August 28, 2023

The high cost of lower priced medicine

By Angelo Katsoras

Introduction

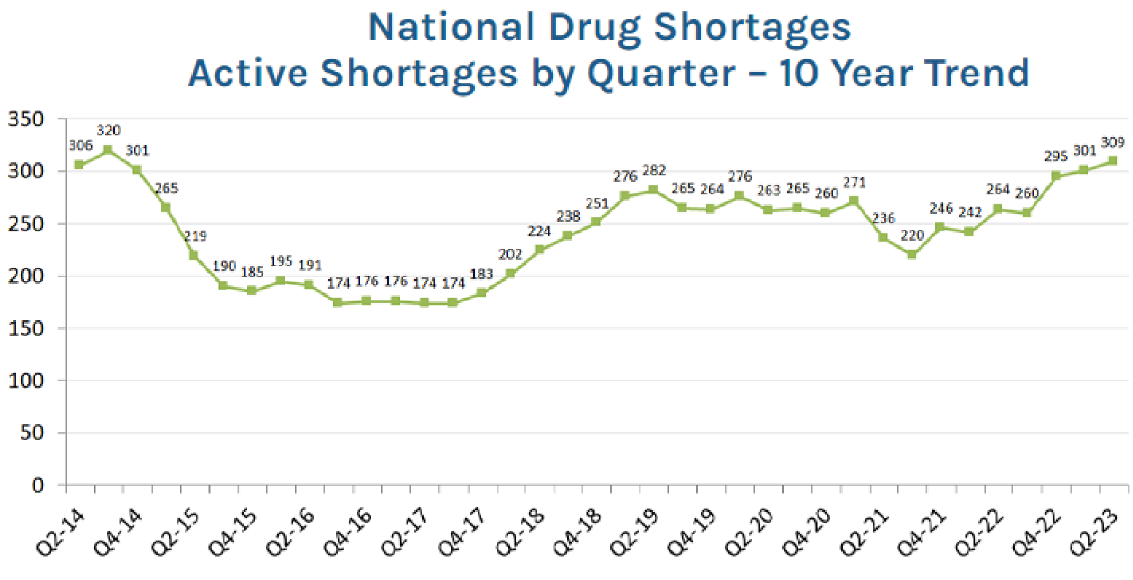
The media and government policymakers often cite the increasingly volatile world as a major reason to re-shore supply chains related to alternative energy, electric vehicles and semiconductors. But it is important not to overlook the fact that few challenges more dramatically illustrate this critical need to relocate production than ensuring access to essential medicines.

This report examines the growing problem of drug shortages, particularly for generic drugs, a crisis increasingly being driven by a combination of low profit margins, market consolidation, and over-reliance on foreign supply chains.

While the main focus of the report is on drug shortages in the United States, we also look at how related factors impact Canada and how, in some ways, Canada faces a much tougher road to finding solutions.

Increasing drug shortages

The United States is having to deal with more and more shortages of medicine, particularly generic drugs for treating conditions such as cancer, heart disease and bacterial infections. As of last March, 309 drugs nationwide were listed as being in short supply. The highest since 2014.



Source: "University of Utah Drug Information Service," 2023

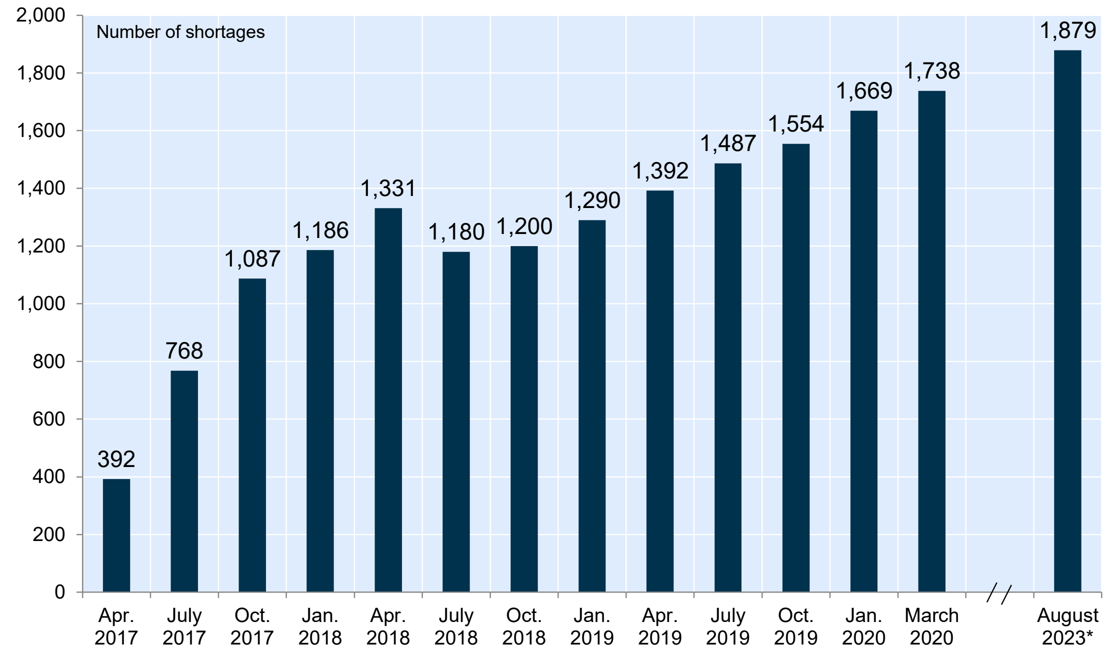
A survey conducted this year by the American Society of Health-System Pharmacists between June 23 and July 14 found that 32% of the 1,123 U.S. hospital pharmacists surveyed have been forced to ration, delay or even cancel treatments because of drug shortages.[1]

Canada also faces drug shortages. According to the Canadian government, 29% of all prescription drugs sold in Canada were reported to be in short supply in 2019/20. Over 90% were generic drugs.[2] Recent examples include the 2022 shortage of cold medicines for children and adults, and the critical shortage of two cancer drugs this year: one used to fight thyroid cancer and the other to fight leukemia (i.e., thyrotropin alfa and asparaginase).[3]

As of August 28, 2023, the Canadian government estimates that 1,879 drugs are in short supply, up from 392 in 2017 (see chart below).[4]

[1] "Severity and impact of current drug shortages," American Society of Health-System Pharmacists, July 2023
[2] "Drug Shortages in Canada and their Impact on Public Drug Plans, 2017/18 to 2019/20," Government of Canada, September 2022
[3] "Canada facing critical shortages of leukemia and thyroid cancer drugs," CTV News, June 6, 2023
[4] "Drug Shortages Canada, " Canadian Federal Government, August 2023

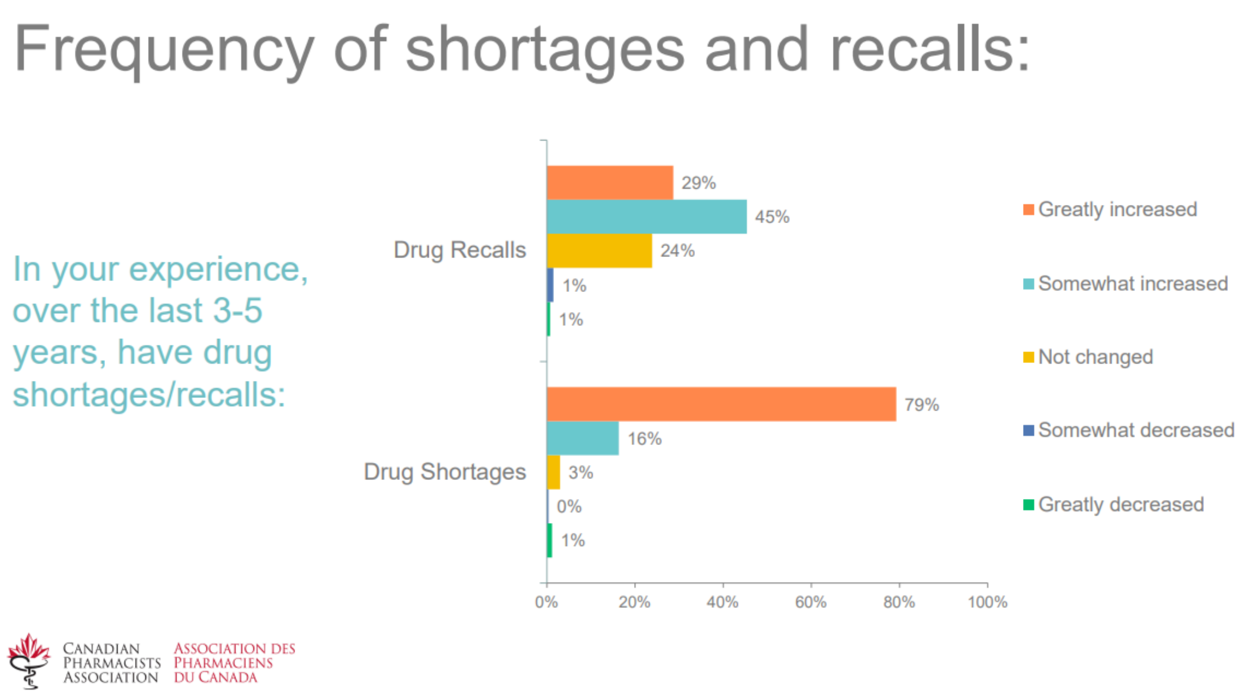
Canada: Number of drug shortages



*No data for 2021 and 2022

NBF Economics and Strategy (data via Statista, Patented Medicine Prices Review Board and drugshortagescanada.ca)

Further evidence that this is a long-standing problem in Canada comes from a survey conducted in 2018. The survey found that the vast majority of Canadian pharmacists (79%) reported that drug shortages had increased in the three to five years prior to 2018. In addition, more than two-thirds of pharmacists (67%) encountered drug shortages on a daily basis during this period.[5]



Source: "CPHA Drug Shortage and Recall Survey 2018," Canadian Pharmacists Association, July 2019

[5] "Drug shortages have 'greatly increased' over the past 3-5 years say Canadian pharmacists," Canadian Pharmacists Association July 2019

The challenge of slim profit margins

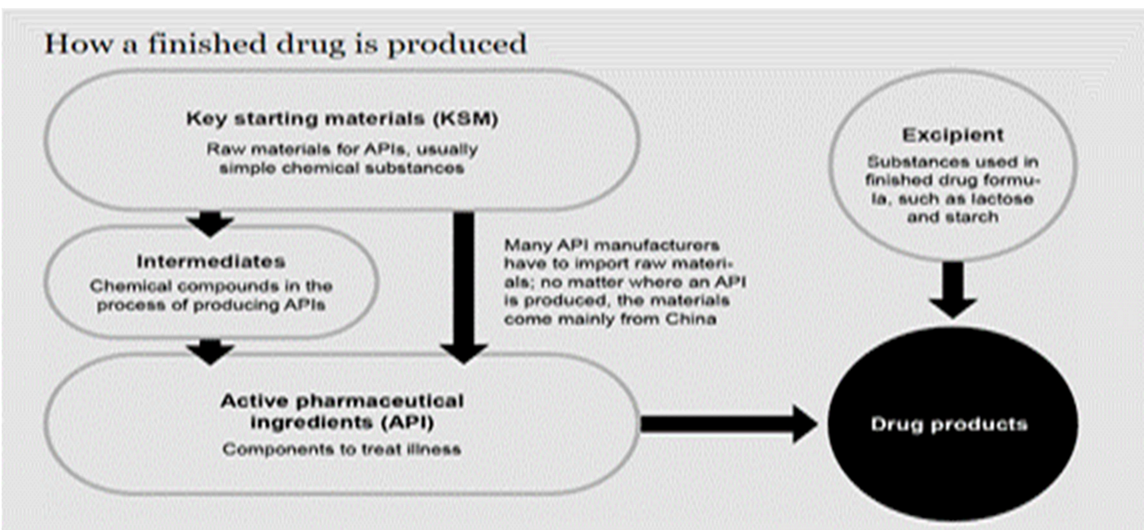
When a company first develops a new drug, the U.S. (and Canada) grants it an exclusive patent for up to 20 years. This protection from competitive pressures allows the company to recoup research and development costs and ensure profitability.

However, when the patent expires, the drug becomes fair game for any other company to produce it in a generic form. Since these manufacturers make essentially the same product, sales are determined by who can produce at the lowest cost. It has been estimated that the average price of U.S. generic drugs fell by more than half from 2016 to 2022.[6] This trend has been driven in part, also, by government pressure on generic manufacturers to produce at ever-lower costs.

On the one hand, these lower prices are a positive for a healthcare sector that has long struggled with rising costs. Generic drugs account for 90% of all drugs sold in the United States but only 18% of total drug costs. Canada has a similar mix, with generics accounting for 74.4% of drugs sold in 2022, but only 21.8% of dollars spent.[7]

On the other hand, lower prices mean lower margins, which discourages some companies from producing generics. As a result, generic drug production is in the hands of fewer and fewer players, making it increasingly vulnerable to supply disruptions.

It is also important to note that, regardless of price, manufacturing certain generic drugs remains a complex process. First, ingredients (i.e., chemicals) must be procured from around the world. Then, they must be combined, often under sterile and strictly regulated conditions.



Source: "The great medicines migration," Nikkei Asian Review, April 4, 2022

For example, while essential generic cancer drugs such as cisplatin and carboplatin are relatively cheap in the United States (about $15 and $23 per vial, respectively), the manufacturing process remains complex. These platinum-based drugs must be produced in a sterile facility where rigorous controls are in place to protect workers from their toxic properties.[8]

Tightening margins are driving manufacturers out of the generic market

Israel-based Teva Pharmaceutical Industries, one of the world's largest makers of generic drugs, is a case in point. Declining profit margins have forced it to downsize. The company operates 52 plants, down from 80 in 2018, and has plans to shut down as many as a dozen more facilities.

U.S.-based Akorn Pharmaceuticals is another example. The company declared bankruptcy in February. It used to manufacture 75 generic drugs. This includes being one of only two U.S. suppliers of liquid albuterol, an essential drug used to treat children's asthma.[9]

Moreover, even when a drug is manufactured by multiple companies, they increasingly rely on the same few suppliers for their ingredients. According to Mariana Socal, a pharmaceutical market expert at Johns Hopkins, one third of the active

[6] "Examining the Root Causes of Drug Shortages: Challenges in Pharmaceutical Drug Supply Chains," Subcommittee on Oversight and Investigations (U.S. Congress), May 9, 2023
[7] "The Canadian Generic Pharmaceutical Association," 2023
[8] "How the Shortage of a $15 Cancer Drug Is Upending Treatment," New York Times, June 26, 2023
[9] "How one U.S. drugmaker contributed to the escalating drug shortage crisis," NBC News, July 16, 2023

pharmaceutical ingredients (APIs) used in the U.S. generic drug supply are produced in only two or three facilities and another third in just one.[10]

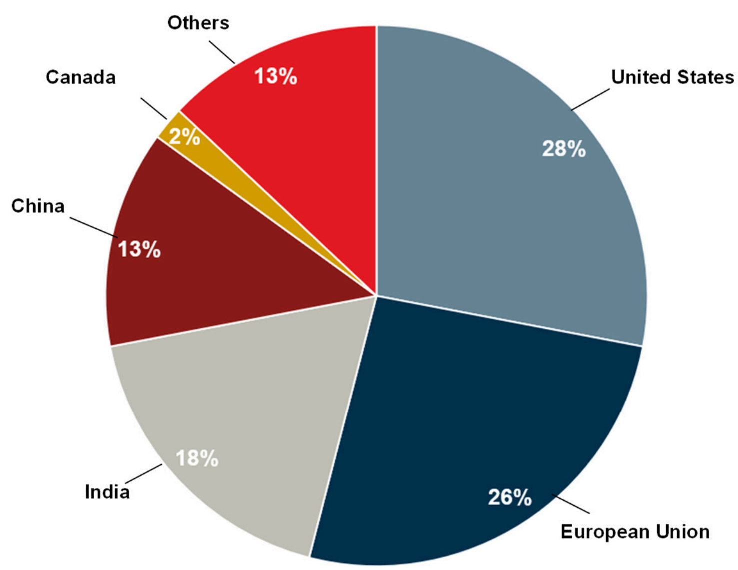
Overdependence on fewer sources means that in some cases a single plant shutdown or quality problem can lead to a major supply disruption.

Production increasingly shifting overseas

Over the past three decades, the manufacturing of pharmaceuticals, especially generics, has not only been consolidated among fewer companies, it has also been increasingly outsourced to countries with lower labour/manufacturing costs and less stringent regulatory environments. China and India are the most prominent of these destinations.

In August 2019, the U.S. Food and Drug Administration (FDA) reported that 72% of the manufacturing facilities that produced ingredients for U.S. drugs were located abroad.[11]

Distribution of facilities manufacturing APIs* for the U.S. pharma market
As of 2019



*Active pharmaceutical ingredients
NBF Economics and Strategy (data via U.S. Food and Drug Administration)

Where generics are concerned, 87% of the FDA-registered manufacturing facilities that produce generic drug ingredients were located in foreign countries over the same period.[12]

What about Canada's dependence on imports?

While an exact comparison with the United States is difficult due to different data sources, Canada is also heavily dependent on imports of pharmaceuticals and related inputs.

Between 2010 and 2020, the percentage of Canada's total spending on medicines that went to imports increased from 74% to 93%.[13]

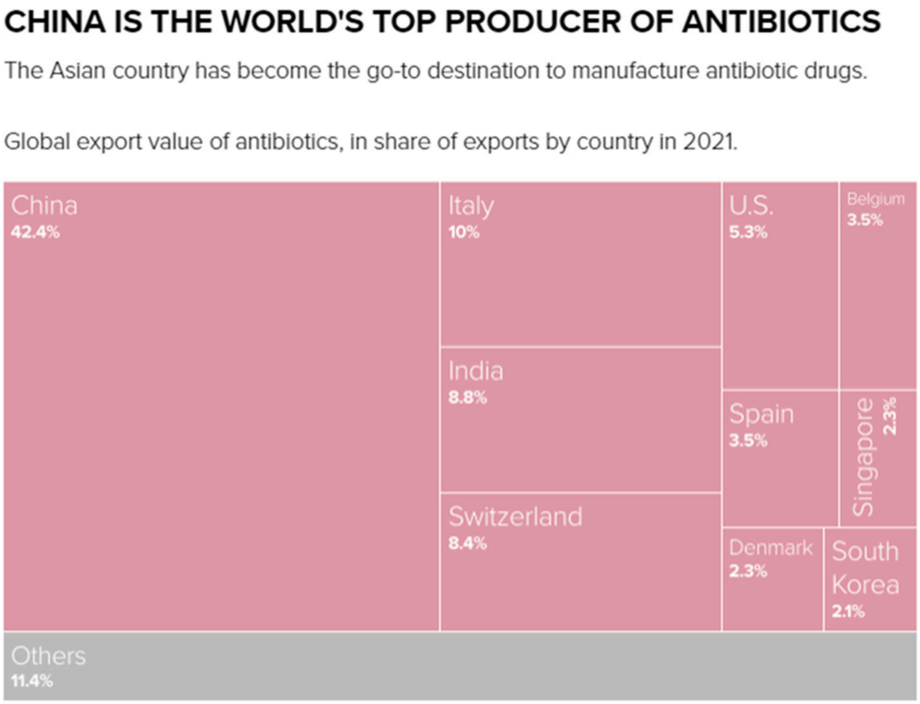
Canada is even more dependent on the ingredients needed to make drugs. While the United States produced about 28% of the active pharmaceutical ingredients needed for its drug supply in 2019, nearly all of the active pharmaceutical ingredients

[10] "The Cancer-Drug Shortage Is Different," Atlantic Monthly, June 26, 2023
[11] "Safeguarding Pharmaceutical Supply Chains in a Global Economy," FDA, October 2019
[12] "Building resilient supply chains, revitalizing American manufacturing and fostering broad-based growth," White House, 2021
[13] "Pharmaceutical security for Canada," Canadian Medical Association Journal, August 22, 2022

needed for Canadian drugs (including those produced locally) came from abroad in 2021. India and China accounted for over 60% of imported ingredients for locally produced generics.[14]

China has become a pharmaceutical powerhouse over the past 20 years

In addition to being a major producer of raw ingredients needed to make drugs, China accounted for 42.4% of global antibiotic exports by value in 2021.



Source: "How China could choke EU supply of medicines," Politico, May 22, 2023 (via International Trade Centre)

The United States is particularly dependent on China for antibiotics. A whopping 97% of the antibiotics consumed in the United States are produced in China.[15]

China is also a major supplier of other medicines to America. In 2019, it was reported that about 70% of the pain reliever acetaminophen and 40-45% of the blood thinner heparin consumed in the United States were produced in China.[16] (Globally, China accounted for about 80 percent of the supply of heparin during the same period.[17]) In addition, the U.S. currently imports over 75% of its vitamins B6, B12, B1, C, and nearly 70% of its vitamin E from China.[18]

At a time of rising tensions between the two superpowers, this dependence on China is increasingly seen in Washington as unsustainable. This concern was very eloquently expressed in Bob Woodward's 2018 book, "Fear: Trump in the White House". In a discussion, Gary Cohn, then Trump's chief economic adviser, argued against a trade war with China, noting that about 97% of all antibiotics in the United States came from China. "If you're the Chinese and you really just want to destroy us, just stop sending us antibiotics," he stated.[19]

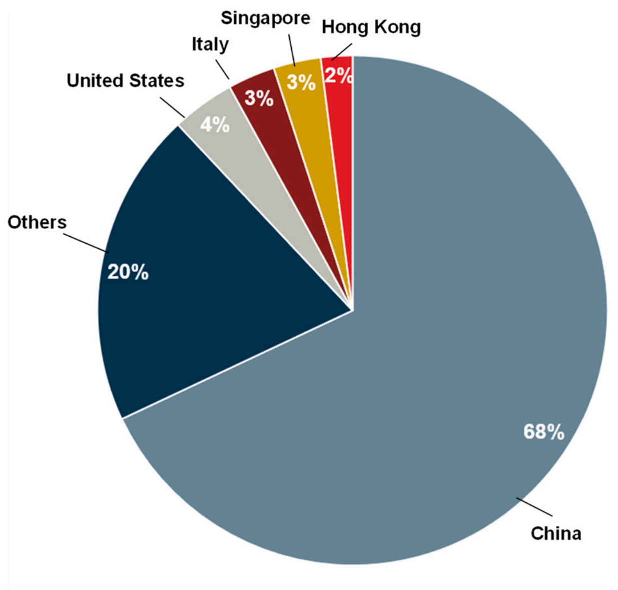
In 2019, Li Daokui, an economics professor at Tsinghua University and a former central bank adviser, reportedly told China's national legislature: "We are at the mercy of others when it comes to computer chips, but we are the world's largest exporter of raw materials for vitamins and antibiotics." He added, "Should we reduce the exports, the medical systems of some western countries will not run well."[20]

[14] "Canadian Generic Pharmaceutical Importing/Manufacturing Capacity Study, Ernst & Young, February 2022
[15] "Drug shortages are an urgent national danger. Here's how we fix them," Washington Post, January 16, 2023
[16] "U.S. policymakers worry about China 'weaponizing' drug exports," South China Morning Post, December 20, 2019
[17] "The day supply chains stood still: What war with China could bring," The Hill, April 19, 2023
[18] "The US is relying more on China for pharmaceuticals – and vice versa," Atlantic Council, April 20, 2023
[19] "U.S. Dependence on Pharmaceutical Products From China," Council of Foreign Relations, August 14, 2019
[20] "China threat to halt US antibiotics supply," The Times, March 11, 2019

India, too, has become a global player in pharmaceuticals

Today, India produces about one-fifth of the world's generic drugs and accounts for 40% of the generics sold in the United States.[21] However, India depends on China for about 70% of the pharmaceutical ingredients needed to make drugs.[22]

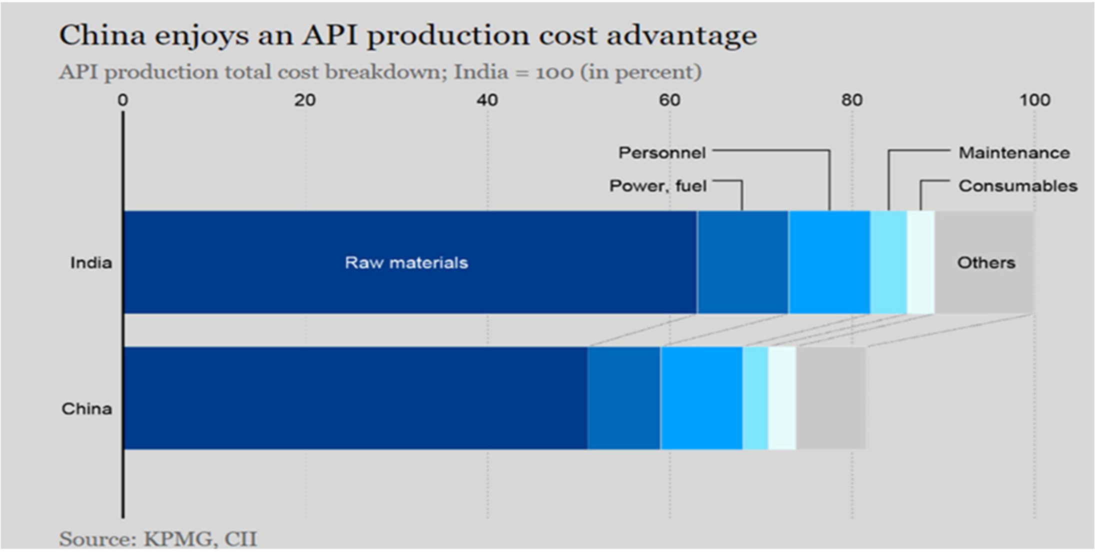
Distribution of facilities manufacturing APIs* for India's pharma market
As of 2019



*Active pharmaceutical ingredients
NBF Economics and Strategy (NBF Economics and Strategy (data via U.S. Food and Drug Administration)

Because of this reliance, when China closed many of its factories during the pandemic, India was forced to temporarily restrict exports of certain drugs to ensure domestic supply.

China can produce the active pharmaceutical ingredients (APIs) needed to make drugs for about 20% less than India can.

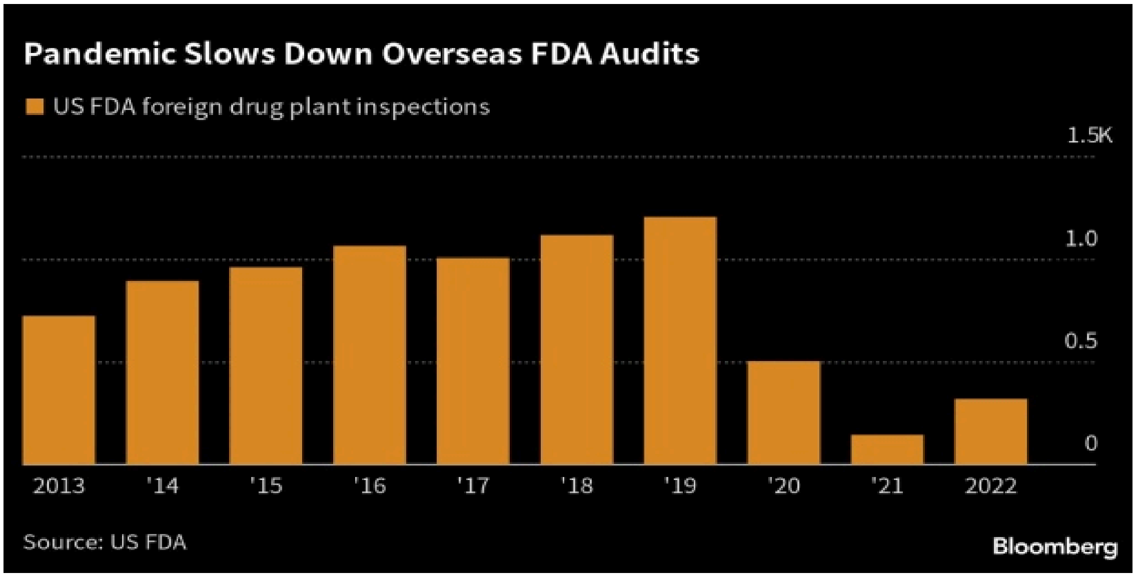


Source: "The great medicines migration," Nikkei Asian Review, April 4, 2022

[21] "Drug Shortages Stem From Quality Problems in Indian Factories," Wall Street Journal, June 19, 2023
[22] "Building resilient supply chains, revitalizing American manufacturing, and fostering broad-based growth," The White House, June 2021

How outsourcing has resulted in increased health-related risks

While overseas manufacturers often enjoy significant cost advantages over their U.S. counterparts, they come with greater health risks. The problem is compounded by the fact that foreign factories are more difficult for the U.S. FDA to monitor. In fact, even before overseas inspections plummeted because of the pandemic, the agency had long been criticized for not inspecting enough facilities abroad. It is estimated that in 2022, the FDA inspected only 6% of the foreign facilities that produce U.S. drugs and their ingredients.[23]



Source: "US FDA Uncovers Fresh Faults at India's Second-Biggest Drugmaker," Bloomberg, June 29, 2023

Approximately 60% of the FDA inspections of pharmaceutical facilities in the Asia-Pacific region result in a Form 483 being issued. This is a notice that flags potential violations of U.S. quality standards.[24]

India has come under increasing scrutiny for quality problems

Last December, Intas Pharmaceuticals, a generic drug manufacturer based in India, suspended production after an FDA inspection revealed numerous quality concerns. The stop caused a widespread shortage of cisplatin and carboplatin, two chemotherapy drugs used to treat a variety of cancers. The situation became particularly serious in the case of cisplatin because the plant accounted for 50% of the U.S. supply.[25]

A few months later, Global Pharma, also based in India, recalled its EzriCare Artificial Tears eye drops after the product was linked to a spate of highly drug-resistant bacterial infections that resulted in over 80 people being infected and four deaths. An FDA inspection found that the company did not follow proper protocols to prevent contamination of its products.[26]

These incidents came on the heels of the deaths of at least 70 children in Gambia last summer linked to cough syrups made by India-based Maiden Pharmaceuticals that contained toxic industrial solvents.[27]

Even before these outbreaks, the FDA warned Congress in 2019 that Indian drug manufacturers had one of the lowest rates of acceptable inspection results. About 83% of plants inspected in India met quality standards, compared with 90% in China and 93% in the United States.[28]

It is important to note, however, that the reason generics produced in the United States or other developed countries are safer is not because manufacturers are more ethical but because they are subject to much greater regulatory oversight. In other words, in the United States, the FDA can make much more frequent surprise visits to keep manufacturers in line.

[23] "After Pandemic Delays, FDA Still Struggling to Inspect Foreign Drug Manufacturers," ProPublica, April 19, 2023
[24] "Drug shortages are an urgent national danger. Here's how we fix them," Washington Post, January 16, 2023
[25] "How troubles at a factory in India led to a U.S. cancer-drug shortage," Washington Post, June 27, 2023
[26] "Drug Shortages Stem From Quality Problems in Indian Factories," Wall Street Journal, June 19, 2023
[27] "India's lax oversight of pharmaceutical manufacturing imperils health around the world," STAT+, January 9, 2023
[28] "Drug Shortages Stem From Quality Problems in Indian Factories," Wall Street Journal, June 19, 2023

Conclusion

Ensuring access to essential medicines is perhaps as important, if not more important, than reshoring alternative energy and semiconductor supply chains. This makes it highly likely to become a major, long-term policy goal for whichever political party happens to be in control of the White House.

To start with, reducing America's reliance on foreign suppliers is a necessary step toward making the nation's vital drug supply chain more resilient in times of heightened geopolitical tension. For example, if China were to cut off pharmaceutical exports because of a war in Taiwan, U.S. drug shelves could quickly be depleted, and many routine treatments would have to be halted. Even drug imports from India could be disrupted because its drug manufacturers rely heavily on ingredients from China.

Reshoring pharmaceutical manufacturing to the United States also has the potential to improve quality control and safety measures. U.S. regulators generally impose much stricter oversight than do those in many other countries.

It must be stressed, however, that the enhanced national security that comes with strengthening drug supply lines brings with it unavoidable higher costs. This is because wages are higher in the United States. U.S.-based pharmaceutical companies that expand U.S. production through reshoring also face additional expenses in complying with stricter domestic regulations, creating local supply chains, and training employees in new skills.

On a global scale, as other countries adopt similar reshoring strategies, there will be a shift away from serving many markets from a single location to locating production and supply chains closer to points of consumption. This will translate into lower economies of scale as supply chains are duplicated and become more regional.

This new global landscape will eventually force governments to either raise the price of certain drugs and/or adopt the same strategy being used to re-shore semiconductor and electric vehicle manufacturing: provide subsidies for domestic production.

In the case of Canada, given that it accounts for only 2% of global pharmaceutical sales (compared to 42.6% for the U.S.),[29] reshoring manufacturing (including ingredients) primarily for its local market would likely be prohibitively expensive. The most cost-effective strategy would be for Canada to align itself with a potential U.S. initiative to bring back manufacturing and advocate for the creation of a more North American-centric supply chain.

Bottom line: Pharmaceutical manufacturing, especially where generics are concerned, will join the growing list of industries where investors will need to assess not only a company's operational efficiency, but also its ability to lobby for subsidies and tariffs. Investors will then have to evaluate whether a combination of price hikes and government support adequately counterbalance the higher operating costs associated with reshoring.

[29] Statista (via IQVIA.com), 2023

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