

# Evolution of the U.S. Overdose Crisis

## Understanding China's Role in the Production and Supply of Synthetic Opioids

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Testimony presented before the House Foreign Affairs Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations on Tackling Fentanyl: The China Connection on September 6, 2018.



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*Evolution of the U.S. Overdose Crisis: Understanding China's Role in the Production and Supply of Synthetic Opioids*

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Before the House Foreign Affairs Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations on Tackling Fentanyl: The China Connection

September 6, 2018

Chairman Smith, Ranking Member Bass, and other distinguished members of the Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations, thank you very much for the opportunity to testify before you today. I am a drug policy researcher at the RAND Corporation. For almost thirty years, the RAND Drug Policy Research Center has worked to help decisionmakers in the United States and throughout the world address issues involving alcohol and other drugs. In doing so, the center brings an objective and data-driven perspective to this often emotional and fractious policy arena. I was asked to speak to you today about ongoing developments related to the current opioid crisis in the United States and China's role in supplying potent synthetic opioids.

The introduction of illicitly manufactured synthetic opioids to U.S. drug markets presents new challenges for contemporary drug policy: The potency of many synthetic opioids increases risk to users and poses challenges for first responders, the development of novel opioids that fall outside existing drug controls complicates regulatory efforts, and their ability to be produced and shipped with ease disrupts traditional supply chains.

Today, I will briefly describe our country's ongoing opioid overdose crisis. Understanding recent developments and the shifting supply of opioids is critical to policy design. I will then describe the emergence of synthetic opioids, which have complicated many of our drug policy efforts. Given the topic of this hearing, I focus most of my testimony on China's role as a source of synthetic psychoactives and chemical precursors, describing what we know about the manufacture and export of potent opioids, such as fentanyl, to the United States. Although most of these substances appear to come from China, many dimensions of this problem remain

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unclear. That said, China's export-led economic strategy and lack of regulatory oversight have created favorable conditions for the production and exportation of synthetic opioids and related chemicals. I conclude with some policy options going forward, aimed at the new challenges posed by these substances.

## Arrival of Synthetic Opioids to Illicit Markets

A decade and a half into the opioid crisis, the number of overdose deaths continues to accelerate, increasing by 6.6 percent from just 2016 to 2017.<sup>3</sup> The crisis was initially fueled by oversupply of prescription painkillers, such as oxycodone and hydrocodone. Yet, in 2017, synthetic opioids, such as fentanyl, were involved in approximately 60 percent of all opioid overdose deaths. Although diversion of prescription fentanyl (e.g., transdermal patches and transmucosal lozenges) has been documented,<sup>4</sup> today's problem largely comes from illicitly manufactured synthetic opioid powders. Unlike traditionally available street-sourced opioids, such as heroin or diverted prescription pills, synthetic opioids found in today's drug markets are often much more potent. Some of these chemicals are active in the tens of micrograms,<sup>5</sup> making precise dosing very difficult without sophisticated equipment. As the supply of fentanyl permeates U.S. markets, so does the risk of fatal overdose.

Provisional numbers from the Centers for Disease Control and Prevention (CDC) suggest that there were as many as 49,000 opioid-involved overdose deaths in 2017. Separating these by drug class shows that there were approximately 29,000 recorded overdoses involving synthetic opioids.<sup>6</sup> This is almost a tenfold increase since 2013. Today's drug overdose crisis now surpasses major public health epidemics of prior generations, including the HIV/AIDS epidemic.

Moreover, overdose figures and law enforcement reports suggest that synthetic opioids, initially sold as powdered heroin or prescription pills, are entering non-opioid drug markets.<sup>7</sup> Although about one-third of heroin-involved deaths in 2016 also involved synthetic opioids, approximately 40 percent of fatal cocaine overdoses included synthetic opioids. Figure 1 shows some trends regarding the presence of synthetic opioids among fatal overdoses with various other drugs. Early numbers for 2017 indicate that overdoses involving heroin and prescription opioids have remained steady since 2016, while overdoses from synthetic opioids increased by almost 50 percent, suggesting a continued diffusion across markets.

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<sup>3</sup> F. B. Ahmad, L. M. Rossen, M. R. Spencer, M. Warner, and P. Sutton, *Provisional Drug Overdose Death Counts*, Hyattsville, Md.: National Center for Health Statistics, 2018.

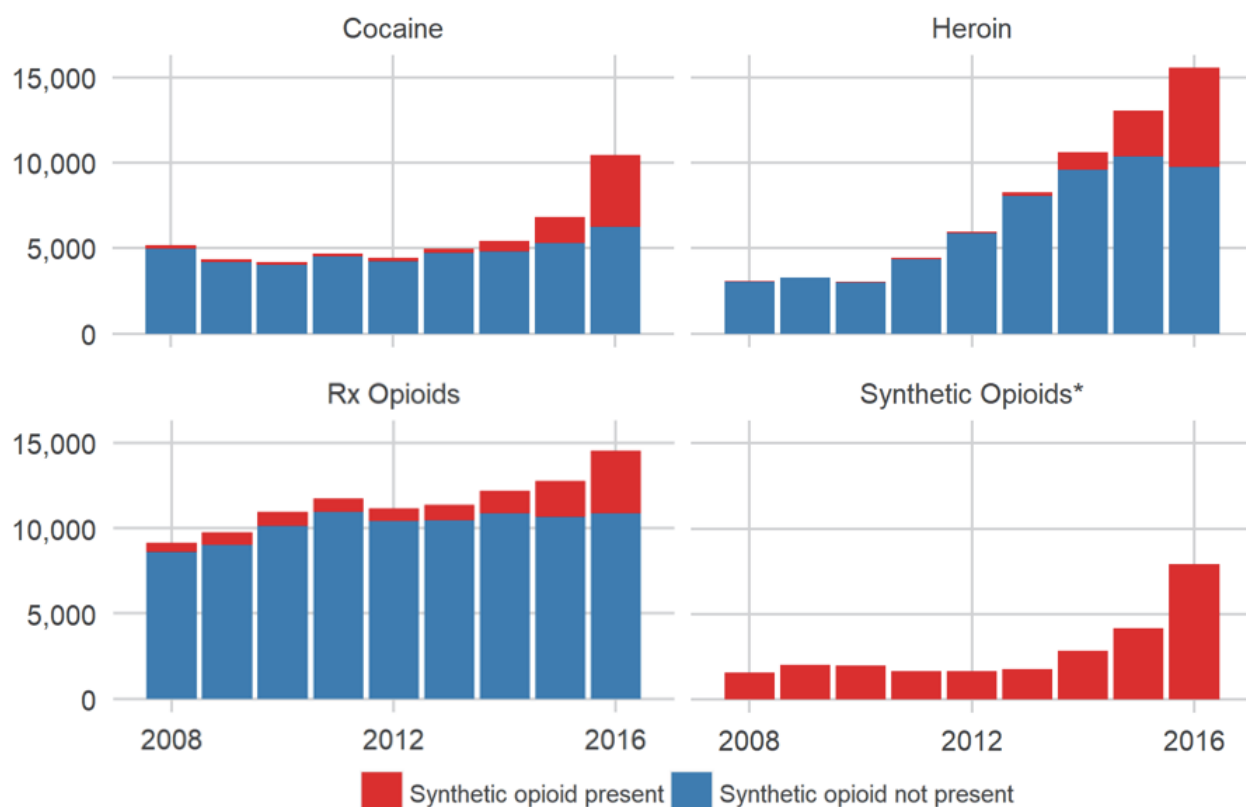
<sup>4</sup> J. Kuhlman, R. McCaulley, T. J. Valouch, and G. S. Behonick, "Fentanyl Use, Misuse, and Abuse: A Summary of 23 Postmortem Cases," *Journal of Analytical Toxicology*, Vol. 27, No. 7, 2003, pp. 499–504.

<sup>5</sup> According to the European Monitoring Centre for Drugs and Drug Addiction, the lethal dose of fentanyl for those without opioid tolerance is approximately two milligrams (2,000 micrograms), roughly the amount of two grains of salt. See <http://www.emcdda.europa.eu/publications/drug-profiles/fentanyl#pharmacology>. Transdermal patches containing fentanyl release 12.5 to 100 micrograms per hour, depending on the prescription.

<sup>6</sup> Ahmad et al., 2018.

<sup>7</sup> U.S. Drug Enforcement Administration, Special Testing and Research Laboratory, *Emerging Threat Report, Annual 2017*, Springfield, Va., 2018.

**Figure 1. Number of Fatal Drug Overdoses in the United States**



\*Excludes cocaine, heroin, Rx opioid, and psychostimulant deaths from synthetic opioid counts

SOURCE: Data are deidentified public-use Multiple Cause of Death certificate files produced by the National Center for Health Statistics for 2008–2016.

The upward trend in overdoses is mirrored by supply-side indicators. U.S. Customs and Border Protection (CBP) seized approximately one kilogram of fentanyl in FY 2013; by FY 2017, CBP seized 675 kilograms.<sup>8</sup> Likewise, reports by the U.S. Drug Enforcement Administration’s (DEA’s) National Forensic Laboratory Information System (NFLIS) show a sharp increase in the number of seizures containing fentanyl submitted to state and local drug laboratories. Although this may be partially explained by changes in law enforcement procedures when handling unknown substances, reports of the number of incidents of fentanyl seizures submitted to NFLIS also jumped, from 978 in 2013 to more than 34,000 in 2016.<sup>9</sup> In addition to the rise in reports of seized fentanyl in domestic drug markets, DEA has noted increases in the number of novel synthetic opioids. According to DEA’s *Emerging Threat Report* for 2017, ten synthetic opioids were seized and identified for the first time.<sup>10</sup> In other words, these chemicals

<sup>8</sup> U.S. Customs and Border Protection, *CBP Border Security Report: Fiscal Year 2017*, Washington, D.C., December 5, 2017.

<sup>9</sup> U.S. Drug Enforcement Administration, Diversion Control Division, *NFLIS Brief: Fentanyl, 2001–2015*, Springfield, Va., 2017; U.S. Drug Enforcement Administration, Diversion Control Division, *NFLIS Brief: Fentanyl and Fentanyl-Related Substances Reported in NFLIS, 2015–2016*, Springfield, Va., 2017.

<sup>10</sup> U.S. Drug Enforcement Administration, Special Testing and Research Laboratory, 2018.

were previously unknown in U.S. drug markets. Even though producers continue to innovate and create new substances, fentanyl remains the dominant synthetic opioid reported in laboratory seizure reports.

Although fentanyl and several of its analogues are controlled substances with recognized medical and veterinary applications in the United States, annual aggregate production quotas and prescriptions have remained relatively stable over time.<sup>11</sup> Today, the most likely source of these drugs is illicit manufacture. There was a brief period in the mid-2000s when illicitly manufactured fentanyl appeared in street markets in the Midwest, claiming about 1,000 lives.<sup>12</sup> The federal and local responses were swift, expanding access to naloxone and seizing product from markets. In May 2006, Mexican law enforcement and DEA identified and closed the illicit manufacturing operation in Toluca, Mexico.<sup>13</sup> Illicitly-manufactured synthetic opioids were not again a concern until late 2013.

Much has changed since the closure of the lab in Toluca. Members of law enforcement in the United States and Canada suggest that most synthetic opioids and precursors originate from manufacturers and vendors in China.<sup>14</sup> One route of supply comes via the international postal system and private express consignment carriers, such as FedEx and DHL.<sup>15</sup> According to DEA, Mexican drug traffickers are the other major source.<sup>16</sup> Given that drug trafficking organizations in Mexico have a history of importing methamphetamine precursors from China,<sup>17</sup> it is likely that they are doing the same with fentanyl precursors.

CBP reports seizing synthetic opioids, such as fentanyl, at land points of entry and checkpoints on the southwest border. Table 1 shows that for FY 2017, seizures of fentanyl near or at the border outweighed those at mail and express consignment carrier facilities. However, after adjusting for reported potency, almost 80 percent of purity-adjusted fentanyl seized by CBP in FY 2017 occurred at mail and express consignment carrier facilities. Law enforcement and

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<sup>11</sup> Production quotas for fentanyl trended upward starting in 2013, but they returned to their baseline levels by 2017. U.S. Drug Enforcement Administration, “Aggregate Production Quota History for Selected Substances,” November 15, 2017; R. Gladden, *Fentanyl Law Enforcement Submissions and Increases in Synthetic Opioid-Involved Overdose Deaths—27 States, 2013–2014*, Atlanta, Ga.: Centers for Disease Control and Prevention, Morbidity and Mortality Weekly Report, August 16, 2016.

<sup>12</sup> Centers for Disease Control and Prevention, *Nonpharmaceutical Fentanyl-Related Deaths—Multiple States, April 2005–March 2007*, Atlanta, Ga., Morbidity and Mortality Weekly Report, July 25, 2008.

<sup>13</sup> U.S. Drug Enforcement Administration, National Drug Intelligence Center, *Fentanyl: Situation Report*, Springfield, Va., SR-000001, June 5, 2006.

<sup>14</sup> C. Bairns, “Charges to Be Laid Involving Fentanyl Shipments from China: RCMP,” *Globe and Mail*, September 18, 2017; U.S. Drug Enforcement Administration, *Counterfeit Prescription Pills Containing Fentanyls: A Global Threat*, Springfield, Va., 2016.

<sup>15</sup> U.S. Senate, Committee on Homeland Security and Governmental Affairs, Permanent Subcommittee on Investigations, *Combatting the Opioid Crisis: Exploiting Vulnerabilities in International Mail*, Washington, D.C., staff report, 2018.

<sup>16</sup> U.S. Drug Enforcement Administration, 2016.

<sup>17</sup> S. O’Connor, *Meth Precursor Chemicals from China: Implications for the United States*, Washington, D.C.: U.S.-China Economic and Security Review Commission, 2016.

congressional investigations have suggested that these packages originated from China.<sup>18</sup> If we think that CBP seizures represent the true nature of trafficking patterns (i.e., that these are minimally biased samples), then these preliminary calculations support law enforcement’s conclusion that the mail and express carrier consignment systems are a substantial supply channel of synthetic opioids coming from China.

**Table 1. Breakdown of CBP Seizures Reported to Contain Fentanyl in FY 2017**

<b>Point of Interdiction</b>	<b>Amount Seized (kg)</b>	<b>Number of Seizures</b>	<b>Average Weight of Seizures (kg)</b>	<b>Reported Purity (%)</b>	<b>Purity-Adjusted Amount (kg)</b>
Express consignment carrier facilities	110	118	0.932	90.0	99.0
International mail network	42	227	0.185	90.0	37.8
Land points of entry (southwest border)	388	65	5.970	7.5	29.1
Remainder* (presumably Border Patrol checkpoints)	135	—	—	7.5	10.1
<b>Total</b>	<b>675</b>				<b>176.0</b>

SOURCE: Owen, 2018.

NOTE: Purity at border is reportedly 5–10 percent; here, we use the midpoint.

\* Remainder was calculated by taking the difference of reported fentanyl seizures from the FY 2017 total of 675 kg.

Nevertheless, smuggling trends may be evolving. In late June 2018, CBP at Philadelphia’s port seized 50 kilograms of 4-flouroisobutyryl fentanyl hidden in barrels of iron oxide in a container ship from China.<sup>19</sup> CBP noted high purity, which would make this single seizure one of the largest to originate from China.

By most accounts, China remains an important source of synthetic opioids and fentanyl precursors entering North America, whether sent by mail or cargo or smuggled over the border by drug trafficking organizations.

## China as a Source of New Drugs and Chemical Precursors

The manufacture of many of these new drugs and precursors, including synthetic opioids, is linked to China’s large and underregulated chemical and pharmaceutical sectors. China is a leading exporter of active pharmaceutical ingredients and chemicals that can be used in the production of controlled substances. These include methamphetamine precursors and cocaine

<sup>18</sup> U.S. Senate, 2018; T. Owen, Executive Assistant Commissioner for Office of Field Operations, U.S. Customs and Border Protection, testimony before the U.S. Senate Committee on Homeland Security and Governmental Affairs, January 25, 2018.

<sup>19</sup> U.S. Customs and Border Protection, “Philadelphia CBP Seizes Nearly \$1.7 Million in Fentanyl Shipped from China,” June 28, 2018.

reagents, such as ephedrine, pseudoephedrine, and potassium permanganate.<sup>20</sup> To avoid detection at points of import, Chinese producers or distributors often employ technically legal workarounds and, when necessary, outright deception. It has been reported that Chinese traffickers and chemical exporters will mislabel shipments, modify chemicals, or ship pre-precursors that fall outside international controls.<sup>21</sup>

As this relates to synthetic opioids, lack of international scheduling has allowed Chinese manufacturers to export fentanyl precursors. Although they have been scheduled in the United States for a decade, N-Phenethyl-4-piperidinone (NPP) and anilino-N-phenethylpiperidine (ANPP) were not listed or subject to international controls until October 2017.<sup>22</sup> In late 2016, the U.S. Department of State identified nearly 260 producers of these precursors, more than half of which were in China.<sup>23</sup> These chemicals were finally scheduled in China this past February.<sup>24</sup> Prior to then, there was little scrutiny on their manufacture, and producers faced little, if any, reporting, production, or exporting restrictions.

Much like circumvention of precursor regulations, Chinese manufacturers have synthesized new substances that fall outside national and international laws, including drugs that mimic the effects of cannabis, stimulants, benzodiazepines, and opioids. In the case of synthetic opioids, such as fentanyl, individuals can order these substances online and have them shipped directly to destinations in the United States.<sup>25</sup> Chinese chemical and pharmaceutical firms openly advertise such drugs on English-language websites accessible by a simple internet search. Vendors will sometimes purposefully conceal shipments through freight forwarding systems, mislabel packages, or route them through a third country to conceal efforts to trace packages to their original source.<sup>26</sup>

To stem the growing production of uncontrolled psychoactives, the Chinese government has added new chemicals to national drug schedules. In late 2015, China added 116 new substances, including 38 synthetic cannabinoids, 26 synthetic cathinones (e.g., “bath salts”), 23 phenethylamines (e.g., MDMA analogues), as well as half a dozen synthetic opioids, to its drug control laws.<sup>27</sup> Since then, China has scheduled additional fentanyl analogues as they are brought to the attention of authorities by U.S. and Canadian law enforcement.<sup>28</sup> In January 2017, China’s

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<sup>20</sup> O’Connor, 2016; U.S. Department of State, *International Narcotics Control Strategy Report*, Washington, D.C., 2017.

<sup>21</sup> O’Connor, 2016.

<sup>22</sup> International Narcotics Control Board, “INCB: Scheduling of Fentanyl Precursors Comes into Force,” October 18, 2017.

<sup>23</sup> J. Whalen, “U.S. Seeks Curb on Chemicals Used to Make Fentanyl, a Powerful Opioid,” *Wall Street Journal*, October 14, 2016.

<sup>24</sup> U.S. Drug Enforcement Administration, “China Announces Scheduling Controls on Two Fentanyl Precursor Chemicals,” January 5, 2018.

<sup>25</sup> U.S. Senate, 2018.

<sup>26</sup> U.S. Senate, 2018.

<sup>27</sup> United Nations Office on Drugs and Crime, “China Announces Controls over 116 New Psychoactive Substances,” October 2015.

<sup>28</sup> U.S. Drug Enforcement Administration, 2018; Royal Canadian Mounted Police, “RCMP and Chinese Ministry of Public Security Commit to Combat the Flow of Fentanyl into Canada,” November 16, 2016.



Ministry of Public Security listed four additional synthetic opioids: acrylfentanyl, carfentanyl, furanylfentanyl, and valerylfentanyl.<sup>29</sup> This was followed six months later with the control of four new substances, including two non-fentanyl synthetic opioids, U-47700 and MT-45.<sup>30</sup>

## Industry Growth and Regulatory Deficiencies

Although the Chinese central government has taken steps to control new chemicals and precursors, the problem persists. There are two likely factors for this. First, as previously mentioned, many manufacturers adapt to controls by designing new drugs. But, more important, regulatory capacity in China appears to be inadequate to effectively police its expansive pharmaceutical and chemical industries. I now turn to this second factor.

Government-led market reforms in the past thirty years have helped China become a global manufacturing center driven by exports. The expansion of e-commerce and inexpensive shipping have made global trade cheaper and more convenient. Together, these phenomena helped make many of China's industries important links in international supply chains. The same is true for its expansive pharmaceutical and chemical industries. Initially, China prioritized the development of these sectors under strong central planning, but, over the years, it has slowly introduced privatization.<sup>31</sup>

As state-run producers privatized, the pharmaceutical and chemical industries experienced rapid economic development. During the 1980s, the pharmaceutical industry grew, on average, by 17 percent per year.<sup>32</sup> During the 1990s, the pharmaceutical industry was one of the fastest-growing sectors in China. By 1995, the number of pharmaceutical manufacturers had hit a peak of 5,300 firms.

Today, China's pharmaceutical industry counts some 5,000 manufacturers that produce more than 2,000 products, with an annual production capacity of more than 2 million tons, making the country the single largest exporter of active pharmaceutical ingredients (APIs) in the world.<sup>33</sup> According to the World Health Organization (WHO), most Chinese APIs are imported by the United States to produce legitimate pharmaceutical products. China's pharmaceutical industry is now the second-largest in the world, with recent annual sales revenues of more than \$100 billion.<sup>34</sup>

In addition to China's pharmaceutical industry, the Department of State estimates that, in China, there are approximately 400,000 chemical manufacturers or distributors, some of which

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<sup>29</sup> Chinese Ministry of Public Security, "Notice on Inclusion of Four Fentanyl Substances, Such as Fentanyl, in the Supplement to the Catalog of Non-Medical Narcotic Drugs and Psychotropic Substances Control," March 1, 2017.

<sup>30</sup> U.S. Drug Enforcement Administration, "China Announces Scheduling Controls of New Psychoactive Substances/Fentanyl-Class Substances," June 19, 2017.

<sup>31</sup> World Health Organization, *China Policies to Promote Local Production of Pharmaceutical Products and Protect Public Health*, Geneva, 2017.

<sup>32</sup> H. Li. and H. Sun, "The Historical Evolution of China's Drug Regulatory System," *Value in Health*, Vol. 17, No. 3, 2014, pp. A30–A31.

<sup>33</sup> World Health Organization, 2017.

<sup>34</sup> World Health Organization, 2017.

are operating without legal approval.<sup>35</sup> These firms produce tons of chemicals each week intended for industrial and commercial use.<sup>36</sup> China is the world's leading chemical exporter by value.<sup>37</sup> One private-sector analysis estimates that China's chemical industry has grown by an annual average of 9 percent in recent years and made up 3 percent of the national economy in 2016, generating more than \$100 billion in profits that year.<sup>38</sup>

Market-oriented reforms have generated rapid growth but also necessitated the creation of an independent regulatory system to police the industry and ensure product quality. Rapid commercial growth has outpaced the capacity and design of China's regulatory regime.<sup>39</sup> Regulatory gaps and bureaucratic fragmentation continue to hamper China's ability to oversee its pharmaceutical and chemical industries.

In 1998, the State Drug Administration (forerunner to today's China Food and Drug Administration [CFDA]) was created to regulate manufacturers of pharmaceutical and medical products. Henceforth, the regulatory authority was formally prohibited from joint ventures or profit-seeking activities in the pharmaceutical industry.<sup>40</sup> In the past decade, efforts have been made to adopt better enforcement and production guidelines, including good manufacturing practices (GMPs). The GMP standards cover most basic aspects of manufacturing, including environmental protections, sanitary working conditions, product testing and tracking, and record keeping.

However, the division of regulatory design and enforcement responsibilities among national governmental entities is a commonly noted problem. Given the confusing and competing overlap among agencies, efforts to regulate the chemical industry have been overlooked at times. By one account, API producers that were registered as non-pharmaceutical chemical manufacturers escaped the CFDA's regulatory oversight until 2014.<sup>41</sup>

Lack of coordination and competing regulatory oversight allow for such gaps to exist. This creates opportunities for some firms to hide unregulated activities in plain sight. According to one report written by staff of the U.S.-China Economic and Security Review Commission, there were eight governmental entities involved in promulgating and enforcing production and export requirements for pharmaceuticals or chemicals. These include the CFDA, the State Council Leading Group on Product Quality and Food Safety, the National Narcotics Control Commission, the Anti-Smuggling Bureau within the General Administration of Customs, the

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<sup>35</sup> U.S. Department of State, *International Narcotics Control Strategy Report*, Washington, D.C.: Bureau of International Narcotics and Law Enforcement Affairs, 2014; U.S. Department of State, *International Narcotics Control Strategy Report*, Washington, D.C.: Bureau of International Narcotics and Law Enforcement Affairs, 2015.

<sup>36</sup> O'Connor, 2016.

<sup>37</sup> International Trade Centre, "Trade Map," yearly trade data, 2018.

<sup>38</sup> Atradius, "Market Monitor: Focus on Chemicals Performance and Outlook," 2017.

<sup>39</sup> Li and Sun, 2014; World Health Organization, 2017.

<sup>40</sup> Li and Sun, 2014.

<sup>41</sup> S. O'Connor, *Fentanyl: China's Deadly Export to the United States*, Washington, D.C.: U.S.-China Economic and Security Review Commission, 2017.

Ministry of Chemical Industry, the Ministry of Agriculture, the Ministry of Commerce, and the General Administration of Quality Supervision, Inspection, and Quarantine.<sup>42</sup>

In addition to the patchwork of responsible agencies, competing incentives between levels of government may impede enforcement. Provincial authorities protect, promote, and sometimes manage local economies and industries.<sup>43</sup> Although the central government, through the CFDA, designs rules to govern GMP standards, it relies on provincial governments to enforce them. According to the WHO, the CFDA inspects manufacturers of products deemed sensitive by the central government (such as radioactive pharmaceuticals and biologics), whereas provincial governments are mainly tasked with inspecting and certifying companies for GMP approval.<sup>44</sup> This creates a principal-agent situation between the central and provincial governments. This division in regulatory design and enforcement generates opportunities for regulatory capture, non-enforcement, or outright corruption when the economic incentives of provincial governments misalign with those of good governance. In some cases, there is little or no independent regulatory oversight of firms.

Beyond gaps in regulatory design and misaligned incentives, the government's regulatory capacity is limited. The division in enforcement strategy, in which the CFDA inspects only a subset of manufacturers, leaving the rest up to provincial authorities, may reflect this limitation. The CFDA and other regulators are unable to effectively inspect and police the large number of pharmaceutical manufacturers. The WHO notes that, although the CFDA is attempting to hire more inspectors, its efforts are complicated by lack of time and resources; private industry salaries are highly competitive, complicating efforts to retain qualified staff.<sup>45</sup>

Data from the CFDA, produced in Table 2, show that regulators are increasing the number of inspections, yet gaps remain. Figures from annual reports show an increase in inspected firms and applicants from 698 in 2015 to 751 in 2017, although there was a dip in inspections in 2016.<sup>46</sup> The number of CFDA inspectors has remained around 2,000 over the same period; however, regulators have shifted focus to GMP certification inspections away from other forms of inspections, such as pre-approval and overseas inspections. These regulatory efforts, which have traditionally been assigned to provincial governments, more than doubled from just over 200 in 2015 and 2016 to 428 in 2017.<sup>47</sup> The number of unannounced inspections remained steady over this period, while those that included international inspectors (such as the U.S. Food and Drug Administration [FDA]) modestly increased in recent years.

Of the 428 GMP inspections carried out in 2017, 37 firms or applicants did not pass, and one-quarter were issued warning letters for violations. According to the most recent CFDA

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<sup>42</sup> O'Connor, 2017.

<sup>43</sup> T. Gong, "Corruption and Local Governance: The Double Identity of Chinese Local Governments in Market Reform," *The Pacific Review*, Vol. 19, No. 1, 2006, pp. 85–102.

<sup>44</sup> World Health Organization, 2017.

<sup>45</sup> World Health Organization, 2017.

<sup>46</sup> China Food and Drug Administration, Center for Food and Drug Inspection, *Annual Report of Drug Inspection 2015*, 2016; China Food and Drug Administration, Center for Food and Drug Inspection, *Annual Report of Drug Inspection 2016*, 2017; China Food and Drug Administration, Center for Food and Drug Inspection, *Annual Report of Drug Inspection 2017*, 2018.

<sup>47</sup> China Food and Drug Administration, Center for Food and Drug Inspection, 2016, 2017, 2018.

annual report, 15 firms that manufacture narcotic or psychotropic drugs, precursors, or pharmaceuticals were inspected that year; three did not pass inspection for failure to properly handle mailing and transportation certificates or failure to control samples.<sup>48</sup> These numbers suggest that regulators are inspecting a small share of companies and that a sizable portion of manufacturers of controlled substances assessed in 2017 failed inspection for improper handling and transport.

**Table 2. China Food and Drug Inspections**

Inspection Type	Number of Inspected Firms/Applicants			Number of Inspectors		
	2015	2016	2017	2015	2016	2017
GMP certification	221	204	428	784	47	1,234
Unannounced	59	39	57	170	155	183
Observation by international inspectors	74	81	84	76	85	92
Other	334	107	182	1,052	990	556
<b>Total</b>	<b>698</b>	<b>431</b>	<b>751</b>	<b>2,082</b>	<b>1,277</b>	<b>2,065</b>

SOURCES: China Food and Drug Administration, Center for Food and Drug Inspection, 2016, 2017, 2018.

The situation is similar for China’s chemical regulators, who cannot adequately enforce regulations on all manufacturers and distributors.<sup>49</sup> Regulatory gaps have led to a large increase in the number of unlicensed or “semi-legitimate” chemical manufacturers or distributors.<sup>50</sup> There are reports that use of shell facilities and weak oversight lets some chemical and pharmaceutical manufacturers avoid scrutiny, allowing companies to produce and sell beyond their legal limits.<sup>51</sup> In 2007, industry insiders estimated that uncertified chemical manufacturers produced half of the APIs sold in China, with most exported to foreign markets.<sup>52</sup> It is unclear what proportion of uncertified manufacturers are supplying international API markets today or what amount of synthetic opioids is produced and exported via shell entities.

Gaps in regulatory design, the division of responsibility between provincial and central governments, and a lack of oversight and government and corporate accountability increase opportunities for corruption. The Regional Representative of the United Nations Office on Drugs and Crime, Jeremy Douglas, has asserted that corruption contributes to the ongoing illicit manufacturing and export of synthetic drugs and precursors. In 2015, after a major seizure of two and half tons of methamphetamine in Hong Kong—one of the biggest seizures in Asia at the time—Douglas stated, “To operate a lab like this, you need a lot of chemicals, which are legitimate, regulated chemicals from the pharmaceutical industry. There is some kind of

<sup>48</sup> China Food and Drug Administration, Center for Food and Drug Inspection, 2018.

<sup>49</sup> O’Connor, 2017.

<sup>50</sup> O’Connor, 2016.

<sup>51</sup> O’Connor, 2016.

<sup>52</sup> W. Bogdanich, “Chinese Chemicals Flow Unchecked onto World Drug Market,” *New York Times*, October 31, 2007.

corruption in the chemical/pharmaceutical industry taking place allowing this to happen.”<sup>53</sup> The Department of State also points to insufficient regulatory oversight and corruption of local government officials as explanations behind illicit drug and chemical production.<sup>54</sup>

Chinese authorities recognize these problems, and the government has made some efforts to expel corrupt officials. The high-profile conviction and execution of the former director of the forerunner to the CFDA in 2007 is one such example.<sup>55</sup> The central government has been tough on local officials and businesses, arresting nearly 2,000 people in a nationwide crackdown on counterfeit drug manufacturers in 2012.<sup>56</sup> In 2015, President Xi Jinping demanded that authorities increase penalties and stiffen drug regulation.<sup>57</sup> This past March, the central government proposed another reorganization of the CFDA, combining it with other regulatory entities.<sup>58</sup> Details are not final, but industry observers suggest that this reorganization is intended to extend the agency’s regulatory reach and reduce gaps in oversight.<sup>59</sup>

## Potential Policy Options

There are several options that Congress and federal authorities could consider. However, given the scope of this problem and the new challenges it presents, Congress must look beyond traditional drug policy tools.

First, given the lack of information about supply and demand, one option that Congress could take is to ensure improved and streamlined data collection and analysis methods. This includes directing law enforcement and public health authorities to improve measurement and analysis of seizures and outcome measures—such as overdoses, which are likely to be undercounted because of the novelty of analogues.<sup>60</sup> Most of our drug policy data collection and analysis systems are inadequate to appropriately assess developments related to the arrival of these new and emerging drugs. Congress could direct federal authorities to reintroduce expanded data collection systems, such as the Arrestee Drug Abuse Monitoring Program (ADAM) and the Drug Abuse Warning Network (DAWN) or other early warning systems. Given how fast new substances emerge in consumer markets, we need to improve measurement and reduce data lags.

Second, Congress could encourage federal authorities to use supply-side interventions strategically by working with Chinese counterparts to strengthen the country’s regulatory and interdiction capabilities. Congress should consider appropriating additional resources to aid U.S. authorities that work with international partners and direct the FDA, DEA, and Department of

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<sup>53</sup> B. Harris, “Corrupt Mainland Drug Firms ‘Fuelling Crystal Meth Scourge,’ Says UN Official,” *South China Morning Post*, February 22, 2015.

<sup>54</sup> U.S. Department of State, 2017.

<sup>55</sup> A. Olesen, “China Ex-Food and Drug Chief Executed,” Associated Press, July 10, 2007.

<sup>56</sup> M. Lee and B. Hirschler, “Special Report: China’s ‘Wild East’ Drug Store,” Reuters, August 28, 2012.

<sup>57</sup> World Health Organization, 2017.

<sup>58</sup> Xinhua News Agency, “Explanation of the State Council’s Institutional Reform Plan,” March 14, 2018.

<sup>59</sup> A. Liu, “China Creates New Drug Regulator in Biggest Government Overhaul in Years,” *FiercePharma*, March 13, 2018.

<sup>60</sup> C. J. Ruhm, “Corrected US Opioid-Involved Drug Poisoning Deaths and Mortality Rates, 1999–2015,” *Addiction*, Vol. 113, No. 7, 2018.

State to improve interagency coordination and cooperation with Chinese counterparts. In some cases, source-country supply controls aimed at eradicating plant-based drugs have been limited in reducing total supply or have been seen as a source of political instability.<sup>61</sup> However, these factors may be less of a concern for synthetic opioids produced illegally by manufacturers. Congress could also encourage U.S. regulators to engage with Chinese counterparts to improve joint monitoring and evaluation efforts of regulation violations, as well as aid the CFDA in hiring, training, and retaining qualified personnel. Through these efforts and high-level diplomatic channels, China should be encouraged to modernize its regulatory regime to effectively address the corruption and oversight problems in its growing pharmaceutical and chemical industries. This includes efforts to improve China's scheduling system and, more importantly, its enforcement capacity.

Third, Congress could encourage the Department of State to engage diplomatically with China for the purposes of discussing an extradition agreement to prosecute and deter suppliers. The United States does not have an extradition agreement with China, but it does with several other major drug-producing and drug-trafficking countries that supply illicit drugs to the United States. The lack of an extradition agreement impedes U.S. law enforcement's ability to prosecute Chinese nationals who traffic synthetic opioids. Although the U.S. Department of Justice has indicted a handful of Chinese nationals since late last year,<sup>62</sup> it is unclear whether these individuals or others will be prosecuted.<sup>63</sup>

Lastly and most importantly, Congress could strengthen federal efforts aimed at reducing demand for illicit opioids. Demand reduction could help lessen economic incentives for drug dealers while saving the lives of those suffering from opioid-use disorder. Demand reduction includes improving access to existing and proven therapies, such as methadone and buprenorphine. Some steps that Congress could take are encouraging the expansion of pharmacological treatments covered by private and public insurance, subsidizing the cost of medication treatments to those who cannot afford them, and reviewing and reducing regulatory barriers on their provision. Congress could also direct federal health authorities, such as the FDA, to assess additional innovative and evidence-informed medication treatments. Similarly, increasing the availability of naloxone is one possible short-term, life-saving intervention. The advent of illicitly manufactured synthetic opioids coming from China creates uncertainty in the supply of drugs in markets. However, there is less uncertainty surrounding the impact of medication therapies when it comes to saving lives.<sup>64</sup>

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<sup>61</sup> P. Reuter, F. Trautmann, R. L. Pacula, B. Kilmer, A. Gageldonk, and D. van der Gouwe. *Assessing Changes in Global Drug Problems, 1998–2007*, Santa Monica, Calif.: RAND Corporation, TR-704-EC, 2009.

<sup>62</sup> U.S. Department of Justice, "Justice Department Announces First Ever Indictments Against Designated Chinese Manufacturers of Deadly Fentanyl and Other Opiate Substances," October 17, 2017; U.S. Department of Justice, "Two Chinese Nationals Charged with Operating Global Opioid and Drug Manufacturing Conspiracy Resulting in Deaths," August 22, 2018.

<sup>63</sup> S. L. Wee and J. Hernández, "Despite Trump's Pleas, China's Online Opioid Bazaar Is Booming," *New York Times*, November 8, 2017.

<sup>64</sup> R. Mattick, C. Breen, J. Kimber, and M. Davoli, "Buprenorphine Maintenance Versus Placebo or Methadone Maintenance for Opioid Dependence," *Cochrane Database of Systematic Reviews*, February 6, 2014.