out of existence, one must also remain attentive to the possibility of reemerging paradoxes. Perhaps the most nettlesome of the paradoxes is revealed by contemplation of the costly, all-too-often counterproductive results of American military interventions and foreign policy initiatives in the years since 9/11. This period, which began a decade after the dissolution of the Soviet Union, should by all traditional measures of power have seen American vital interests well-served and policy goals promptly achieved. Yet results have proved to be very far from satisfactory, with a seemingly endless sea of troubles looming straight ahead. To be sure, part of the problem lies in the rise of irregular modes of conflict—but such challenges have been met and mastered in the past. Curiously, what may be adding to the difficulty in parsing them today is the very concept of the gray zone.

By creating the notion of a space that lies between war and peace, rather than simply recognizing the rise of irregular warfare to a leading position on the spectrum of conflict, American strategists have hobbled themselves, like horses whose tethered legs allow little movement. The failure to see that the gray zone is actually *in and an essential part of* the realm of war conveys huge advantages to insurgents, terrorist networks, and roguish nations. Understanding why this failure of perception has occurred reveals another paradox: how the Marxist worldview—that failed socially, politically, and economically—and a radical offshoot of Islam—that is overwhelmingly rejected by Muslims—have both come to life owing to the fuzzy thinking about conflict in the United States that has diffused among its allies and friends.

The problem with gray zone thinking is that it confounds the very paradigms that have generally guided the behavior of the world's more progressive, or at least more advanced, nation-states. One foundational body of thought is classical liberalism—not to be confused with today's meaning of the word "liberal"—that grew from the economic thinking of Adam Smith and David Ricardo. Both favored free markets instead of the controls imposed by mercantilist policies. And both saw the rational individual as the prime unit of analysis in commercial affairs. The heirs to their thinking became devoted to the "Manchester Creed," a belief system based on the notion of an enduring harmony of interests. War in this paradigm is a clear aberration. Thus classical liberalism has a hard time with the notion of a gray zone between a harmony of interests and open conflict. Perhaps the best example of the great difficulty this world view has had with creeping aggression of the gray-zone sort is provided by the befuddlement of England, France, and even the League of Nations in the face of Nazi actions and annexations during the 1930s. Edward Hallett Carr, the great historian and analyst of this period, was the first to critique the liberal paradigm as inadequate, noting of this time that it was "no longer possible to believe that every state, by pursuing the greatest good of the whole world, is pursuing the greatest good of its own citizens, and *vice versa*." He concluded that "[t]he inner meaning of the modern international crisis is the collapse of the whole structure of utopianism based on the concept of the harmony of interests."[25]

Despite the travails of World War II and the Cold War, in the half-century between Hitler's invasion of Poland in 1939 and the fall of the Berlin Wall in 1989 sustained efforts arose to rehabilitate notions of the harmony of interests. "Neoliberal"

thought, which emphasizes the importance of global institutions and agreements, operates under the assumption of harmony. As Robert Jervis has noted, neoliberals believe that the onset of armed conflict is just evidence that "international politics represents tragedy rather than evil."[26] Even the polar opposite of liberal thought, flinty Realism with its emphasis on power calculations in matters of war and peace, makes clear that there are "rules of the game" even at this level that are not lightly disregarded. The father of the realist school of thought, Hans Morgenthau, went so far as to argue "there is the misconception . . . that international politics is so thoroughly evil that it is no use looking for ethical limitations of the aspirations for power." Instead, he noted, it was more proper to focus on "the increasing awareness on the part of most statesmen of certain ethical limitations restricting the use of war as an instrument of international politics."[27]

The structural realists who have come after Morgenthau have seen war as a disturbance—what leading realist John Mearsheimer, echoing Jervis, describes as tragedy—of an equilibrium to be restored by balancing behavior.[28] In sum, classic liberalism and realism, along with their neoliberal and structural realist descendants, remain key, guiding paradigms that tend to see sharp, clearly delineated dividing lines between states of peace and war. The gray zone concept poses a challenge they are not particularly well-suited to address which may help to explain, in part, the difficulty liberal- and realist-oriented policymakers have had in coping with the crises of the post–9/11 era.

By way of contrast, the seemingly defunct Marxist paradigm actually provides a more useful way to think about the low-level conflicts that populate the gray zone and bedevil our time. Like classic liberalism, Marxism draws its basic tenets from economic analysis. But a key difference is that, whereas liberal thought was based on a belief in the harmony of interests, Marxism sees the world, in the phrasing of Jeffry Frieden and David Lake, as "necessarily conflictual."[29] And it is quite clear that Marxists did not simply see this conflict as limited to the economic realm. For V.I. Lenin a perpetual war was to be fought, often of subversion and various forms of low-level violence. The aim was to meet what he described as "the preliminary condition for every people's revolution . . . the smashing, the *destruction* of the ready-made State machine."[30] His successor Josef Stalin reaffirmed this point in his 1924 monograph, "The Foundations of Leninism," in which he argued "the law of violent proletarian revolution . . . is an inevitable law." The coming of peace, he thought, could happen only "in the remote future, if the proletariat is victorious."[31]

The gray zone construct, as noted earlier in the mention of formal definitions in current use, includes irregular and guerrilla war, as well as acts of terrorism. The Marxist paradigm makes no effort to employ such fine distinctions. Instead, all these phenomena are forms of *war*. Mao Zedong argues this point unambiguously in his writings, affirming that "guerrilla operations must not be considered as an independent form of war. They are but one step in the total war." He returns to this theme repeatedly, linking irregular warfare to overall goals, and finally concluding that "the strategy of guerrillas is inseparable from war strategy as a whole."[32] Vietnam's Vo Nguyen Giap, who was influenced to a significant degree by Mao's thinking, adhered to this notion in his and Ho Chi Minh's long, successful fight against the French and, later, the Americans.

For all the continuing value of Marxist strategic thought today—Russia and China, two heirs of Marx, are showing real mastery of our so-called gray zone—there is another conceptual paradox that has been regained: Islamism. And not just the odd, fringe beliefs so widely and overwhelmingly rejected by the world's Muslims. Rather, the paradox is to be found in the rebirth of the early notion of the obligation to wage perpetual warfare against "unbelievers."

This idea animated the first great sweep of Arab conquests in the 7th century and thereafter, shored up resistance to repeated "crusades," and sparked continuing conflict that was waged for many centuries in the Mediterranean, and at times beyond, by the corsairs of Barbary—who eventually ended up fighting U.S. Marines early in the 19th century. Of this true "long war" mentality Sir John Bagot Glubb, a soldier who did much service with Arab forces, wrote tellingly about how their forebears

> *swept irresistibly forward without organization, without pay, without plans, and without orders. They constitute a perpetual warning to technically advanced nations who rely for their defence on scientific progress rather than the human spirit.*[33]

Could there be any more cautionary, telling explanation of the true antecedents of the zeal and tenacity modern Muslim extremists have shown since the great war between nations and terrorist networks erupted in the wake of the 9/11 attacks on America? I don't think so. Just like the heirs of Marx, today's Islamist fighters see war as a quite unitary construct. A phenomenon that, from very early days, saw the jihadis skillfully blending conventional and irregular modes of conflict. As G.E. von Grunebaum, a leading scholar of Islam from the 7th to the 13th centuries, observed, "guerrilla warfare, apart from several larger expeditions, *continued without interruption*."[34] Those who oppose the present-day jihadis may try to slice and dice conflict in different ways, based on their habits of mind and institutional biases against treating something other than conventional war as "war." But they do so at their increasing peril.

Conclusion

This article has sharply critiqued the very notion of the "gray zone." It is an intellectual construct that confuses rather than clarifies the spectrum of conflict, and plays into the hands of smart, motivated aggressors who see war in simpler ways. That is, today's aggressors are most willing to accept insurgency, terror, subversion and covert action as war—right alongside increasingly rare occurrences of conventional conflict. The irony of the situation is that the victors in the Cold War, the champions of democracy, modernization and the "new world order," hamstring themselves by dithering over new definitions for old concepts that an earlier generation of their own strategists had thought about deeply and insightfully. Meanwhile, the heirs of Marx and of classical militant Islam—two paradigms long seen as defunct and widely rejected—come to 21st century conflict better prepared, in terms of mindset, for the waging of protracted war in all its many dimensions.

If we must have a fresh definition for war in this era—and I am still far from convinced that we should—let it be "hybrid warfare," the term for present and future conflict that then-Defense Secretary Robert Gates first used in 2009. He was no doubt inspired by "hybrid thinking" going on in the Marine Corps, and the thoughtful 2007 policy study by Frank Hoffman, *Conflict in the 21st Century: The Rise of the Hybrid Wars*. In it, he posed the prospect that "we can expect to face competitors who employ all forms of war and tactics, perhaps simultaneously."[35] At least this term recognizes the irregular as a full-blooded form of conflict, right alongside conventional war. Thus it gives those on the defensive—and make no mistake, the United States and its allies and friends are on the defensive—good reason to sharpen their wits in the face of aggressive actions by major powers and regional states, rogues, and terrorist and insurgent networks. There is a world war under way, waged in hot, cold, and cool modes. The aggressors see no gray zone "between war and peace." They see all as war. So must we. PRISM

Notes

[1] The Uppsala Conflict Data Program (UCDP), Peace Research Institute Oslo (PRIO), and the Global Terrorism Database (GTD) maintained at the University of Maryland all concur broadly with this assertion. In 2001, there were roughly 2,000 terrorist incidents that caused an estimated 14,000 deaths and injuries. By 2015 that number had risen to 15,000 attacks and more than 80,000 total casualties. The upward trend continues.

[2] UCDP and PRIO figures for conflicts exceeding 1,000 battle deaths in a given year.

[3] Perhaps the broadest depiction of Iran's global capabilities was offered in a hearing before the House Committee on Foreign Affairs, Subcommittee on Terrorism, Nonproliferation, and Trade on March 20, 2013. See especially I*ran's Global Force Projection Network: IRQC Quds Force and Lebanese Hezbollah* (statement of Will Fulton, American Enterprise Institute Critical Threats Project Iran Analyst and IRGC Project Lead).

[4] Josh Rogin, "NSA Chief: Cybercrime Constitutes the 'Greatest Transfer of Wealth in History'," *Foreign Policy Magazine*, July 9, 2012.

[5] I borrow and slightly expand the meaning of the term from Frederik Pohl's classic dystopian novel, *The Cool War* (New York: Del Rey Books, 1981), in which many of the world's leading nations engage in protracted, covert conflicts against each other.

[6] For details, see Marcus Weisgerber, "Peeling the Onion Back on the Pentagon's Special Operations Budget," *Defense One*, January 27, 2015.

[7] Hal Brands, "Paradoxes of the Gray Zone," (Philadelphia: Foreign Policy Research Institute, February 2016). Another thoughtful exposition of the concept can be found in Michael Mazarr, *Mastering the Gray Zone: Understanding a Changing Era of Conflict* (Carlisle, PA: U.S. Army War College Press, 2015).

[8] International Security Advisory Board, Hon. Gary Hart Chairman, *Report on Gray Zone Conflict* (Washington, DC: Government Printing Office, 2017), 1.

[9] Clausewitz's *On War* scarcely touched on the irregular—e.g. see Book Six, Chapter 26, "The People in Arms." But he lectured extensively at the Prussian War College on the guerrilla wars against Napoleon conducted in Spain and in the Austrian Tyrol. Christopher Daase and James Davis edited and translated these lectures in the fine *Clausewitz on Small War* (Oxford: Oxford University Press, 2015). C.E. Callwell's seminal work was *Small Wars: Their Principles and Practice* (London: University of Nebraska Press, [1896]1996). One of the best general surveys of irregular wars in this era can be found in Walter Laqueur, *Guerrilla: A Historical and Critical Study* (Boston: Little, Brown & Co., 1976).

[10] See Mao Zedong, *On Guerrilla Warfare*, Samuel B. Griffith translation (New York: Frederick A. Praeger, 1962), Ernesto "Che" Guevara, *Reminiscences of the Cuban Revolutionary War*, V. Ortiz translation (New York: Grove Press, 1963), Vo Nguyen Giap, *Big Victory, Great Task* (New York: Frederick A. Praeger, 1968), David Galula, *Counterinsurgency Warfare* (New York: Praeger Security International, 1964), Otto Heilbrunn, *Partisan Warfare* (New York: Frederick A. Praeger, 1962), and Lewis Gann, *Guerrillas in History* (Stanford: Hoover Institution Press, 1970).

[11] Brands, "Paradoxes of the Gray Zone,"4.

[12] Kenneth N. Waltz, *Man, the State, and War: A Theoretical Analysis* (New York: Columbia University Press, 1954), p. 236.

[13] Robert Taber, *The War of the Flea* (New York: The Citadel Press, 1965), 29.

[14] Regarding al-Suri's keen interest in Taber's work, see Brynjar Lia's biography of him, *Architect of Global Jihad* (Oxford: Oxford University Press, 2009).

[15] See *U.S. Army Field Manual 3-24 and Marine Corps Warfighting Publication 3-33.5*, jointly published as The U.S. Army and Marine Corps Counterinsurgency Field Manual (Chicago: University of Chicago Press, 2007).

[16] Eliot A. Cohen, *Commandos and Politicians* (Cambridge: Harvard University Center for International Affairs, 1978), 45.

[17] Gregory F. Treverton, *Covert Action: The Limits of Intervention in the Postwar World* (New York: Basic Books, Inc., 1987) provides an excellent survey of the American practice of covert action from the early 1950s to the late 1980s.

[18] See Andrew J.R. Mack, "Why Big Nations Lose Small Wars: The Politics of Asymmetric Conflicts," *World Politics*, Vol. 27, No. 2 (January 1975), 175–200. Important studies that have built upon this theme include: T.V. Paul, *Asymmetric Conflicts: War Initiation by Weaker Powers* (Cambridge: Cambridge University Press, 1994), which explores both successes and failures of asymmetric approaches; and Ivan Arreguín-Toft, *How the Weak Win Wars: A Theory of Asymmetric Conflict* (Cambridge: Cambridge University Press, 2005), which argues that conventional strategies for opposing irregular opponents do rather poorly.

[19] Ironically, Russia also signed the Memorandum—that extends the guaranty to Belarus and Kazakhstan as well—in return for their and Ukraine's agreement to give up the nuclear weapons they inherited upon the dissolution of the Soviet Union.

[20] Friedrich August Freiherr von der Heydte, *Modern Irregular Warfare in Defense Policy and as a Military*

Phenomenon, translated by George Gregory (New York: New Benjamin Franklin House, [1972]1986), 3.

[21] See Claire Sterling, *The Terror Network: The Secret War of International Terrorism* (New York: Holt, Rinehart and Winston, 1981).

[22] Gann, *Guerrillas in History*, 89–90. With regard to information-gathering, Gann advanced the clever idea of reversing the terrorist tactic of using threatening "night letters" aimed at intimidating the populace. Instead, he outlined a means by which the people caught in the middle of a guerrilla war could be encouraged to inform anonymously on the insurgents while retaining secure means for later proof of the valued information they provided.

[23] Ben Connable and Martin C. Libicki, *How Insurgencies End* (Santa Monica: RAND, 2010), note of the 89 cases from the modern era they examine that the counter-insurgents won slightly more than half of the clearly decided conflicts.

[24] Otto Heilbrunn, "When the Counter-Insurgents Cannot Win," *Royal United Services Institution Journal*, Vol. 114, No. 653, (1969), 55–58.

[25] E.H. Carr, *The Twenty Years' Crisis, 1919–1939* (London: Macmillan, 1939), 62.

[26] Robert Jervis, "Realism, Neoliberalism, and Cooperation," in Colin Elman and Miriam Fendius Elman, eds., *Progress in International Relations Theory* (London: MIT Press, 2003), 289.

[27] Hans Morgenthau, *Politics Among Nations* (New York: Alfred A. Knopf, 1948), 174–80. Morgenthau goes on at some length to condemn the killing of innocents in peacetime and noncombatants in wartime.

[28] See John Mearsheimer, *The Tragedy of Great Power Politics* (New York: W.W. Norton, 2001); and Kenneth N. Waltz, Theory of International Politics (New York: McGraw-Hill, 1979).

[29] See Jeffry Frieden and David Lake, *International Political Economy* (New York: St. Martin's Press, 1987), 9.

[30] V.I. Lenin, *Selected Works* (Moscow: Progress Publishing, [1904] Second Edition 1965), 37. Emphasis in the original.

[31] Cited in David McLellan, ed., *Marxism: Essential Writings* (Oxford: Oxford University Press, 1988), 303.

[32] Mao Zedong, *On Guerrilla Warfare*, 41, 95.

[33] General Sir John Bagot Glubb, *The Great Arab Conquests* (London: Hodder and Stoughton, 1963), 359.

[34] G.E. von Grunebaum, Classical Islam (New York: Barnes & Noble, 1997), 97. Emphasis added. See further affirmation of this view in Robin Wright, S*acred Rage: The Wrath of Militant Islam* (New York: Touchstone, 2001).

[35] Cited in Paul Brister, William H. Natter III, and Robert R. Tomes, eds., *Hybrid Warfare and Transnational Threats: Perspectives for an Era of Persistent Conflict* (New York: Council for Emerging National Security Affairs, 2011), 13.

Photos

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SECTION 6: FACTS AND BACKGROUND

H. OPCW Senior Dir. Andrea Hall for WMD National Security Council Statement – Dec. 2017

OPCW **Conference of the States Parties**

Twenty-Second Session
27 November – 1 December 2017

C-22/NAT.7*
27 November 2017
ENGLISH only

UNITED STATES OF AMERICA

STATEMENT BY ANDREA HALL

SENIOR DIRECTOR FOR WEAPONS OF MASS DESTRUCTION AND COUNTERPROLIFERATION, NATIONAL SECURITY COUNCIL DELEGATION OF THE UNITED STATES OF AMERICA TO THE TWENTY-SECOND SESSION OF THE CONFERENCE OF THE STATES PARTIES

Mr Chairperson, Mr Director-General, distinguished ambassadors and delegates,

It is an honour to join you at the Conference of the States Parties in this twentieth anniversary year of the entry into force of the Chemical Weapons Convention. As we reflect collectively on the many accomplishments that we as States Parties and the Organisation for the Prohibition of Chemical Weapons (OPCW) have made over the years, I am pleased to take this opportunity to salute the tremendous contributions of Director-General Üzümcü, who has provided stalwart and visionary leadership to the OPCW during a period of unprecedented challenges. In this context, I am also pleased to congratulate Ambassador Fernando Arias on his nomination to assume the weighty responsibilities of the Director-General next year. The United States of America looks forward to joining other States Parties in confirming his appointment and supporting his future endeavours as the next Director-General.

Even as we acknowledge the important achievements that we have gained through two decades of implementation of the Convention, we must not be complacent or naïve regarding the challenges we face today. The international community is at a critical juncture in the fight to maintain the international norm against chemical weapons use. I see three issues that have forced us to this precipice – the Assad regime's continued use of chemical weapons on its own people; the increased interest in and use of chemical weapons by non-State actors; and the growing concern that States are deliberately developing central nervous system (CNS)-acting chemicals for warfare or for other harmful purposes, cloaking these efforts under the guise of non-prohibited purposes such as law enforcement or medical research. I will address each of these issues. And, I have four recommendations that we in the international community should take to address them.

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First, let me start with the threat posed by the continued use of chemical weapons by a State Party to the Chemical Weapons Convention—Syria.

Chemical weapons use by the Syrian Arab Republic remains the most serious violation of the Chemical Weapons Convention in the Convention's twenty year history, and the greatest modern challenge to the global norm against chemical weapons use. The Syrian regime was found responsible by the OPCW-United Nations Joint Investigative Mechanism (JIM), an independent and impartial international body of experts, for three separate attacks using the toxic chemical chlorine as a chemical weapon in 2014 and 2015, and for the 4 April 2017, sarin attack in Khan Shaykhun, an opposition-held territory, where most of the victims were women and children. And the JIM would likely investigate numerous additional cases if the mandate were extended. The OPCW Fact-Finding Mission (FFM) has in front of it an additional 60 allegations of chemical weapons use in Syria to investigate. Syria's continued use of chemical weapons in blatant contravention of international law presumably continues because the Assad regime believes these weapons have military utility and psychological effect, and that they help the regime make gains in the ongoing civil war in Syria. While the civil war continues, we have seen the real effects on television – Syrian civilians with little to no defence against these abhorrent weapons dying in the streets. Use of chemical weapons is barbaric and must not be tolerated by the international community.

Second, I will turn to the increased interest in and use of chemical weapons by non-State actors.

The threat of non-State actor interest in development, acquisition, and use of chemical weapons is not a new challenge, but the threat is real, and the risks to our collective security are great. The technical pathway to a chemical weapon capability is clearly within the grasp of non-State actors. Non-State actors like ISIS are pursuing and using rudimentary chemical agents, like chlorine and mustard, in improvised explosive devices in Iraq and Syria. ISIS has used industrial chemicals and sulfur mustard in improvised explosive devices, mortars, and rockets in both Iraq and Syria. So far, the JIM has concluded that ISIS was responsible for two chemical weapons attacks using mustard, one in Marea in August 2015, and one in Um-Housh in September 2016. The counter ISIS campaign report detailed continued chemical weapons use in 2016 and 2017 beyond those attributed to ISIS by the JIM. Further, these actors are difficult to deter. While our ISIS-specific sanctions are important to limiting the outside support for these groups, non-State actors will continue to pose threats to international security because they shrug off accountability and the basic tenets of human decency. Chemical weapons terrorism can affect us all, and we must work together to stop it.

Finally, I would like to highlight the threat posed by central nervous system-acting chemicals, or so-called "incapacitants."

CNS-acting chemicals raise a new spectre of chemical weapons re-emergence. Since 2002, there has been a growing interest, evident through academic articles and press pieces, in the utility of these chemicals for law enforcement purposes. When it comes to these chemicals, the aerosolised use is not consistent with the law enforcement exception to the Chemical Weapons Convention as a purpose not prohibited by the Convention. President Trump recently announced that the opioid crisis in the United States of America is a public health emergency. As part of our response, the White House issued safety recommendations for first responders when handling and encountering fentanyl, the most well-known of the CNS-acting chemicals. If our first responders are at risk when they encounter illicit fentanyl,

how can our unsuspecting populations be safe when fentanyl is aerosolised and used as a law enforcement tool? The simple answer is that they cannot. Despite these dangers, countries continue to pursue these chemicals. If we do not seriously confront this issue here in The Hague, we would be turning a blind eye to the threat that CNS-acting chemicals pose to the Chemical Weapons Convention – a threat that will increase, not decrease, over time.

Call to Action

The international community must take action now or risk a reversal of a trend we have worked so hard to establish. We must take every opportunity to deter states from using chemical weapons. If we fail to take action now, non-State actor use will also rise. And, the number of countries pursuing nefarious CNS-acting chemical programmes will rise as well. We have made a commitment to put an end to chemical weapons use, and to fulfil that commitment, I recommend four concrete steps.

Step One: Hold Accountable Those Who Use Chemical Weapons

The international community must continue to take steps to hold the Syrian regime accountable for its chemical weapons use and take additional steps to deter future use. Holding the regime appropriately accountable would require effective United Nations Security Council and OPCW Executive Council action. But accountability cannot occur without appropriate resources. The United States of America has provided millions of dollars to the United Nations and OPCW trust funds set up specifically for the investigation of chemical weapons use in Syria. And we are not alone – the EU, Japan, and a number of other countries have made contributions to these funds, which have facilitated the OPCW and United Nation's ability to continue to investigate chemical weapons use in Syria. The Executive Council demonstrated accountability with the adoption of its 11 November 2016 decision, and it must do so again. While we sought an accountability resolution earlier this year at the United Nations, our efforts were undercut by Syria's ally the Russian Federation, which made a blatant decision to choose politics over human decency and our collective international obligations. The use of the veto has not deterred us, and many countries have enacted national sanctions on entities involved in the use of chlorine as a chemical weapon in Syria in 2014 and 2015, and we will again seek United Nations action on the latest JIM conclusions. We urge every State Party to condemn the use of chemical weapons by Syria and non-State actors. Unified condemnation and action are key to deterring future use and upholding the international norm against chemical weapons use. Everyone here in this room has a responsibility to respond to these atrocious acts.

Step Two: Full and Effective Implementation of Article VII of the Chemical Weapons Convention

The threat of non-State actor development, acquisition, and use of chemical weapons is a complex problem, and the response from the OPCW and States Parties – individually and collectively – must equal the challenge. We must fully and effectively implement our Chemical Weapons Convention Article VII obligations, specifically, comprehensive penal and export control legislation at the national level. This is the best way to ensure that there are no jurisdictions where non-State actors who commit or seek to commit chemical weapons-related crimes may seek safe harbour. Further, like-minded States Parties could share information regarding their relevant national domestic policies and laws. This would serve not only as a confidence-building measure, but would also strengthen the prohibitions

in the Convention and provide other stakeholders examples that could shorten their own routes to stronger national policies. Implementation of Article VII helps us deter not only those who would use chemical weapons but also those who would support them or provide them materials, knowledge, or a safe haven. It might deny terrorists or other non-State actors the tools they need to succeed and drive them away from these heinous weapons.

Step Three: Improve Chemical Defences

The international community should work to improve the defence of those populations most vulnerable to chemical weapons use. I specifically recommend providing support to the NGO medical community and to countries that may be a risk of attack, but are currently inadequately prepared to defend themselves. The establishment of the Rapid Response and Assistance Mission is an excellent step towards providing necessary assistance to States Parties affected by chemical weapons use, but we can do more. We should provide these entities training, defensive equipment, and appropriate medical countermeasures. Indeed, within the U.S. Government, the State Department has committed to providing up to USD 15 million in chemical weapons threat reduction equipment and training to medical personnel and first responders. I know we are not alone in wanting to improve our collective security and defence against chemical weapons use. Furthermore, denying those that would use these weapons their desired effect is, in itself, a deterrent to use.

Step Four: Endorse a CNS-acting Chemical Non-Use Policy Statement

Lastly, I call on States to endorse a non-use policy regarding aerosolisation of CNS-acting chemicals that reiterates the tenets of the Chemical Weapons Convention, to include that we are "determined for the sake of all mankind, to exclude completely the possibility of the use of chemical weapons." This endorsement would include international support recognising that the aerosolised use of CNS-acting chemicals is not consistent with law enforcement exception to the Chemical Weapons Convention. Together we can preserve the norm against chemical weapons use, but we have to do it now.

On 6 April 2017, President Trump said, "It is in the vital national security interest of the United States to prevent and deter the spread and use of deadly chemical weapons." I would argue that preventing the spread and use of chemical weapons is also strongly in the international community's security interest. It is important that the international community take steps now, such as those I have outlined, to improve the chances of deterring future use of chemical weapons.

Mr Chairperson, I request that this statement be considered an official document of the Twenty-Second Session of the Conference of the States Parties and posted on the external server.

Thank you.

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SECTION 6: FACTS AND BACKGROUND

I. Weapons of Mass Destruction Definition – Sept. 2019

18 U.S. Code § 2332a. Use of weapons of mass destruction

U.S. Code Notes

(a) Offense Against a or Within the United States.—A person who, without lawful authority, uses, threatens, or attempts or conspires to use, a weapon of mass destruction—

(1) against a national of the United States while such national is outside of the United States;

(2) against any person or property within the United States, and

(A) the mail or any facility of interstate or foreign commerce is used in furtherance of the offense;

(B) such property is used in interstate or foreign commerce or in an activity that affects interstate or foreign commerce;

(C) any perpetrator travels in or causes another to travel in interstate or foreign commerce in furtherance of the offense; or

(D) the offense, or the results of the offense, affect interstate or foreign commerce, or, in the case of a threat, attempt, or conspiracy, would have affected interstate or foreign commerce;

(3) against any property that is owned, leased or used by the United States or by any department or agency of the United States, whether the property is within or outside of the United States; or

(4) against any property within the United States that is owned, leased, or used by a foreign government,

shall be imprisoned for any term of years or for life, and if death results, shall be punished by death or imprisoned for any term of

years or for life.

(b) Offense by Outside of the United States.—
Any national of the United States who, without lawful authority, uses, or threatens, attempts, or conspires to use, a weapon of mass destruction outside of the United States shall be imprisoned for any term of years or for life, and if death results, shall be punished by death, or by imprisonment for any term of years or for life.

(c) Definitions.—For purposes of this section—

(1) the term "national of the United States" has the meaning given in section 101(a)(22) of the Immigration and Nationality Act (8 U.S.C. 1101(a)(22));

(2) the term "weapon of mass destruction" means—

(A) any destructive device as defined in section 921 of this title;

(B) any weapon that is designed or intended to cause death or serious bodily injury through the release, dissemination, or impact of toxic or poisonous chemicals, or their precursors;

(C) any weapon involving a biological agent, toxin, or vector (as those terms are defined in section 178 of this title); or

(D) any weapon that is designed to release radiation or radioactivity at a level dangerous to human life; and

(3) the term "property" includes all real and personal property.

(Added Pub. L. 103–322, title VI, § 60023(a), Sept. 13, 1994, 108 Stat. 1980; amended Pub. L. 104–132, title V, § 511(c), title VII, § 725, Apr. 24, 1996, 110 Stat. 1284, 1300; Pub. L. 104–294, title VI, § 605(m), Oct. 11, 1996, 110 Stat. 3510; Pub. L. 105–277, div. I, title II, § 201(b)(1), Oct. 21, 1998, 112 Stat. 2681–871; Pub. L. 107–188, title II, § 231(d), June 12, 2002, 116 Stat. 661; Pub. L. 108–458, title VI, § 6802(a), (b), Dec. 17, 2004, 118 Stat. 3766, 3767.)

SECTION 7: COUNTERMEASURES

A. LDRD Capture Annual Report (LDRD) – 2018

Cyclodextrin-Based Nanometer-Scale Scaffolds for Capture and Catalytic Degradation of Chemical Warfare Agents

Carlos Valdez (14-ERD-048)

Abstract

New technologies for capturing and catalytically degrading chemical weapon agents represent a critical national security need. This project addressed the use of molecular-complex scaffolds known as cyclodextrins that possess chemical and physical characteristics suitable for detection and analysis, decontamination, and medical countermeasures where the demand for broad-spectrum solutions is urgent. The project's dual components allowed us to obtain results with the overall goal of capturing and degrading chemical warfare agents. The first component focused on the synthesis and evaluation of zinc-based amino complexes that can be used as catalytic and stoichiometric entities for the destruction of organophosphorus-based compounds—that is, pesticides and nerve agents. The second component involved using carbohydrate-based scaffolds known as cyclodextrins as hosts for the capture and in some instances the degradation of toxic substances of interest in the chemical warfare arena as well as illicit, highly toxic substances such as fentanyls, which are potent, synthetic opioid pain medications.

Background and Research Objectives

An urgent need exists for the development of technologies directly aimed at high-priority chemical weapon agents in three areas: decontamination protocols, specificity of detection and analysis, and medical countermeasures. Current strategies to mitigate the environmental and physiological effects of exposure to chemical weapon agents have included complex biological solutions for patient care and stoichiometric, small-molecule approaches to surface decontamination. Our plan was to develop and validate an integrated experimental and computational approach for developing cyclodextrin-based nanometer-scale scaffolds for the capture and catalytic destruction of organophosphorus nerve agents and fentanyls. Successful technologies have been developed to mitigate individual issues for known chemical threats. However, establishing broadly applicable and rapidly responsive methodologies, targeted at known and more importantly emerging threats, remains critical. Although our research addressed the development of designer cyclodextrin molecules for two classes of agents, the foundation of our work was an integrated experimental and computational strategy for the discovery of efficacious cyclodextrins for broad-spectrum application.

Our project explored the use of cyclodextrins, which are supramolecular scaffolds possessing chemical and physical characteristics uniquely suitable for demonstrating the efficacy of this capability in the three areas described above. Our research focused on two classes of chemical warfare agents: the organophosphorus-based nerve agents and a series of incapacitating agents known as fentanyls. Both classes of agents are high priority given their ease of production and availability and their toxicity at very low doses. We planned to develop an understanding of the mechanism of action of fentanyl on protein receptors, which is key to the development of cyclodextrin for sequestration of these toxic chemicals. Elucidating conditions under which zinc-based organometallic catalysts most efficiently degrade organophosphorus agents provides insight into the development of effective metallocyclodextrins for decontamination. While the cyclodextrins themselves are important for mitigating organophosphorus- and fentanyl-specific threats, the development, demonstration, and validation of an integrated design approach capable of optimizing arbitrary host□–guest complexes was the central focus of our research.

Scientific Approach and Accomplishments

Synthesis of Fentanyl and Analogs

We completed the alternate and optimized syntheses of the parent opioid fentanyl and its analogs. After optimization studies were carried out for each synthetic step, the published routes exhibited high-yielding transformations leading to these powerful analgesics. The general three-step strategy produced a panel of four fentanyls in excellent yields (73–78%) along with their more commonly encountered hydrochloride and citric acid salts. The strategy offers the opportunity for the gram-scale, efficient production of these opioid alkaloids.

Kinetics and Speciation of Paraoxon Hydrolysis by Zinc(II)–Azamacrocyclic Catalysts

In this work, we investigated four zinc(II)-azamacrocyclic complexes for their ability to catalyze the hydrolysis of the toxic organophosphate pesticide diethyl paraoxon. Of the four complexes studied, zinc(II)-1,5,9-triaza-cyclododecane was found to be the most effective catalyst with a pseudo-first order reaction rate of k = 6.08 ± 0.23 x 10^{-4} min^{-1}. Using phosphorus-31 nuclear magnetic resonance spectroscopy, we identified the two products diethyl phosphate and ethyl (4-nitrophenyl) phosphate for both catalyzed and background hydrolysis of paraoxon. Reaction rate and selectivity for forming the non-toxic diethyl phosphate correlated with the catalyst's pK_a, which is a constant indicating the strengths of acids. We found that background hydrolysis at elevated reaction temperatures (50°C) displayed no preference for diethyl paraoxon over that of ethyl (4-nitrophenyl) phosphate, despite substantial differences between the pK_a values of the two leaving groups (ethoxide versus 4-nitrophenoxide anions). Kinetic rates for catalytic hydrolysis displayed an overwhelming propensity for diethyl paraoxon formation and suggest the importance of steric restrictions on transition state structure, namely a concerted arrangement of the azamacrocycle in opposition to the bulky 4-nitrophenoxy group.

Figure 1 shows the decrease in the phosphorus-31 signal intensity of paraoxon associated with the degradation of paraoxon by the four catalysts under study. Paraoxon degradation in the presence of the zinc(II)-1,5,9-triaza-cyclododecane catalyst occurred rapidly, compared to the other catalysts and the buffer. The cyclen-based complex displayed a slightly lower activity, while the cyclam-based complex displayed a small, but still enhanced activity.

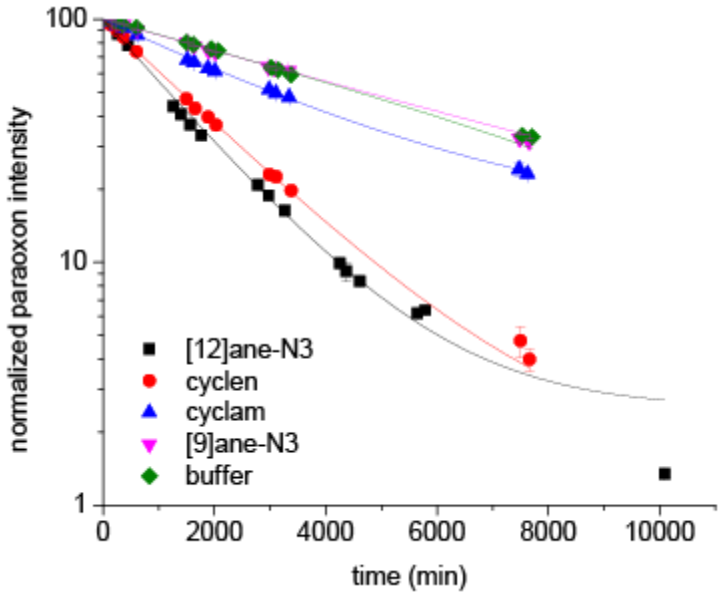

Figure 1. Degradation of paraoxon at initial pH of 8.1 (0.1 M of the buffer AMPSO) at 50°C in the presence of each catalyst and a control consisting of buffer alone.

Solution-State Structure and Affinities of Cyclodextrin:Fentanyl Complexes by Nuclear Magnetic Resonance Spectroscopy and Molecular Dynamics Simulation

We also investigated cyclodextrins for their ability to form inclusion complexes with the analgesic fentanyl and three similar molecules: acetylfentanyl, thiofentanyl, and acetylthiofentanyl. Stoichiometry, binding strength, and complex structure were revealed through nuclear magnetic resonance techniques and discussed in terms of molecular dynamics simulations. We found that β- cyclodextrin is generally capable of forming the strongest complexes with the fentanyl panel. We used two-dimensional nuclear magnetic resonance data and computational chemical calculations to derive solution-state structures of the complexes. Binding of the fentanyls to the cyclodextrins occurs at the amide phenyl ring, leaving the majority of the molecule solvated by water, an observation common to all four fentanyls.

Two-dimensional data using rotating frame nuclear Overhauser effect spectroscopy (ROESY) was employed to determine the proper choice of reporter protons in the fentanyl molecule. Figure 2(a) shows letter designations that

have been assigned to the base fentanyl protons, while Figure 2(b) shows the ROESY spectrum for β-cyclodextrin:fentanyl–hydrogen-chloride. The presence of cross-peaks between protons on the two molecules demonstrates definitively that association occurs, as the cutoff distant for the presence of ROESY peaks is roughly 5 to 6 Å. Particularly strong correlations are observed between protons on the amide end of the fentanyl and the interior H3 and H5 protons of cyclodextrin. Specifically, all five amide phenyl protons, labelled k to m in Figure (2a), have observable correlations with H3 and H5. The propionyl methyl and methylene groups, labelled i to j in Figure 2(a), also correlate to these protons, though more weakly. These peaks indicate that the amine half of fentanyl is buried within the cyclodextrin core. The essentially nonexistent cross-peaks between H3 and H5 and any protons on the phenethyl side chain of fentanyl lead us to conclude that it dangles above the H2/H3 rim of cyclodextrin and experiences relatively unrestricted mobility.

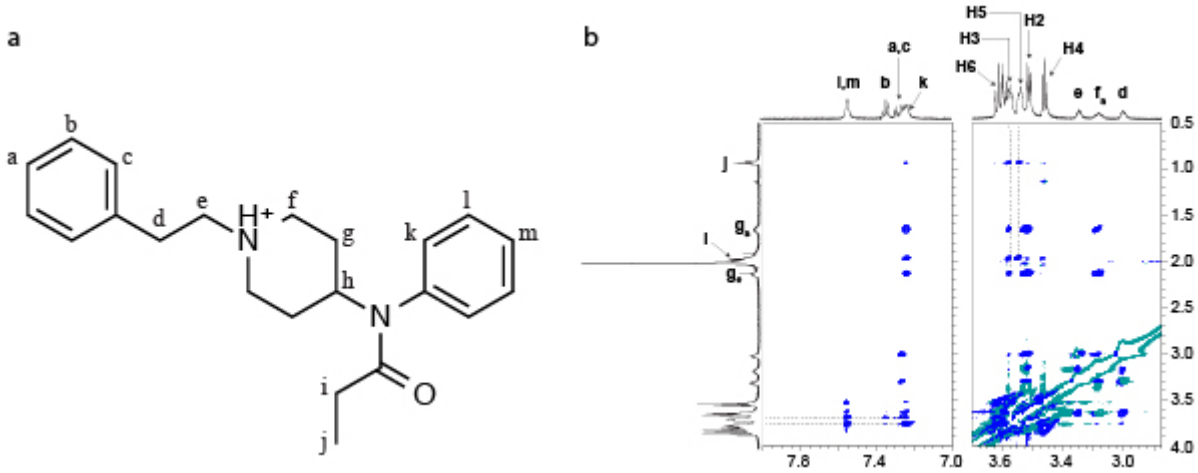

Figure 2. (a) Structure of the protonated fentanyl with protons labelled alphabetically and (b) proton−proton ROESY spectrum for 1:2 [β-cyclodextrin]:[fentanyl hydrogen-chloride], showing only the important chemical shift regions.

Discovery of Cyclodextrins with Even Higher Affinity for Fentanyl

In the follow-up work to our studies above, which yielded cyclodextrins exhibiting modest equilibrium binding affinities (*K* of approximately 100 to 200 M^{-1}) for fentanyl, we evaluated a library of newly synthesized cyclodextrin possessing extended thioalkylcarboxylate or thioalkylalcohol moieties. This library turned out to display remarkable affinity for fentanyl (*K* = 66,500 M^{-1}), the largest value reported for such complexes to date. Nuclear magnetic resonance experiments compounded with molecular dynamics simulations suggested an unexpected binding behavior where fentanyl binds in one of two distinct energetically favorable orientations (Figure 3). Binding energies derived from computational work were found to correlate strongly with affinities derived from nuclear magnetic resonance. These correlations signified the utility of this computational work as a predictive tool for the discovery of superior cyclodextrin binders in future follow-on work of the project. The significant performance of these host molecules portends their application as medical countermeasures for opioid exposure, as biosensors, and in other forensic platforms. The synthesized cyclodextrins are shown in Figure 3.

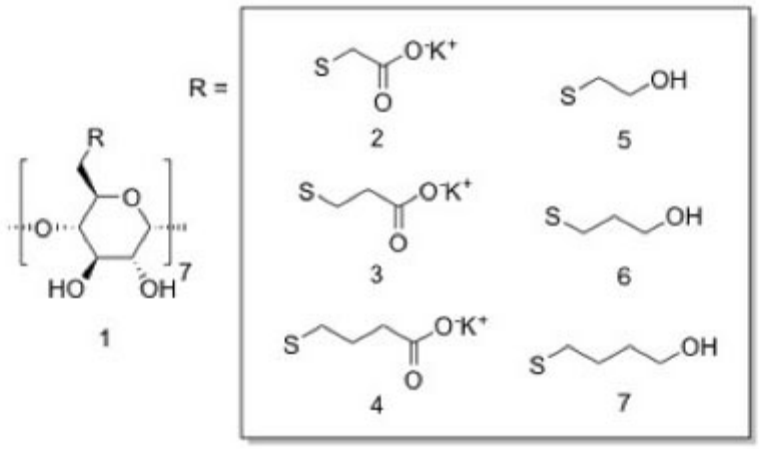

Figure 3. Basic structural scheme of a β-cyclodextrin with a primary, 6-position alcohol moiety replaced with a generalized R group (left). The box on the right shows the R group moieties investigated in this work (numbers associated with suβ indicate difference in carbon atoms in comparison to the R groups 3 and 6, while "n" denotes the hydroxylated analogue): (2) 2-mercaptoacetayl (suβ−1), (3) 3-mercaptopropionyl (suβ−0), (4) 4-mercaptobutanoyl (suβ+1), (5) 2-mercaptoethyl (suβ-1n), (6) 3-mercaptopropyl (suβ−0n), and (7) 4-mercaptobutyl (suβ+1n).

To visualize the complexes studied in the project, we conducted molecular dynamics simulations involving two distinct fentanyl orientations within the charged cyclodextrin, however, both fentanyl orientations within the cavity were shown to be favorable with relatively small differences in energies between the two possible conformations (0.8 to 5.8 kcal mol^{-1}), as shown in Figure 4(c). In the case of suβ−1, the orientation with the amide half of fentanyl pointed “down” toward the anionic chain ends is energetically favored over fentanyl in the opposite direction, as shown in Figure 4(a). Figure 4(b) shows that for suβ+1, the reversed configuration is favored with the amide half pointed “up” toward the unmodified secondary rim of cyclodextrin. For suβ−0, the two conformations are roughly equally favorable.

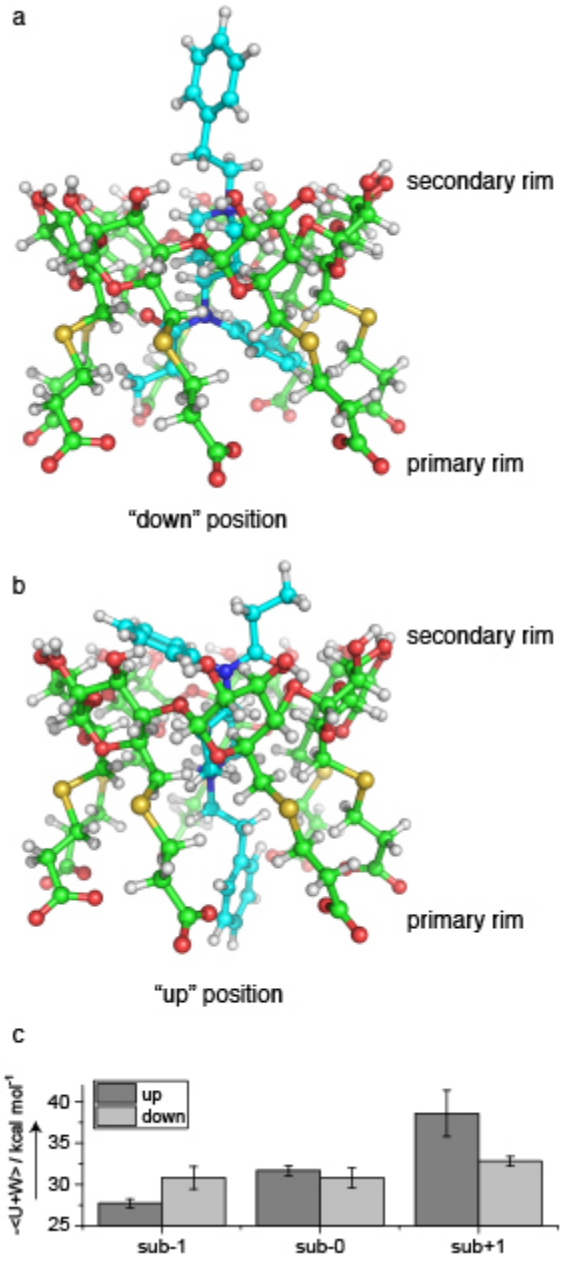

Figure 4. Molecular dynamic results for the host–guest complex with two orientations: (a) fentanyl, with the carbon atoms in cyan, aligned “down” with amide half near the primary rim of suβ−0, with carbon atoms in green; (b) fentanyl in alternate “up” position within suβ−0; and (c) binding energies for all three carboxylate subetadex complexes.

Accomplishments

During the course of this project, we:

- Obtained data on the binding affinities of a number of commercially available cyclodextrins and fentanyls. The binding constants for fentanyl and other congeners were obtained for their cyclodextrin complexes.[1]
- Discovered an efficient route to fentanyl and analogs thereof.[2]
- Initially identified a panel of zinc(II)-based azamacrocyclic scaffolds capable of catalyzing the destruction of organophosphorus-based nerve agents. The catalytic nature of these scaffolds was demonstrated using paraoxon as a test organophosphorus-based agent. With the aid of one- and two-dimensional nuclear magnetic resonance spectroscopy and phosphorus-31 nuclear magnetic resonance, we were able to identify two scaffolds that catalyzed the degradation of paraoxon, effectively thus providing support to their potential use as entities capable of degrading chemical warfare agents.[3]
- Identified better cyclodextrin scaffolds for fentanyl and its analogs. To this end, we identified and synthesized more complex cyclodextrins that can bind the drug with an affinity that is over 100 times that of commercially available cyclodextrins. These new thiocarboxylate-based cyclodextrins possess great affinity for fentanyl. Because of their nontoxic nature, these cyclodextrins could be potentially used to capture the drug from surfaces and contaminated environmental samples, and as a medical countermeasure against a drug overdose.
- Discovered that the same panel of zinc(II)-based azamacrocyclic scaffolds used against paraoxon also work relatively well against the nerve agent O-ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothioate (VX). Although they destroy the nerve agent stoichiometrically, they carry out its destruction in a region-selective manner yielding a nontoxic byproduct instead of the equally toxic EA-2192 byproduct.

The technologies developed were submitted as LLNL records of invention, and a total of three patent applications were produced from these records.[4-7]

Impact on Mission

Our strategy focused on the development of physical and medical countermeasures against fentanyls and organophosphorus nerve agents, which supports the Laboratory's strategic focus area in chemical and biological security for the rapid mitigation of evolving and unknown threats. This project also supported the LLNL core competency in bioscience and bioengineering by evolving an integrated computational and experimental capability for the rapid discovery of highly effective, broadly applicable scaffolds. This effort provides a foundation for future progress in environmental remediation technologies, exposure detection capabilities, and the production of advanced materials for use against known and emerging threats.

Conclusion

Our project team accomplished the goals initially set out for this project. Among those goals, we discovered and synthesized a powerful cyclodextrin core with high affinity for fentanyl that now opens new opportunities in scientific fields dealing with this drug such as medical countermeasures, decontamination protocol development, medical treatment and antidote development, and forensic science applications. The technologies we developed with this research resulted in three patent applications. We will continue to work with this newly identified scaffold and test its potential in binding other classes of drugs utilizing our established experimental and computational methods.

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SECTION 7: COUNTERMEASURES

B. Trubloc: Capture– Nov. 2019

THE NEW + THE NEXT

IS WEAPONIZED FENTANYL THE NEXT TERROR THREAT?

WHY YOU SHOULD CARE

Because it's not just users who can get sick from this drug.

The nightmare scenario for narcotics specialist John "Jake" Kelton goes as follows.

A man smuggles a pen filled with fentanyl onto a flight from New York to Los Angeles. Somewhere over Las Vegas, he flings the pen's contents into the aisle. A dozen passengers immediately fall unconscious. With fentanyl in their lungs, they'll have six minutes before they overdose.

"You're going to see panic at 37,000 feet," Kelton says. "You're not going to have enough Narcan to help everyone. You'd have to have *drums* of it. And the sad thing is, the pilot will never land that plane in time."

Excerpt From: https://www.ozy.com/the-new-and-the-next/the-cop-fighting-weaponized-fentanyl/224377/

Although it sounds like a psychological thriller, incidents of open-air fentanyl exposure have been recorded in increasing amounts since 2016, when the cheap, synthetic opioid exploded across the Midwest. That year, the Drug Enforcement Administration released a memo alerting police departments about fentanyl's threat in "small amounts." In March 2017, a patrol officer in East Liverpool, Ohio, Chris Green, had to be rushed to the emergency room after he brushed an "unknown powder" off his uniform. In August 2018, at the Ross Correctional Institution in Chillicothe, Ohio, 29 officers, first responders and nurses were sped to the hospital after an inmate blew three grams of heroin-fentanyl mix around his cell. Ross ran entirely out of lifesaving Narcan.

With police departments continuing to buff up their white powder policies, even as some experts warn the fears are overblown, the question of how to prevent a chemical disaster is not just a speculative pitch to Delta Air Lines executives. Catastrophes are already happening.

I PUT [A METH KINGPIN] IN JAIL FOR FIVE YEARS, AND I STILL GET CHRISTMAS CARDS FROM HIM EVERY YEAR.

JAKE KELTON

The idea arrived at 9:30 pm, June 14, 2017 — he remembers the precise time — when Kelton, 54, was staying at his second home in Bay St. Louis, Mississippi, training local law enforcement on "how to invest in meth labs and buy narcotics." On the news was a story about two patrol officers who had overdosed

Excerpt From: https://www.ozy.com/the-new-and-the-next/the-cop-fighting-weaponized-fentanyl/224377/

due to fentanyl exposure on the job. Kelton, who worked as a forensic scientist for the Pennsylvania State Police for nine years, was taken aback when the TV reporter said the substance went through the officers' skin.

"That's impossible," thought Kelton. He knew the exposure came from inhalation, not from touch. "That's like pulling a rhinoceros through a garden hose."

A week and a half later, he met with Tom Nachtman, a product manager for InstaCote in Erie, Michigan, urging him to reshape a "deployable spray" into a patented mist that could cover unidentified powders and stop them from dispersing into the air. In November 2017, Kelton finished a working prototype of Bloc: a 4-inch tall canister that could disperse (without air) a translucent orange mist that cures into a membrane. When the powder is under such a film, Kelton thought, any possibility of inhaling passive fentanyl would be completely eliminated.

Along with Nachtman, Kelton brought on a Cleveland, Ohio-based investor named Joe Lopez to try and sell Bloc to police chiefs across the country. Kelton, a father of three, put his career on hold. "We invested millions," he says. "Everything in my life is tied up by this right now."

A self-described black sheep of his family, Kelton grew up in Pittsburgh as a kid piqued by a life in the sciences. To fund a bachelor's degree at the University of California in chemistry and biology, he enlisted in the Marines as a police officer. A self-motivated fast talker, Kelton landed a job in 1996 as a forensic scientist with the Pennsylvania State Police in charge of everything from "prepping the SWAT teams to interviewing meth lab cooks." Starting in 2009, he led an undercover investigation into the Barber family, a $1 million ring of methamphetamine makers hidden in the hills of Mercer County. The resulting takedown of Rockne "Rocky" Barber and 60 other participants would earn Kelton an agent of the year award from the Pennsylvania Narcotic Officers' Association, and spark his nuanced philosophy on drug traffickers.

"When you first go in there, undercover, you think they're all bad people — but they're not," Kelton says. "Most of them are just like you or me." He smiles in a type of nostalgia. "I mean, I put [Barber] in jail for five years, and I still get Christmas cards from him every year."

Around the same time Barber was being arraigned, one of Kelton's nephews in Pittsburgh died from a heroin overdose. Appalled by the negligence, Kelton cut off contact with his family shortly after ("I've never even smoked a *joint*," Kelton claims). Since Bloc's official release in February, he spends most days managing the company out of his garage in Erie, Pennsylvania, or driving around neighboring states to convert hospital CEOs or college lab techs. He's sold Bloc in canister form ($40 a pop) to 28 police departments this year, and he says the federal Department of Homeland Security is considering a purchase for TSA agents.

The Painesville Police Department in Ohio was his first customer last November. The town of about 20,000 has seen fentanyl overdoses skyrocket from zero in 2015 to nearly 70 last year. Lieutenant Toby Burgett, who knew Kelton by reputation, bought 48 canisters. "He's been a narc guy for a while," Burgett says. "He knows drugs. And he knows what he's talking about — that this is scary."

Excerpt From: https://www.ozy.com/the-new-and-the-next/the-cop-fighting-weaponized-fentanyl/224377/

Kelton training the 94th CST (Citizen Support Team), customs and police in Guam, to investigate and process clandestine fentanyl operations.

But how legitimate is the scare? Critics often note that the media's reportage on exposure can be vague, and officer reactions may be psychosomatic. "We believe that such responses to passive casualties from fentanyl are excessive," Lewis Nelson and Jeanmarie Perrone, two university experts in emergency medicine, wrote for health policy site STAT News. "[They] may actually interfere with the ability of first responders and others to do their jobs." (Nelson and Perrone did not respond to calls for comment.)

Kelton maintains the fentanyl exposure fears are real and says he'll "calmly debate" anyone who tries to prove otherwise (he once deactivated Bloc's Twitter page due to "total bullshit" needless arguments with strangers). He's easily irritated by the status quo for officers but thinks this problem is bigger: He wants to get it on the radar for the Centers for Disease Control and major airlines.

"People said the same thing about the bulletproof vest when it came out," Kelton says. "And, well, look how that turned out."

Mark Oprea, OZY Author

SECTION 7: COUNTERMEASURES

C. Decon7: Decontamination – Nov. 2018

Corrections Products -- Corrections Fentanyl Protection

Defend yourself against exposure to drugs and diseases with a ready-to-use decontamination spray

The BDAS+ from Decon7 provides a tool to help COs reduce potential exposure to infectious diseases and dangerous narcotics like fentanyl

Nov 13, 2018

Sponsored by Decon7 Systems

By CorrectionsOne BrandFocus Staff

Corrections officers deal with plenty of nasty stuff in a day's work, but too often the toxic effects created by exposure to contraband drugs or bodily fluids take a backseat to managing the incident and restoring order.

Gloves, soap and water simply aren't enough to prevent harmful effects from exposure to drugs like fentanyl. The D7 decontamination formula from Decon7 Systems can neutralize these hazards and comes in the ready-to-use BDAS+ spray unit as well as bulk liquid. (image/Decon7 Systems)

Gloves, soap and water simply aren't enough. What can COs do to avoid exposure to dangerous narcotics like fentanyl or infectious diseases when they have to deal with a contaminated scene?

You need a solution that will neutralize germs and the toxic properties of drugs, not just remove them from your hands to a towel or sink where they remain a hazard.

Decon7 Systems provides the patented D7 formula, which can neutralize toxic or infectious hazards posed from threats like fentanyl and bloodborne pathogens like hepatitis within minutes. The decontamination solution is available in the ready-to-use BDAS+ unit as well as bulk liquid and laundry.

A READY-TO-USE DECONTAMINATION TOOL

Washing with soap and water can remove contaminants from a surface, such as your hands or the floor of a cell, but it doesn't eliminate potential threats like bacteria or trace drug residue.

Unlike most decontamination products that must be mixed at the time of use, The BDAS+ provides the detergent, neutralization and accelerant in a single package and mixes them for one-step application. Simply pull the yellow safety tab from the nozzle, point it at the surface to be decontaminated, then pull the trigger.

"Officers have more important things to worry about than spending 10 or 20 minutes preparing and mixing a decontaminant that they need on the spot and not well after the fact," said Joe Hill, vice president of defense and public safety for Decon7. "With the BDAS+, you can pull a ready-to-use unit and spray it. There's no manual mixing."

The handheld unit, which weighs less than 2 pounds, can be kept on hand and deployed within seconds when needed. In addition to enabling rapid response, the BDAS+ eliminates potential for human error because it automatically mixes the solution's three components.

HOW DOES IT WORK?

Once the D7 solution is mixed and applied to a surface and in contact with the threat, the neutralization process begins. The formula disinfects, decomposes and partially digests pathogens like bacteria and viruses and breaks down contaminants like fentanyl and other drugs. Positively charged micelles, or clusters of molecules, draw germs and contaminants into the liquid, where the hazard is chemically altered to render the mess harmless in a matter of minutes.

D7 can reduce the number of germs present by at least 1 million times, and tactically relevant testing shows that the formula eliminates more than 99.9 percent of fentanyl in under seven minutes. The formula is not flammable, is minimally corrosive and is environmentally friendly.

"It's about as corrosive as the shampoo you use on your hair," said Hill. "The process ends with a final neutral pH."

SAFE FOR FREQUENT USE

While chlorine and bleach solutions will neutralize many biological and chemical agents, the runoff of these solutions is still hazardous. Also, bleach itself is highly corrosive and can cause damage to many surfaces, particularly plastics. Alcohol and ammonia present similar inhalation hazards and potential damage to surfaces.

Excerpt From: https://www.correctionsone.com/products/fentanyl-protection/articles/defend-yourself-against-exposure-to-drugs-and-diseases-with-a-ready-to-use-decontamination-spray-Ubk8FwwEnCgv4Nk9/

D7 can kill most pathogens – without harmful fumes like bleach – and neutralize dangerous narcotics like fentanyl by breaking them down into nontoxic substances. The formula is safe to apply on a variety of surfaces, including plastics and metals, and it creates no noxious fumes or odors.

Although D7 complies with environmental regulations, D7 is not FDA-approved for skin application. Users should wear gloves and goggles, plus a mask and protective clothing when applying the solution in close quarters.

PROTECT YOUR HEALTH

D7 also eradicates smells, a definite plus in close quarters like a jail or prison.

“If you can smell it, you are being exposed,” said Hill. “D7 attacks the source of the smells, whether it’s from vomit, feces or urine, and in doing so neutralizes the health threat officers are being exposed to.”

In addition to instant application with the BDAS+ unit, the bulk D7 solution can be applied with a foaming apparatus, low-pressure sprayer, mop or soaking system as well. Fogging can be especially effective for deodorization, whether in a cell or the infirmary.

“If you fog a cell with D7, in addition to applying D7 to the gross contamination from the BDAS+ or another applicator, not only are you removing the odor, you are also removing what causes the odor, both in the air and on any surfaces,” said Hill.

Corrections officers face numerous threats on the job, including exposure to hazardous narcotics like fentanyl and infectious diseases like hepatitis. Make sure you have adequate protection and decontamination tools so you can protect yourself from these threats.

SECTION 7: COUNTERMEASURES

D. Naloxone: Revive – Nov. 2019

Naloxone

From Wikipedia, the free encyclopedia

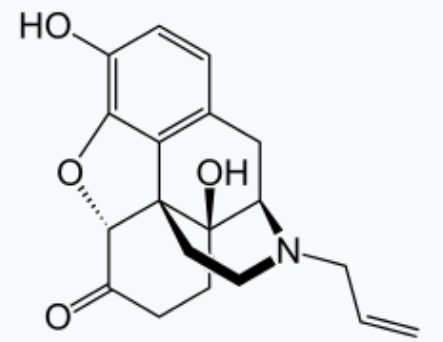
Not to be confused with Naltrexone.

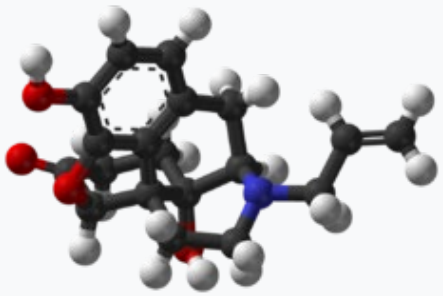
Naloxone, sold under the brand name **Narcan** among others, is a medication used to block the effects of opioids .[1] It is commonly used for decreased breathing in opioid overdose .[1] Naloxone may also be combined with an opioid (in the same pill) to decrease the risk of opioid misuse.[1] When given intravenously , naloxone works within two minutes, and when injected into a muscle, it works within five minutes;[1] it may also be sprayed into the nose.[3] The effects of naloxone last about half an hour to an hour.[4] Multiple doses may be required, as the duration of action of most opioids is greater than that of naloxone.[1]

Administration to opioid-dependent individuals may cause symptoms of opioid withdrawal , including restlessness, agitation, nausea, vomiting, a fast heart rate, and sweating.[1] To prevent this, small doses every few minutes can be given until the desired effect is reached.[1] In those with previous heart disease or taking medications that negatively affect the heart, further heart problems have occurred.[1] It appears to be safe in pregnancy, after having been given to a limited number of women.[5] Naloxone is a non-selective and competitive opioid receptor antagonist.[6][7] It works by reversing the depression of the central nervous system and respiratory system caused by opioids.[1]

Naloxone was patented in 1961 and approved for opioid overdose in the United States in 1971.[8] It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system.[9] Naloxone is available as a generic medication.[1] Its wholesale price in developing countries is between $0.50 and $5.30 per dose.[10] Vials of naloxone are not very expensive (less than $25) in the United States.[11] However, the price for a package of two auto-injectors in the US has increased from $690 in 2014 to $4,500 in 2016.[12] The 2018 price for the NHS in the [13]

Naloxone





Clinical data	
Trade names	Narcan, Evzio, others
Other names	EN-1530; *N*-Allylnoroxymorphone; 17-Allyl-4,5α-epoxy-3,14-dihydroxymorphinan-6-one
AHFS/Drugs.com	Monograph
License data	EU EMA: by INN
Pregnancy category	AU: B1 US: C (Risk not ruled out) [1]
Routes of administration	Endotracheal, intranasal, IV, IM, IO
ATC code	A06AH04 (WHO) V03AB15 (WHO)
Legal status	
Legal status	AU: S3 (Pharmacist only) [2] DE: § 48 AMG/§ 1 MPAV (Prescription only) UK: POM (Prescription only) US: R-only
Pharmacokinetic data	

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Edit links

United Kingdom is about £5 per dose. In Australia, a single dose without prescription costs AU$20 while with a prescription five doses is AU$40.[14]

Contents [hide]

Bioavailability	2% (by mouth , 90% absorption but high first-pass metabolism) 50% (intranasally)
Metabolism	Liver
Onset of action	2 min (IV), 5 min (IM)[1]
Elimination half-life	1–1.5 h
Duration of action	30–60 min [1]
Excretion	Urine, bile
Identifiers	
IUPAC name	[show]
CAS Number	465-65-6
PubChem CID	5284596
IUPHAR/BPS	1638
DrugBank	DB01183
ChemSpider	4447644
UNII	36B82AMQ7N
KEGG	D08249
ChEBI	CHEBI:7459
ChEMBL	ChEMBL80
CompTox Dashboard (EPA)	DTXSID8023349
ECHA InfoCard	100.006.697
Chemical and physical data	
Formula	$C_{19}H_{21}NO_4$
Molar mass	327.380 $g \cdot mol^{-1}$
3D model (JSmol)	Interactive image
SMILES	[show]
InChI	[show]

(what is this?) (verify)

Medical uses [edit]

Opioid overdose [edit]

Naloxone is useful in treating both acute opioid overdose and respiratory or mental depression due to opioids.[1] Whether it is useful in those in cardiac arrest due to an opioid overdose is unclear.[15]

A naloxone kit as distributed in British Columbia, Canada

It is included as a part of emergency overdose response kits distributed to heroin and other opioid drug users and emergency responders. This has been shown to reduce rates of deaths due to overdose.[16] A prescription for naloxone is recommended if a person is on a high dose of opioid (>100 mg of morphine equivalence/day), is prescribed any dose of opioid accompanied by a benzodiazepine , or is suspected or known to use opioids nonmedically.[17] Prescribing naloxone should be accompanied by standard education that includes preventing, identifying, and responding to an overdose; rescue breathing; and calling emergency services.[18]

If minimal or no response is observed within 2–3 minutes, dosing may be repeated every 2 minutes until the maximum dose of 10 mg has been reached. If no response occurs at this time, alternative diagnosis and treatment should be pursued. Depending on the severity of overdose, a high dose exceeding 10 mg may be needed.[19] The effects of naloxone may wear off before those of the opioids, and they may require repeat dosing at a later time. Patients experiencing effects should be monitored for respiratory rate, heart rate, blood pressure, temperature, ABGs and level of consciousness. Those with a greater risk for respiratory depression should be identified prior to administration and watched closely.[20]

Clonidine overdose [edit]

Naloxone can also be used as an antidote in overdose of clonidine , a medication that lowers blood pressure.[21] Clonidine overdoses are of special relevance for children, in whom even small doses can cause significant harm.[22] However, there is controversy regarding naloxone's efficacy in treating the symptoms of clonidine overdose, namely slow heart rate , low blood pressure , and confusion/somnolence .[22] Case reports that used doses of 0.1 mg/kg (maximum of 2 mg/dose) repeated every 1–2 minutes (10 mg total dose) have shown inconsistent benefit.[22] As the doses used throughout the literature vary, it is difficult to form a conclusion regarding the benefit of naloxone in this setting.[23] The mechanism for naloxone's proposed benefit in clonidine overdose is unclear, but it has been suggested that endogenous opioid receptors mediate the sympathetic nervous system in the brain and elsewhere in the body.[23] Some poison control centers recommend naloxone in the setting of clonidine overdose, including intravenous bolus doses of up to 10 mg naloxone.[24][25]

Preventing opioid abuse [edit]

Naloxone is poorly absorbed when taken by mouth, so it is commonly combined with a number of oral opioid preparations, including buprenorphine and pentazocine , so that when taken by mouth, only the opioid has an effect.[1][26] However, if the opioid and naloxone combination is injected, the naloxone blocks the effect of the opioid.[1][26] This combination is used in an effort to prevent abuse.[26]

Other uses [edit]

In people with shock , including septic , cardiogenic, hemorrhagic, or spinal shock, those who received naloxone had improved blood flow. The importance of this is unclear.[27]

Naloxone is also experimentally used in the treatment for congenital insensitivity to pain with anhidrosis ,[28] an extremely rare disorder that renders one unable to feel pain or differentiate temperatures.[29]

Naloxone can also be used to treat itchiness brought on by opioid use,[30] as well as opioid-induced constipation.[31]

Special populations [edit]

Pregnancy and breastfeeding [edit]

Naloxone is pregnancy category B or C in the United States. [1] Studies in rodents given a daily maximum dose of 10 mg naloxone showed no harmful effects to the fetus, although human studies are lacking and the drug does cross the placenta , which may lead to the precipitation of withdrawal in the fetus. In this setting, further research is needed before safety can be assured, so naloxone should be used during pregnancy only if it is a medical necessity.[32]

Whether naloxone is excreted in breast milk is unknown, however, it is not orally bioavailable and therefore is unlikely to affect a breastfeeding infant. [33]

Children [edit]

Naloxone can be used on infants who were exposed to intrauterine opiates administered to mothers during delivery. However, there is insufficient evidence for the use of naloxone to lower cardiorespiratory and neurological depression in these infants.[34] Infants exposed to high concentrations of opiates during pregnancy may have CNS damage in the setting of perinatal asphyxia . Naloxone has been studied to improve outcomes in this population, however the evidence is currently weak.[35][36]

Intravenous, intramuscular, or subcutaneous administration of naloxone can be given to children and neonates to reverse opiate effects. The American Academy of Pediatrics recommends only intravenous administration as the other two forms can cause unpredictable absorption. After a dose is given, the child should be monitored for at least 24 hours. For children with low blood pressure due to septic shock , naloxone safety and effectiveness is not established.[37]

Geriatric use [edit]

For patients 65 years and older, unclear if there is a difference in response. However, older people often have decreased liver and kidney function that may lead to an increased level of naloxone in their body.[38]

Side effects [edit]

Naloxone has little to no effect if opioids are not present. In people with opioids in their system, it may cause increased sweating, nausea, restlessness, trembling, vomiting, flushing, and headache, and has in rare cases been associated with heart rhythm changes, seizures , and pulmonary edema .[39][40]

Besides the side effects listed above, naloxone also has other adverse events, such as other cardiovascular effects (hypertension, hypotension, tachycardia, ventricular fibrillation, ventricular tachycardia) and central nervous system effects, such as agitation, body pain, brain disease, and coma. In addition to these adverse effects, naloxone is also contraindicated in people with hypersensitivity to naloxone or any of its formulation components.[41]

Naloxone has been shown to block the action of pain-lowering endorphins the body produces naturally. These endorphins likely operate on the same opioid receptors that naloxone blocks. It is capable of blocking a placebo pain-lowering response, if the placebo is administered together with a hidden or blind injection of naloxone.[42] Other studies have found that placebo alone can activate the body's μ-opioid endorphin system, delivering pain relief by the same receptor mechanism as morphine.[43][44]

Naloxone should be used with caution in people with cardiovascular disease as well as those that are currently taking medications that could have adverse effects on the cardiovascular system such as causing low blood pressure , fluid accumulation in the lungs (pulmonary edema), and abnormal heart rhythms . There have been reports of abrupt reversals with opioid antagonists leading to pulmonary edema and ventricular fibrillation.[45]

Hypersensitivities [edit]

Naloxone preparations may contain methylparaben and propylparaben and is inappropriate for use by people with a paraben hypersensitivity. If a person is sensitive to nalmefene or naltrexone , naloxone should be used with caution as these three medications are structurally similar. Cross-sensitivity among these drugs is unknown.[46] Preservative-free preparations are available for those with paraben hypersensitivities.

Pharmacology [edit]

Pharmacodynamics [edit]

Naloxone is a lipophilic compound that acts as a non-selective and competitive opioid receptor antagonist.[6][7] The pharmacologically active isomer of naloxone is (−)-naloxone.[48][50]

Naloxone at opioid receptors

Compound	Affinities (K_i)			Ratio	Ref
	MOR	DOR	KOR	MOR:DOR:KOR	
Naloxone	1.1 nM	16 nM	12 nM	1:15:11	[47]
(−)-Naloxone	0.559 nM 0.93 nM	36.5 nM 17 nM	4.91 nM 2.3 nM	1:65:9 1:18:2	[48] [49]
(+)-Naloxone	3,550 nM 1,000 nM	122,000 nM 1,000 nM	8,950 nM 1,000 nM	1:34:3 ND	[48] [49]

Naloxone's binding affinity is highest for the μ-opioid receptor, then the δ-opioid receptor, and lowest for the κ-opioid receptor;[6] naloxone has negligible affinity for the nociceptin receptor .[51]

If naloxone is administered in the absence of concomitant opioid use, no functional pharmacological activity occurs, except the inability for the body to combat pain naturally. In contrast to direct opiate agonists, which elicit opiate withdrawal symptoms when discontinued in opiate-tolerant people, no evidence indicates the development of tolerance or dependence on naloxone. The mechanism of action is not completely understood, but studies suggest it functions to produce withdrawal symptoms by competing for opiate receptor sites within the CNS (a competitive antagonist, not a direct agonist), thereby preventing the action of both endogenous and xenobiotic opiates on these receptors without directly producing any effects itself.[52]

Pharmacokinetics [edit]

When administered parenterally (nonorally or nonrectally, e.g. intravenously or by injection), as is most common, naloxone has a rapid distribution throughout the body. The mean serum half life has been shown to range from 30 to 81 minutes, shorter than the average half life of some opiates, necessitating repeat dosing if opioid receptors must be stopped from triggering for an extended period. Naloxone is primarily metabolized by the liver. Its major metabolite is naloxone-3-glucuronide, which is excreted in the urine.[52] For people with liver diseases such as alcoholic liver disease or hepatitis , naloxone usage has not been shown to increase serum liver enzyme levels.[53]

Naloxone has low systemic bioavailability when taken by mouth due to hepatic first pass metabolism, but it does block opioid receptors that are located in the intestine.[31]

Chemistry [edit]

Naloxone, also known as N-allylnoroxymorphone or as 17-allyl-4,5α-epoxy-3,14-dihydroxymorphinan-6-one, is a synthetic morphinan derivative and was derived from oxymorphone (14-hydroxydihydromorphinone), an opioid analgesic.[54][55][56] Oxymorphone, in turn, was derived from morphine , an opioid analgesic and naturally occurring constituent of the opium poppy.[57] Naloxone is a racemic mixture of two enantiomers , (–)-naloxone (levonaloxone) and (+)-naloxone (dextronaloxone), only the former of which is active at opioid receptors.[58][59] The drug is a highly lipophilic, allowing it to rapidly penetrate the brain and to achieve a far greater brain to serum ratio than that of morphine.[54] Opioid antagonists related to naloxone include cyprodime , nalmefene , nalodeine , naloxol , and naltrexone .[60]

The chemical half-life of naloxone is such that injection and nasal forms have been marketed with 24-month and 18-month shelf-lives, respectively.[61] A 2018 study noted that the nasal and injection forms presented

as chemically stable to 36- and 28-months, respectively, which prompted an as yet incomplete five year stability study to be initiated.[61] This suggests that expired caches of material in community and healthcare settings may still be efficacious substantially beyond their labeled expiration dates.[61]

History [edit]

Naloxone was patented in 1961 by Mozes J. Lewenstein, Jack Fishman, and the company Sankyo .[8] It was approved for opioid abuse treatment in 1971 by the FDA with opioid abuse kits being distributed by many states to medically untrained people beginning in 1996. From the period of 1996 to 2014, the CDC estimates over 26,000 cases of opioid overdose have been reversed using the kits.[62]

Society and culture [edit]

Names [edit]

Naloxone is the generic name of the medication and its INN, BAN, DCF, DCIT, and JAN, while *naloxone hydrochloride* is its USAN and BANM.[63][64][65][66]

The patent has expired and it is available as a generic medication . Brand names of naloxone include Narcan, Nalone, Evzio, Prenoxad Injection, Narcanti, Narcotan, among others.

Identification [edit]

The CAS number of naloxone is 465-65-6; the anhydrous hydrochloride salt has CAS 357-08-4 and the hydrochloride salt with 2 molecules of water, hydrochloride dihydrate, has CAS 51481-60-8

Routes of administration [edit]

Intravenous [edit]

Naloxone is commonly injected intravenously , with an onset of 1–2 minutes and a duration of up to 45 minutes.[67] While the onset is achieved fastest through IV than through other routes of administration, it may be difficult to obtain venous access in patients who use IV drugs chronically. This may be an issue under emergency conditions.[68]

Intramuscular or subcutaneous [edit]

Naloxone can also be administered via intramuscular or subcutaneous injection. The onset of naloxone provided through this route is 2 to 5 minutes with a duration of around 30-120min.[69] Naloxone administered intramuscularly are provided through pre-filled syringes, vials, and auto-injector. Evzio is the only auto-injector on the market and can be used both intramuscularly and subcutaneously. It is pocket-sized and can be used in non-medical settings such as in the home.[15] It is designed for use by laypersons, including family members and caregivers of opioid users at-risk for an opioid emergency, such as an overdose.[70] It is speculated that a generic version will be available mid 2019 in the US.[71]

Intranasal [edit]

Administration of naloxone intranasally is recommended for people are unconscious or unresponsive.[69] While the onset of action is slightly delayed in this method of administration, the ease of use and portability are what make naloxone nasal sprays useful.[67][69] Narcan Nasal Spray was approved in 2015 and was the first FDA-approved nasal spray for emergency treatment or suspected overdose.[72] Narcan Nasal Spray is prepackaged, requires no assembly, and delivered a consistent dose.[73] It was developed in a partnership [74]

between LightLake Therapeutics and the National Institute on Drug Abuse. The approval process was fast-tracked.[75] A generic version of the nasal spray was approved in the United States in 2019.[76]

However, a wedge device (nasal atomizer) can also be attached to a syringe that may also be used to create a mist to deliver the drug to the nasal mucosa .[77] This is useful near facilities where many overdoses occur that already stock injectors.[78]

Storage [edit]

Naloxone should be stored at room temperature and protected from light. For the auto-injector, naloxone should be stored in the outer case provided.[79] If the product is cloudy, discolored, or contains particulate matter, use is not recommended.[46]

Legal status [edit]

In the United States , naloxone is available without a prescription in every state with the exception of Hawaii.[80][81] However, not all pharmacies stock or dispense naloxone.[82][83] Depending on the pharmacy, a pharmacist may have to write a prescription or not be able to give naloxone to comply with accounting rules regarding prescription medications, as naloxone is still considered a prescription only medication under FDA rules.

While paramedics have carried naloxone for decades, law enforcement officers in many states throughout the country carry naloxone to reverse the effects of heroin overdoses when reaching the location prior to paramedics. As of July 12, 2015, law enforcement departments in 28 states are allowed to or required to carry naloxone to quickly respond to opioid overdoses.[84]

In Australia, as of February 1, 2016, naloxone is now available "over the counter" in pharmacies without a prescription.[85] It comes in single-use filled syringe similar to law enforcement kits.

In Canada, naloxone single-use syringe kits are distributed and available at various clinics and emergency rooms. Alberta Health Services is increasing the distribution points for naloxone kits at all emergency rooms, and various pharmacies and clinics province-wide. Also in Alberta , take-home naloxone kits are available and commonly distributed in most drug treatment or rehabilitation centres, as well as in pharmacies where pharmacists can distribute single-use take-home naloxone kits or prescribe the drug to addicts. All Edmonton Police Service and Calgary Police Service patrol cars carry an emergency single-use naloxone syringe kit. Some Royal Canadian Mounted Police patrol vehicles also carry the drug, occasionally in excess to help distribute naloxone among users and concerned family/friends. Nurses, paramedics, medical technicians, and emergency medical responders can also prescribe and distribute the drug.

Following Alberta Health Services, Health Canada reviewed the prescription-only status of naloxone, resulting in plans to remove it in 2016, allowing naloxone to be more accessible.[86][87] Due to the rising number of drug deaths across the country, Health Canada proposed a change to make naloxone more widely available to Canadians in support of efforts to address the growing number of opioid overdoses.[88] In March 2016, Health Canada did change the prescription status of naloxone, as "pharmacies are now able to proactively give out naloxone to those who might experience or witness an opioid overdose."[89]

Prehospital access [edit]

Laws in many jurisdictions have been changed in recent years to allow wider distribution of naloxone.[90][91] Several states have also moved to permit pharmacies to dispense the medication without the person first seeing a physician or other non-pharmacist professional.[92] Over 200 naloxone distribution programs utilize licensed prescribers to distribute the drug, often through the use of standing medication orders [93][94]

whereby the medication is distributed under the medical authority of a physician or other prescriber (such as a pharmacist under California's AB1535). Additionally, 36 states have passed laws that provide naloxone prescribers with immunity against both civil and criminal liabilities.[95] Third-party prescriptions are also available for people, such as family and friends of people at risk for an overdose, who may find themselves in a situation that requires them to administer naloxone. Local schools, government agencies, and nonprofit organizations hold training programs to educate laypeople on proper use of naloxone. It is estimated that programs like these have helped to reverse more than 26,000 overdoses.[95]

Following the use of the nasal spray device by police officers on Staten Island in New York, an additional 20,000 police officers will begin carrying naloxone in mid-2014. The state's Office of the Attorney General will provide US$1.2 million to supply nearly 20,000 kits. Police Commissioner William Bratton said: "Naloxone gives individuals a second chance to get help".[96] Emergency Medical Service Providers (EMS) routinely administer naloxone, except where basic Emergency Medical Technicians are prohibited by policy or by state law.[97] In efforts to encourage citizens to seek help for possible opioid overdoses, many states have adopted Good Samaritan laws that provide immunity against certain criminal liabilities for anybody who, in good faith, seeks emergency medical care for either themselves or someone around them who may be experiencing an opioid overdose.[98]

A survey of US naloxone prescription programs in 2010 revealed that 21 out of 48 programs reported challenges in obtaining naloxone in the months leading up to the survey, due mainly to either cost increases that outstripped allocated funding or the suppliers' inability to fill orders.[99] The approximate cost of a 1 ml ampoule of naloxone in the US is estimated to be significantly higher than in most Western countries.[93]

Projects of this type are under way in many North American cities.[99][100] CDC estimates that the US programs for drug users and their caregivers prescribing take-home doses of naloxone and training on its use have prevented 10,000 opioid overdose deaths.[99] States including Vermont and Virginia have developed programs that mandate the prescription of naloxone when a prescription has exceeded a certain level of morphine milliequivalents per day as preventative measures against overdose.[101] Healthcare institution-based naloxone prescription programs have also helped reduce rates of opioid overdose in North Carolina , and have been replicated in the US military.[93][102] Programs training police and fire personnel in opioid overdose response using naloxone have also shown promise in the US, and effort is increasing to integrate opioid fatality prevention in the overall response to the overdose crisis.[103][104][105][106]

Pilot projects were also started in Scotland in 2006. Also in the UK, in December 2008, the Welsh Assembly government announced its intention to establish demonstration sites for take-home naloxone.[107]

As of February 2016, Pharmacies across Alberta and some other Canadian jurisdictions are allowed to distribute take-home naloxone kits. Additionally, the Minister of Health issued an order to change basic life support provider's medical scope, within EMS, to administer naloxone in the event of a suspected narcotic overdose. These are part of the government's plan to tackle a growing fentanyl drug crisis. [108]

In 2018, a maker of naloxone announced it would provide a free kit including two doses of the nasal spray, as well as educational materials, to each of the 16,568 public libraries and 2,700 YMCAs in the U.S.[109]

Media [edit]

The 2013 documentary film *Reach for Me: Fighting to End the American Drug Overdose Epidemic* interviews people involved in naloxone programs aiming to make naloxone available to opioid users and people with chronic pain .[110]

See also [edit]

- Oxycodone/naloxone
- Buprenorphine/naloxone

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External links [edit]

- Chicago Recovery Alliance's naloxone distribution project
- Report on Naloxone and other opiate antidotes , by the International Programme on Chemical Safety
- What Is Naloxone? via Substance Abuse and Mental Health Services Administration| SAMHSA
- Naloxone Overdose Prevention Laws | PDAPS.org

v · t · e **Antidotes (V03AB)** [show]

v · t · e **Opioid receptor modulators** [show]

v · t · e **Sigma receptor modulators** [show]

Medicine portal

Categories : Tertiary alcohols | Allyl compounds | Antidotes | Chemical substances for emergency medicine | GABAA receptor negative allosteric modulators | Kappa antagonists | Ketones | Morphinans | Opioid antagonists | Phenol ethers | Sigma antagonists | World Health Organization essential medicines

SECTION 7: COUNTERMEASURES

E. Naltrexone: Block – Oct. 2019

Naltrexone

From Wikipedia, the free encyclopedia

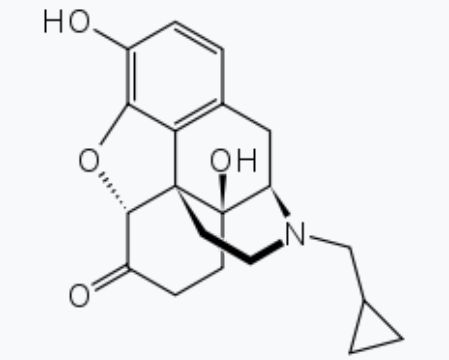
Not to be confused with Naloxone or Nalmexone.

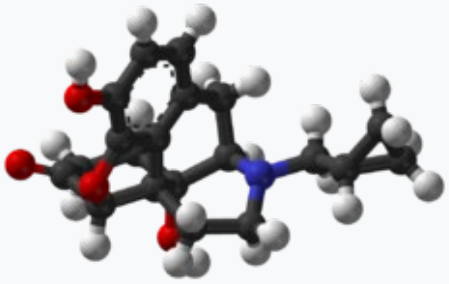
Naltrexone, sold under the brand names **ReVia** and **Vivitrol** among others, is a medication primarily used to manage alcohol or opioid dependence.[1] An opioid-dependent person should not receive naltrexone before detoxification.[1] It is taken by mouth or by injection into a muscle.[1] Effects begin within 30 minutes.[1] A decreased desire for opioids, though, may take a few weeks.[1]

Side effects may include trouble sleeping, anxiety, nausea, and headaches.[1] In those still on opioids, opioid withdrawal may occur.[1] Use is not recommended in people with liver failure.[1] It is unclear if use is safe during pregnancy.[1][2] Naltrexone is an opioid antagonist and works by blocking the effects of opioids, both those from inside and outside the body.[1]

Naltrexone was first made in 1965 and was approved for medical use in the United States in 1984.[1][3] As of 2019, the wholesale cost of tablets is about US$0.78 per day in the United States.[4] The extended-release injections cost about $1,267 per month ($41.20 per day).[4] Naltrexone, as bupropion/naltrexone, is also used to treat obesity.[5]

Naltrexone





Clinical data	
Trade names	ReVia, Vivitrol, others
Other names	EN-1639A; UM-792; *N*-Cyclopropyl-methylnoroxymorphone; *N*-Cyclopropylmethyl-14-hydroxydihydro-morphinone; 17-(Cyclopropylmethyl)-4,5α-epoxy-3,14-dihydroxymorphinan-6-one
AHFS/Drugs.com	Monograph
MedlinePlus	a685041
Pregnancy category	AU: B3 US: C (Risk not ruled out)
Routes of administration	By mouth, intramuscular injection, subcutaneous implant
ATC code	N07BB04 (WHO)
Legal status	
Legal status	AU: S4 (Prescription only) CA: R-only

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17 more

Edit links

	UK: POM (Prescription only) US: R-only In general: ℞ (Prescription only)
Pharmacokinetic data	
Bioavailability	5–40%
Protein binding	21%
Metabolism	Liver
Elimination half-life	Naltrexone: 4 hours 6β-Naltrexol: 13 hours
Excretion	Urine
Identifiers	
IUPAC name	[show]
CAS Number	16590-41-3
PubChem CID	5360515
IUPHAR/BPS	1639
DrugBank	DB00704
ChemSpider	4514524
UNII	5S6W795CQM
KEGG	D05113
ChEBI	CHEBI:7465
ChEMBL	ChEMBL19019
CompTox Dashboard (EPA)	DTXSID4046313
ECHA InfoCard	100.036.939
Chemical and physical data	
Formula	$C_{20}H_{23}NO_4$
Molar mass	341.401 g/mol g·mol $^{-1}$
3D model (JSmol)	Interactive image
Melting point	169 °C (336 °F)
SMILES	[show]
InChI	[show]
(what is this?) (verify)	

Medical uses [edit]

Alcoholism [edit]

Naltrexone has been best studied as a treatment for alcoholism .[6] Naltrexone has been shown to decrease the amount and frequency of drinking.[7] It does not appear to change the percentage of people drinking.[8] Its overall benefit has been described as "modest".[9]

Acamprosate may work better than naltrexone for eliminating drinking, while naltrexone may decrease the desire for alcohol to a greater extent.[10]

The Sinclair method is a method of using opiate antagonists such as naltrexone to treat alcoholism. The person takes the medication about an hour (and only then) before drinking to avoid side effects that arise from chronic use.[11][12] The opioid antagonist blocks the positive-reinforcement effects of alcohol and allows the person to stop or reduce drinking.[12]

Opioid use [edit]

Long-acting injectable naltrexone decreases heroin use more than placebo.[13] It has benefits over methadone and buprenorphine in that it is not a restricted medication.[13] It may decrease cravings for opioids after a number of weeks, and decreases the risk of overdose .[1][14] It is given once per month and has better compliance than the oral formulation. [15]

A 2011 review found insufficient evidence to determine the effect of naltrexone taken by mouth in opioid dependence.[16] While some do well with this formulation, it must be taken daily, and a person whose cravings become overwhelming can obtain opioid intoxication simply by skipping a dose. Due to this issue, the usefulness of oral naltrexone in opioid use disorders is limited by the low retention in treatment. Naltrexone by mouth remains an ideal treatment for a small number of people with opioid use, usually those with a stable social situation and motivation. With additional contingency management support, naltrexone may be effective in a broader population.[17]

Others [edit]

Naltrexone is not useful for quitting smoking .[18] It has been used in chronic pain such as fibromyalgia with tentative evidence of benefit.[19][20]

Available forms [edit]

Naltrexone is available and most commonly used in the form of an oral tablet (50 mg). [21] Vivitrol, a naltrexone formulation for depot injection containing 380 mg of the medication per vial, is also available.[21][22] Additionally, naltrexone subcutaneous implants that are surgically implanted are available.[23] While these are manufactured in Australia, they are not authorized for use within Australia, but only for export.[24] By 2009, naltrexone implants showed encouraging results.[25]

Contraindications [edit]

Naltrexone should not be used by persons with acute hepatitis or liver failure, or those with recent opioid use (typically 7–10 days).

Side effects [edit]

The most common side effects reported with naltrexone are gastrointestinal complaints such as diarrhea and abdominal cramping. These adverse effects are analogous to the symptoms of opioid withdrawal , as the mu receptor blockade will increase GI motility.

Naltrexone has been reported to cause liver damage (when given at doses higher than recommended). It carries an FDA boxed warning for this rare side effect. Due to these reports, some physicians may check liver function tests prior to starting naltrexone, and periodically thereafter. Concerns for liver toxicity initially arose from a study of nonaddicted obese patients receiving 300 mg of naltrexone.[26] Subsequent studies have suggested limited toxicity in other patient populations.

Naltrexone should not be started until several (typically 7-10) days of abstinence from opioids have been achieved. This is due to the risk of acute opioid withdrawal if naltrexone is taken, as naltrexone will displace most opioids from their receptors. The time of abstinence may be shorter than 7 days, depending on the half-life of the specific opioid taken. Some physicians use a naloxone challenge to determine whether an individual has any opioids remaining. The challenge involves giving a test dose of naloxone and monitoring for opioid withdrawal. If withdrawal occurs, naltrexone should not be started.[27]

Pharmacology [edit]

Pharmacodynamics [edit]

Naltrexone and its active metabolite 6β-naltrexol are competitive antagonists at the μ-opioid receptor (MOR), the κ-opioid receptor (KOR) to a lesser extent, and, to a far lesser extent, at the δ-opioid receptor (DOR).[30]

Naltrexone at opioid receptors

Affinities (K_i)			Ratio	Ref
MOR	DOR	KOR	MOR:DOR:KOR	
1.0 nM	149 nM	3.9 nM	1:149:4	[28]
0.0825 nM	8.02 nM	0.509 nM	1:97:6	[29]

Mechanism of action [edit]

The blockade of opioid receptors is the basis behind naltrexone's action in the management of opioid dependence—it reversibly blocks or attenuates the effects of opioids. Its mechanism of action in alcohol dependence is generated via κ-opioid receptor antagonism,[31] which blocks the actions of the endogenous opioid peptide dynorphin .[32] Dynorphin typically instates drug-seeking behavior when it binds to the κ-opioid receptor, as well as decreasing dopamingeric signalling in the nucleus accumbens.[33]

Pharmacokinetics [edit]

Naltrexone is metabolized in the liver mainly to 6β-naltrexol by the enzyme dihydrodiol dehydrogenase. Other metabolites include 2-hydroxy-3-methoxy-6β-naltrexol and 2-hydroxy-3-methoxy-naltrexone. These are then further metabolized by conjugation with glucuronide .[*citation needed*] The plasma half-life of naltrexone and its metabolite 6β-naltrexol are about 4 hours and 13 hours, respectively.[*citation needed*]

Pharmacogenetics [edit]

Tentative evidence suggests that family history and presence of the Asn40Asp polymorphism predicts naltrexone being effective.[34][35]

Chemistry [edit]

Naltrexone can be described as a substituted oxymorphone – here the tertiary amine methyl -substituent is replaced with methylcyclopropane . Naltrexone is the N-cyclopropylmethyl derivative of oxymorphone.[*citation needed*]

Analogues [edit]

The closely related medication, methylnaltrexone , is used to treat opioid-induced constipation, but does not treat addiction as it does not cross the blood–brain barrier . Nalmefene is similar to naltrexone and is used for the same purposes as naltrexone. Naltrexone should not be confused with naloxone , which is used in emergency cases of opioid overdose . Other related opioid antagonists include nalodeine and samidorphan .

History [edit]

Naltrexone was first synthesized in 1963 by Metossian at Endo Laboratories, a small pharmaceutical company in New York City.[36] It was characterized by Blumberg, Dayton, and Wolf in 1965 and was found to be an orally active , long-acting, and very potent opioid antagonist. [36][37][38][3] The drug showed advantages over earlier opioid antagonists such as cyclazocine , nalorphine , and naloxone, including its oral activity, a long duration of action allowing for once-daily administration, and a lack of dysphoria , and was selected for further development.[3] It was patented by Endo Laboratories in 1967 under the developmental code name EN-1639A and Endo Laboratories was acquired by DuPont in 1969. [39] Clinical trials for opioid dependence began in 1973, and a developmental collaboration of DuPont with the National Institute on Drug Abuse for this indication started the next year in 1974.[39] The drug was approved by the FDA for the oral treatment of opioid dependence in 1984, with the brand name Trexan, and for the oral treatment of alcohol dependence in 1995, when the brand name was changed by DuPont to ReVia.[39][21] A depot formulation for intramuscular injection was approved by the FDA under the brand name Vivitrol for alcohol dependence in 2006 and opioid dependence in 2010.[22][21]

Society and culture [edit]

Generic names [edit]

Naltrexone is the generic name of the drug and its INN, USAN, BAN, DCF, and DCIT, while naltrexone hydrochloride is its USP and BANM.[40][41][42][43]

Brand names [edit]

Naltrexone is or has been marketed under a variety of brand names, including Adepend, Antaxone, Celupan, Depade, Nalorex, Narcoral, Nemexin, Revia/ReVia, Trexan, and Vivitrol.[40][41][42][43] It is also marketed in combination with bupropion (bupropion/naltrexone) as Contrave and was marketed with morphine (morphine/naltrexone) as Embeda.[43] A combination of naltrexone with buprenorphine (buprenorphine/naltrexone) has been developed, but has not been marketed.[44]

Controversies [edit]

The FDA authorized use of injectable naltrexone for opioid addiction using a single study[45] that was led by Evgeny Krupitsky at Bekhterev Research Psychoneurological Institute, St Petersburg State Pavlov Medical University, St Petersburg, Russia,[46] a country where opioid agonists such as methadone and buprenorphine are not available. The study was a "double-blind, placebo-controlled, randomized", 24-week trial running "from July 3, 2008, through October 5, 2009" with "250 patients with opioid dependence disorder" at "13 clinical sites in Russia" on the use of injectable naltrexone (XR-NTX) for opioid dependence. The study was funded by the Boston-based biotech Alkermes firm which produces and markets naltrexone in the United States. A 2011 article reported that this single trial of naltrexone was performed not by comparing it to the best available, evidence-based treatment (methadone or buprenorphine), but by comparing it with a placebo.[47] A subsequent RCT in Norway did compare injectable naltrexone to buprenorphine and found them to be similar in outcomes.[48]

In May 2017, United States Secretary of Health and Human Services Tom Price, praised [Vivitrol] as the future of opioid addiction treatment after visiting the company's plant in Ohio.[49] His remarks set off sharp criticism with almost 700 experts in the field of substance abuse submitting a letter to Price cautioning him about Vivitrol's "marketing tactics" and warning him that his comment "ignore widely accepted science".[50] The experts pointed out that Vivitrol's competitors, buprenorphine and methadone, are "less expensive", "more widely used", and have been "rigorously studied".

Price had claimed that buprenorphine and methadone were "simply substitute[s]" for "illicit drugs"[49] whereas according to the letter, "the substantial body of research evidence supporting these treatments is summarized in guidance from within your own agency, including the Substance Abuse and Mental Health Services Administration, the US Surgeon General, the National Institute on Drug Abuse, and the Centers for Disease Control and Prevention. To briefly summarize, buprenorphine and methadone have been demonstrated to be highly effective in managing the core symptoms of opioid use disorder, reducing the risk of relapse and fatal overdose, and encouraging long-term recovery."[50]

According to a June 11, 2017, *The New York Times* article, Alkermes "has spent years coaxing, with a deft lobbying strategy that has targeted lawmakers and law enforcement officials. The company has spent millions of dollars on contributions to officials struggling to stem the epidemic of opioid abuse. It has also provided thousands of free doses to encourage the use of Vivitrol in jails and prisons, which have by default become major detox centers".[49]

Research [edit]

Depersonalization [edit]

Naltrexone is sometimes used in the treatment of dissociative symptoms such as depersonalization and derealization .[51][52] Some studies suggest it might help.[53] Other small, preliminary studies have also shown benefit.[51][52] Blockade of the KOR by naltrexone and naloxone is thought to be responsible for their effectiveness in ameliorating depersonalization and derealization.[51][52] Since these drugs are less efficacious in blocking the KOR relative to the MOR, higher doses than typically used seem to be necessary.[51][52]

Low-dose [edit]

Main article: Low-dose naltrexone

"Low-dose naltrexone" (LDN) describes the " off-label " use of naltrexone at low doses for diseases not related to chemical dependency or intoxication, such as multiple sclerosis .[54] More research needs to be done before it can be recommended for clinical use.

Although some scientific studies show its efficacy in some conditions such as fibromyalgia ,[55] other, more dramatic claims for its use in conditions such as cancer and HIV have less scientific support.[54] This treatment has received significant attention on the Internet , especially through websites run by organizations promoting its use.[56]

Self-injury [edit]

One study suggests that self-injurious behaviors present in persons with developmental disabilities (including autism) can sometimes be remedied with naltrexone.[57] In these cases, the self-injury is believed to be done to release beta-endorphin , which binds to the same receptors as heroin and morphine.[58] If the "rush" generated by self-injury is removed, the behavior may stop.

Behavioral disorders [edit]

Some indications exist that naltrexone might be beneficial in the treatment of impulse-control disorders such as kleptomania , compulsive gambling, or trichotillomania (compulsive hair pulling), but evidence of its effectiveness for gambling is conflicting.[59][60][61] A 2008 case study reported successful use of naltrexone in suppressing and treating an internet pornography addiction .[62]

Interferon alpha [edit]

Naltrexone is effective in suppressing the cytokine -mediated adverse neuropsychiatric effects of interferon alpha therapy. [63][64]

See also [edit]

- Opioid antagonist § List of opioid antagonists
- *One Little Pill* (2014 film) - documentary about using naltrexone to treat alcohol use disorder

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v · t · e **Treatment of drug dependence (N07B)** [show]

v · t · e **Opioid receptor modulators** [show]

Categories : Alcohol abuse | Cyclopropanes | Diols | Ethers | GABAA receptor negative allosteric modulators | Kappa antagonists | Ketones | Morphinans | Phenols | Opioid antagonists