

## Opinion

# Our Drug Supply Is Sick. How Can We Fix It?

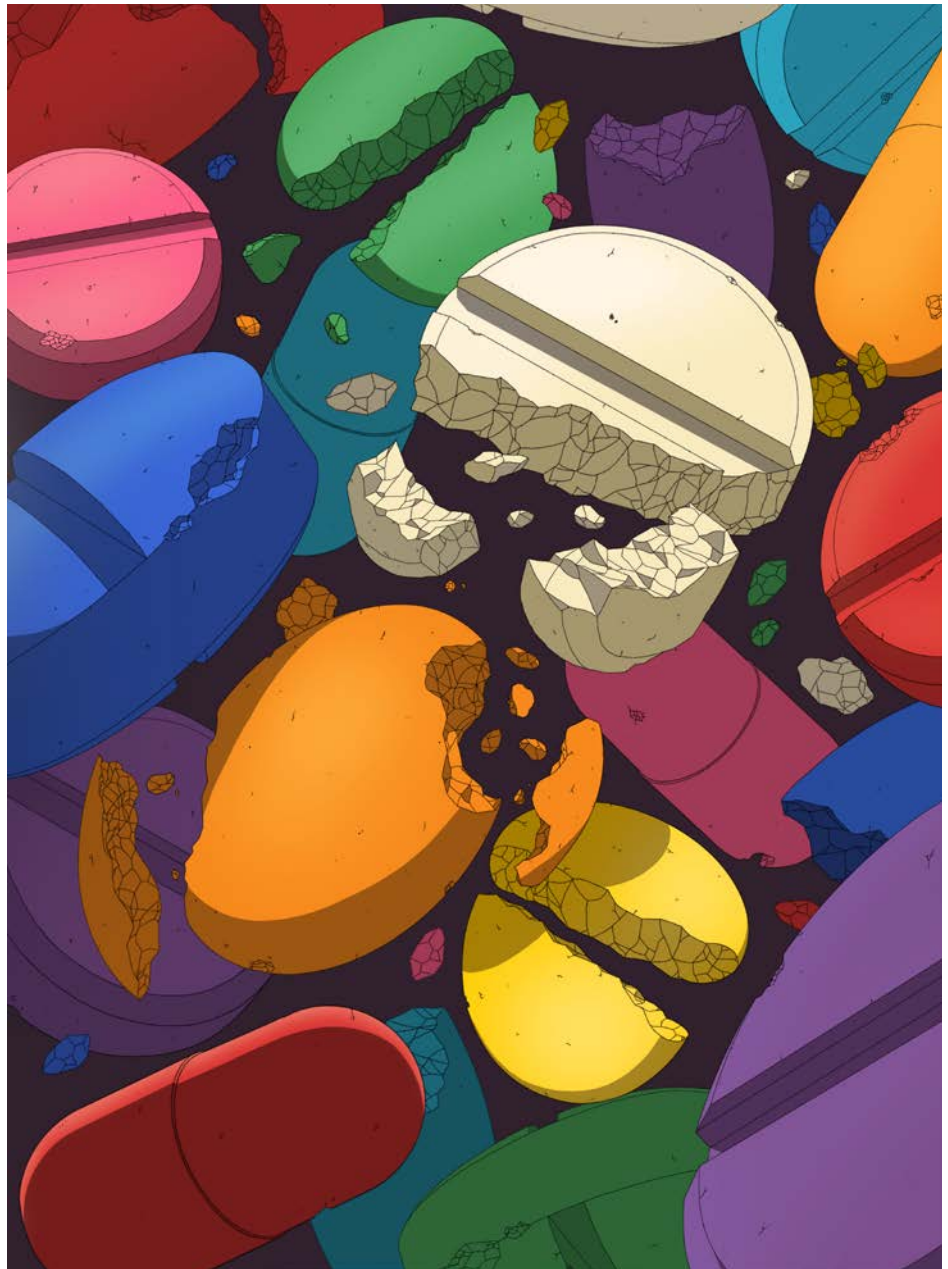
By FARAH STOCKMAN

*A member of the editorial board.*

The American health care system is built on the idea that a pill is a pill. Generic drugs are considered equal to and interchangeable with one another — and also with the name brand. This gospel has existed since 1984, when a law known as Hatch-Waxman was passed, allowing companies to make drugs that had gone off patent without having to replicate the same expensive clinical trials. For the most part, all they had to do was prove that the generic was manufactured using good practices and worked in the body in a similar way, within an acceptable range.

Hatch-Waxman has been a stunning success. Americans have grown increasingly comfortable with generic medications, which now represent 90 percent of the prescriptions that are filled in this country. Their widespread use has translated into trillions of dollars in savings. Politicians and experts agree that any hope we have for affordable, universal health care rests on generic drugs.

But in recent years, the generic drug supply has been plagued by problems. Whereas name-brand drugs can be so expensive that people can't afford them, generics are often so cheap that companies stop making them or cut corners to turn a profit. Competition for market share at rock-bottom price points has led to chronic shortages, unpredictable price-spikes, allegations of illegal price-



fixing, and substandard and even dangerous practices.

Production of generics has shifted overseas, where it's harder for the Food and Drug Administration to inspect factories. Major companies have been caught faking and manipulating the data that is supposed to prove that drugs are effective and safe. Probable carcinogens have been discovered in the drug supply. During the pandemic, which caused several countries to ban the export of medical supplies, a new fear has arisen: that faraway factories might one day cut Americans off from their drugs. Dozens of lifesaving medications are made with ingredients no longer manufactured in the United States.

I got interested in the generic drug supply this summer, after I heard that the nation's largest generic drug factory — the old Mylan plant in Morgantown, W.Va. — was slated to close. Its looming closure flew in the face of promises by Presidents Donald Trump and Joe Biden to encourage more drug production on U.S. soil. The factory workers in Morgantown, aided by activists from Our Revolution, were pushing for the facility to be declared critical infrastructure, essential for national security. "They say they want to shore up domestic production. If that's true, you can't have a better scenario," Joe Gouz, the president of the factory's union, United Steelworkers Local 8-957, told me. "This is a turn-key facility."

When I visited Morgantown in July, pill coaters reminisced to me about the drugs they'd made over the years. They told me that Levothyroxine, a thyroid medication — a synthetic version of a hormone that was once taken from animals like sheep — still had its own area on the factory floor. Levothyroxine is known for being tricky to make. Even small variations in a Levothyroxine pill can have a big impact on the body, so much so that endocrinologists recommend that patients refrain from switching brands, even between generics. (The F.D.A. does not agree. A pill is a pill, the agency insists.)

The workers took pride in the fact



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that their "Levo" had never faced a recall, while other companies repeatedly failed to get the potency right. "One of the hardest things to do in the pharmaceutical industry is run a fluid bed," Chad McCormick, a 43-year-old material handler told me, referring to the process that produces the tiny granules that go inside some pills. "I can run a fluid bed in my sleep."

Mr. McCormick and others told me a familiar story of a once-proud factory that had been picked apart by greedy corporate bosses. But I came to see the saga of the plant as a tale of how everything had gone wrong with the generic drug supply itself.

Built in 1965 by a paternalistic entrepreneur, Milan Puskar, the million-square-foot plant churned out pills 24 hours a day, seven days a week. Mr. Puskar knew his workers by name and treated them like family. In 1984, when Hatch-Waxman passed, Mylan's stock soared. There was a fortune to be made in generic drugs. But competition was brutal. A pill was just a pill, but the first company to get approval to make it had an advantage over the rest.

In 1987, a private investigator hired by Mylan discovered that rival companies were bribing F.D.A. officials to get faster approvals and sometimes faking their

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test results by using the name brand rather than their own product. The revelations sparked a scandal that the F.D.A. worked hard to fix, but the cheating and corruption didn't go away. Two decades later, Mylan found itself again competing with unscrupulous rivals. This time, they were based in India and China.

"Mylan was losing market share to Indian drug companies that made their own active ingredients in-house and operated at rock-bottom costs," wrote Katherine Eban in her book "Bottle of Lies: The Inside Story of the Generic Drug Boom," which chronicles how Ranbaxy, the now-disgraced Indian drug giant, faked data and engaged in other forms of fraud in its bid to get F.D.A. approval to sell drugs in the United States. "By contrast, Mylan was ordering ingredients from Chinese and Indian suppliers. Mylan couldn't beat their price — unless it joined them and went global."

Drug production moved to Asia for the same reasons that other American manufacturing did: labor was cheap, environmental regulations were weak and the continent was full of new potential customers. But drug companies had an additional incentive: Over there, F.D.A. inspectors didn't drop in on factories unannounced.

In 2012, Heather Bresch, Mylan's then-C.E.O. and the daughter of Senator Joe Manchin, complained at a congressional hearing that U.S.-based plants like hers got inspected every two years, but the same was not required of foreign factories. Congress responded by setting up a system in which generic drug companies paid a fee that gave the F.D.A. more resources to conduct international inspections.

By then, Mylan had already joined the offshoring trend. In 2007, it became the first American drug company to buy a

publicly traded Indian company, shifting some of its production to the western city of Nashik. About 400 workers in West Virginia lost their jobs. But the production of Levothyroxine, which was hard to make, remained in Morgantown.

Just how dependent Americans are on faraway factories is difficult to tell, since the place a drug was made — and even the name of the company contracted to make it — are considered trade secrets in the pharmaceutical industry. You read that right. Americans have no way of knowing where their pills come from. In theory, the F.D.A. knows where drugs are made, but the agency can't disclose that information publicly.

This secrecy, combined with the shift to low-wage countries, doesn't bode well for quality, according to John Gray, an Ohio State professor who studies the relationship between drug recalls and countries of origin. Because of the industry's lack of transparency, Professor Gray has to get creative to find data to crunch. "We know where our shirts are made, but not where our drugs are made, which is arguably more important," he told me. "If our shirts are shoddily made, we can tell and we are not going to buy them again." But we often don't know if our drugs are shoddily made, unless something terrible happens.

In 2008, at least 81 people died from a poisoned blood thinner traced back to a Chinese supplier in what has been described as a "deliberate scheme to adulterate a lifesaving medication." Ten years later, Valsartan, a generic drug used to treat high blood pressure, was found to contain a probable carcinogen. Even without high-profile catastrophes, drugs that don't work as well as they should can take a quiet toll. For instance, when New Zealand's national health system switched to a generic antidepressant, some patients reported a worsening in their condition.

Adam Clark-Joseph, an assistant professor at the University of Illinois Urbana-Champaign, co-founded Valisure, an online pharmacy that tests every batch of medicine it sells, after he took a pill that seemed to have no effect on him at

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all. Valisure rejects about 10 percent of batches because of impurities or inaccurate dosages. When the company tested generics of Lisinopril, a popular blood-pressure medicine, it found that some generics made overseas were as consistent as the name brand, while others had dosages that varied widely from one batch to the next. "If somebody taking blood pressure medication gets stuff that doesn't work, and they die of a stroke," Mr. Clark-Joseph asked, "are you going to blame the drugs?"

A former F.D.A. official who asked not to be named because he has left the agency and is now in the private sector told me that the agency had made progress on overseas inspections, but that it shouldn't let down its guard. "Is the house on fire now? No," he told me. "Is the risk of the house being on fire higher than it should be? Yes." But he warned me not to make the public afraid of their drug supply. Nobody wants Grandma to stop taking her pills.

The reality is that we don't know how close the house is to catching fire. Because of the pandemic, the F.D.A. managed to perform just three foreign inspections in 2020, according to the Government Accountability Office. More than a thousand inspections had to be postponed. While Covid opened Americans' eyes about their dependence on faraway drug factories, it also further reduced the visibility into what is going on inside those plants.

I figured that offshoring the U.S. drug supply could have two possible outcomes: Either the quality of drugs worldwide would rise to American standards — or American standards would sink. The demise of the Mylan plant seems to be a story of sinking. When Mr. Puskar was alive, Morgantown had a nearly unblemished F.D.A. record. It

had a reputation as such a well-run facility that the F.D.A. trained its inspectors there. But after his death, in 2011, things began to go downhill.

In 2016, Ms. Bresch got hauled in to Congress to explain why Mylan had jacked up the price of lifesaving EpiPens by 400 percent. (Mylan owns the patents to some brand-name products, including EpiPen.) The following year, Mylan's president, Rajiv Malik, was accused of an illegal conspiracy to hike generic drug prices by colluding with other executives in what Connecticut's attorney general, William Tong, has called "the largest corporate cartel in history." (Mr. Malik has denied the allegations; the case is ongoing.) The F.D.A. also issued a damning warning letter about Mylan's flagship factory in India, noting that it had systematically ignored or deleted troubling test results and "failed to establish an adequate quality control unit."

In 2018, F.D.A. inspectors swarmed the Morgantown plant itself, uncovering a host of problems, according to documents archived by Redica Systems, a company that maintains a searchable database of F.D.A. inspection reports. The raid appears to have been triggered by a whistle-blower at the plant who alleged that Mr. Malik, a former leader at Ranbaxy, ordered employees to manipulate drug test results and cover it up by intentionally crashing the company's computers. (A spokeswoman for the company dismissed the allegations as "unproven and baseless" and expressed "deep faith in the integrity" of Mr. Malik.)

Nonetheless, the F.D.A. raid on the Morgantown plant left Mylan's reputation in tatters. Investor lawsuits piled up. In response, Mylan announced that it was simplifying operations at the plant and halting the production of several drugs, sparking nationwide shortages. The factory had been supplying about a third of all doses of buspirone, an anti-anxiety medicine. Suddenly, patients couldn't buy it. One pharmacy drug shortage list identified Mylan as the nation's sole supplier of thiothixene, which treats schizophrenia. Suddenly it was no-

where to be found.

Quality control issues like the ones found at Mylan are a leading cause of drug shortages, both at American plants and overseas. Sometimes the F.D.A. shuts down a plant after discovering violations, dramatically reducing a medicine's supply. Other times, companies with quality control issues simply opt to stop making a drug rather than invest in expensive upgrades to their aging facilities. The current system simply doesn't reward investments in quality. If a pill is just a pill, it doesn't matter if it's made in a state-of-the-art plant or a rusty one.

For example, in 2011, F.D.A. inspectors discovered a host of problems at Ben Venue Laboratories, an Ohio-based drug manufacturer, including poorly maintained equipment that shed particles into the drugs and an inexplicable bucket of urine on the factory floor. Eventually, the company shut its factory down instead of fixing it. The plant happened to be the country's sole supplier of Doxil, an injectable chemotherapy drug used to treat certain types of cancer. The supply of Doxil dried up. The price of what was left skyrocketed.

In 2016, an explosion at a chemical plant in Eastern China led to a global shortage of an antibiotic combination used intravenously in intensive care. The plant appears to have been the world's sole supplier of active ingredients needed to make it. Over the past two decades, China has become the world's top producer of antibiotics, and its aggressive market tactics have driven some American factories out of business. According to the 2018 book "China Rx: Exposing the Risks of America's Dependence on China for Medicine," Chinese companies flooded the U.S. market with penicillin so cheap that American companies could not compete. The last American factory making key ingredients for penicillin closed in 2004.

Drug shortages rarely make the newspaper because doctors can usually switch from a preferred drug to another one. But make no mistake: Shortages are costly, and they can be deadly. A study found that a shortage of an inject-

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able cancer drug in 2009 led to higher rates of relapse in children because the substitute didn't work as well.

Chronic drug shortages of lifesaving medicines that have been around for decades are perhaps the clearest signal that our drug supply is sick. "The system that we have right now is so broken that we need a big shake-up," Erin Fox, director of drug information at University of Utah Health and one of the nation's top experts on drug shortages, told me.

Mylan's executives decided that the company needed a big shake-up, too. Under mounting pressure from bad publicity and the F.D.A., they merged Mylan with a spinoff of Pfizer. Mylan ceased to exist. It was replaced by Viatrix, a new entity with global centers in Pittsburgh, Shanghai and Hyderabad. So far, things have turned out all right for Ms. Bresch, who retired with a windfall, and for Mr. Rajiv, who is now president of Viatrix. Of course, their factory workers fared worse. In December 2020, the company announced that it was restructuring to cut costs and closing five plants around the world, including the one in Morgantown. A total of 1,431 West Virginians would lose their jobs.

For months, workers hung on to hope that the global pandemic would convince people that the plant had to be saved. They knew that Mr. Trump had directed the F.D.A. to come up with a list of critical drugs, which included everything from aspirin to zanamivir, an antiviral medicine used to treat the flu, as a first step in figuring out where vital medicines are made. Months later, President Biden ordered a committee to whittle down the list. The report, released in June, painted a grim picture: Of more than 100 supercritical medications, about half are made with ingredients that are not produced in the United States.

A recent study based on data from Clarivate, an analytics firm cited in

the White House report, was even more alarming. It found that, of the top 100 generic medicines that Americans consume, 83 had no U.S. source of active pharmaceutical ingredients. No American source existed for 97 percent of the most commonly prescribed antivirals and 92 percent of the most commonly prescribed antibiotics.

Nonetheless, the F.D.A. determined that closing the Morgantown plant wouldn't create any critical shortages. White House officials told me that their hands were tied: They didn't have the authority to save the plant. On July 31, the facility closed its doors. Bill Hawkins, a 47-year-old pill coater, told me that Americans might end up wishing it was still around. "If there is a worldwide pandemic and India is making all the drugs, they are going to take care of their people first," he said. "I can't blame them."

The truth is, a pill is not just a pill. A pill that was made in a top-notch factory with a spotless track record is better than one that was made in a plant that barely passed inspection. A pill that was stored in a cool dark place is better than one left baking on an airport tarmac for weeks.

Kevin Schulman, a professor of medicine at Stanford, believes the salvation of the generic drug industry lies in acknowledging this simple fact. If the market believes that all pills are created equal, then price is the only metric that matters. Contracts are written so that bulk buyers can jump to a new supplier that comes along charging a penny less. Patient prescriptions are filled and reimbursed based on the cheapest version available. Generic drugs are bought and sold as a commodity, like corn or crude oil. When a drug comes off patent, its price declines steeply, as competitors enter the market. But then the price gets so low that companies don't find it profitable to make. They exit the market, even if patients still need the drug to survive. At that point, prices rise astronomically. Quality and long-term accessibility never enter into the picture.

Professor Schulman concluded that the free market simply wasn't working for

generic drugs. “The economics of this market, the theoretical ideas of what this market could be, are all from 1984,” he told me.

Since the 1980s, almost every other kind of product has evolved to develop sophisticated rating systems to let customers balance quality and cost, and make decisions accordingly. “You go on Amazon and you see three different manufacturers making something,” he told me. “One’s got five stars. Another has one star. What the American public should want is the five-star product. And we should be given the tools to pick that out. Who cares if it is a nickel more if it’s a much better drug?”

If customers could see a quality ranking on a drug, they might be willing to pay more for it. Insurance companies might refuse to reimburse for drugs that aren’t at least three stars, to avoid paying for a placebo. The U.S. government could pledge to only buy drugs for its veterans that receive a rating of four stars or above. If quality were rewarded, more companies would invest in it.

The idea of establishing a quality rating system — either for drugs or the fac-

ories that make them — has been batted around in Washington for years. It was included as a “next step” in the Biden administration’s new supply chain resiliency plan. But privately, administration officials told me that they expected it to be an uphill battle, since quality ratings upend the foundational mythology upon which the entire industry has been built.

The realization that the free market isn’t working for generic drugs has led some to turn to nonprofits as a solution. In 2018, Dan Liljenquist, a Utah health care executive fed up with drug shortages and price spikes, brought together a group of hospital administrators and philanthropists to create a buyers club. Members agree on the drugs they want, and then the organization, Civica Rx, enters into long-term contracts with licensed manufacturers to produce them. Since the collective is funded by its members, not investors, it can prioritize need and quality over profit.

Civica doesn’t pretend that all drugs are equal. It sources drugs from the United States and Europe so it has more visibility into the supply chain. It stock-

piles several months of supply, bucking the trend of just-in-time manufacturing. And it supplies drugs that the market has failed to reliably produce. Today, it counts more than 50 health systems as members — over a third of all licensed hospital beds in the United States.

In January, a month after the announcement that the old Mylan plant would shut down, Civica unveiled plans to build a 120,000-square-foot factory in Virginia to make sterile injectable drugs, which have been particularly hard to source. The nonprofit has begun to supply hospitals with vancomycin, an antibiotic used to treat severe pneumonia, which had been scarce and expensive for years prior. Civica’s prices are competitive, but not rock-bottom.

“As of today, we’re still paying a little more for that product,” Mohammad Kharbat, the regional vice president of pharmacy services at SSM Health, a founding member of Civica, told me. But he doesn’t mind. “Sometimes, for the stability of the supply chain, and that peace of mind,” he said, “You are willing to pay a little bit more.”