Statement on

Designing A Resilient U.S. Drug Supply: Efficient Strategies to Address Vulnerabilities

at the Commission Hearing on

Dominance by Design: China Shock 2.0 and the Supply Chain Chokepoints Eroding U.S. Security

Panel II: Preparing for China's Counterpunch: Vectors for Supply Chain Coercion

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Statement of

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Introduction

Thank you, Co-Chair Miller, Co-Chair Shmavonian, and members of the Commission for this opportunity to address "Designing A Resilient U.S. Drug Supply: Efficient Strategies to Address Vulnerabilities".

I am Stephen W. Schondelmeyer, a Professor of Pharmaceutical Management & Economics at the University of Minnesota where I serve as Co-Principal Investigator for the Resilient Drug Supply Project (RDSP). In addition, I am Director of the *PRIME* Institute which focuses on research and policy issues related to the pharmaceutical market and its impact on society. These remarks are my own views based upon my research and experience in studying the pharmaceutical marketplace over the past fifty years. During my career, I have had the opportunity to interact with many federal entities that shape and influence our nation's healthcare system including the Department of Health and Human Services (DHHS), many of its divisions such as FDA, CMS, ASPE, ASPR, BARDA, as well as other federal agencies such as the FTC, DOJ, GAO, USTR, and OMB.

My testimony will address China's dominance by design of the global drug supply chain and various chokepoints that have developed, intentionally or unintentionally, over time to erode the security of the U.S. drug supply chain. Vulnerabilities in the U.S. upstream prescription drug supply chain will be identified, and efficient strategies for strengthening and securing our upstream prescription drug supply chain will be described. The potential economic, health, and national security impact of not using effective strategies to secure the U.S. drug supply is examined.

First, let me point out that the U.S. prescription drug supply chain has had a large number of drug shortages for more than two decades and that the relatively recent COVID-19 pandemic is not responsible for this chronic presence of drug shortages in the U.S. market. However, COVID-19 has exposed and highlighted several new and emerging vulnerabilities including quality of production issues, economic failures, geopolitical risk, and potential trade barriers.

Landscape of the U.S. and Global Pharmaceutical Markets

Virtually all Americans have used, or will use, a prescription drug at some point in their lifetime. Prescription medicines when appropriately used provide life-saving therapy, life-extending care, and improvements in the quality of life. Inability to access critical prescription drugs for any reason, when they are needed, can lead to life-changing, or even, life-ending consequences for an individual and can threaten the health, economic, and national security of the United States, its citizens, and its military.[1]

In 2024, Americans consumed more than 215 billion days of therapy that were provided through over 7 billion outpatient prescriptions.[2] The U.S. represented 4.2% of the global population in 2024 with 340 million of the 8.1 billion people in the world.[3] The

U.S. accounted for 40.1% of the global pharmaceutical spending ($639.2 billion of $1,593.7 billion) for 2024.[4] This is a disproportionately high share of pharmaceutical spending in the United States compared to other developed countries and results, in large part, from a higher rate of drug utilization and the highest drug prices in the world.[5]

Nine out of ten (90%) U.S. prescriptions were filled with a generic or biosimilar medication, yet these prescriptions accounted for only 13.1% of U.S. prescription drug spending in 2024.[6] For the 90% of U.S. daily doses that are generics, about 60% are made in either India (47.2%) or China (13.0%), while only 10.5% were made in the U.S.[7] Upon further examination, both the Indian pharmaceutical industry and the Indian government acknowledge that Indian firms heavily rely on China for about 65% to 70% of their API sourcing.[8] After adjusting for India's secondary dependence on China for API sourcing, it is estimated that 46.0% of U.S. daily doses of generics have API from China and 14.2% have API from India for a total of 60.2% from China or India. When an adjustment is made for the 10% of U.S. prescriptions that are not generics, China and India account for about 54.2% of all U.S. daily doses of prescription medicines. Clearly, the U.S. is dependent upon China and India for the daily doses of generic drug products. Among the many possible root causes of generic drug shortages, both quality issues and economic market failure due to over-competition and low prices are often reported.[9] For example, more than 6 of 10 generic drugs that are in shortage have a price of $1 per unit or less."[10] Overall, the U.S. generic market is heavily dependent upon China and India for more than one-half of all daily doses consumed by Americans.

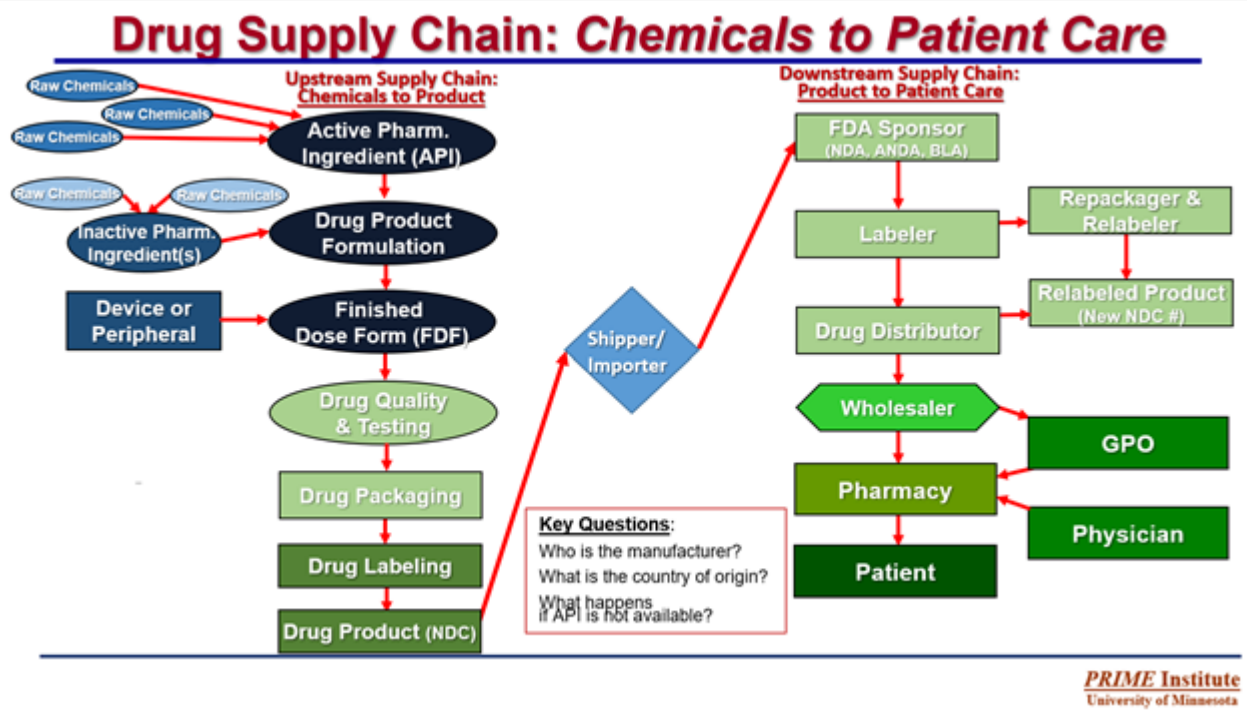
Branded drugs and biologics, in contrast, represented 10% (by units) of U.S. prescriptions used and accounted for 86.9% of U.S. prescription drugs by spending.[11] The greatest share (73%) of branded prescription drug spending in the U.S. is imported from the European Union and Europe—especially Ireland, Germany and Switzerland.[12,13] Intellectual property-protected (IP-protected) brand drugs in the U.S. account for nearly two-thirds (63.4%) of total U.S. drug spending. Growth in the annual cost of new branded drugs in the U.S. is a major concern with the median annual list price for a new drug at over $370,000 based on a survey of 45 new medicines in 2024—more than doubling from $180,000 in 2021.[14] Some major pharma and biotech firms are partnering with firms in China to make their IP-protected products.[15] China is still a relatively small exporter of IP-protected brand name products. As China's experience in this area grows, there is concern that China will develop the technology for making new biological and high-tech drugs. As China learns from working with this technology, it is expected to shift toward innovation to find new IP it can own and protect. In summary, the U.S. brand name market is heavily dependent upon Europe for nearly two-thirds of its drug spending on branded products.

The U.S. pharmaceutical market is a global market with heavy dependence on Europe for brand name products and on India and China for generic products. Since the branded and generic pharmaceutical markets are structurally and substantially different, these two markets should be analyzed and addressed separately from a policy standpoint.

Understanding the Upstream Drug Supply Chain

The "upstream drug supply chain" refers to the series of steps that must occur before a drug or biological product is ready for sale in the U.S. market. In contrast, the "downstream supply chain" is the series of steps that must occur after a pharmaceutical product is approved by the U.S. FDA and offered for sale in the U.S. market. In the downstream supply chain, the finished drug product moves from the drug sponsor to one or more distributors, wholesalers, group purchasing organizations (GPOs), health systems and clinics, providers, pharmacies, and, ultimately, to individual patients.

Figure 1. Drug Supply Chain: Chemicals to Patient Care



The upstream supply chain for making a finished, ready-to-market pharmaceutical product is not a simple or singular process. Pharmaceutical products may have as few as four or five steps to as many as fifty or more steps in the upstream supply chain process. Some of these steps may occur at different factory locations and a product-in-process may travel to several different locations, and even different countries, before it is finished. It is quite rare for the entire upstream process to be performed from start to finish at only one location or by just one firm or company. Several key steps are shown, although not all steps and functions needed to meet the voluntary Good Manufacturing Practice (GMP) standards in the United States are included. Simplistically, one begins the process with raw chemicals or "Key Starting Materials" (KSMs, *e.g.*, simple raw chemicals) that are then combined and mixed with reagents, solvents and other chemicals in multiple steps to create "Intermediates". Intermediates are further processed to create the "Active Pharmaceutical Ingredient" (API). The API is next combined with excipients and other

inactive ingredients into a formulation that can be put in a final dosage form and used to treat a patient. This final dosage form (*e.g.*, a tablet, capsule, liquid, etc.) is made and placed in a delivery device, if needed, (*e.g.*, a syringe, an auto-injector, an inhaler) and packages (*e.g.*, in vials, bottles, or boxes) that can be used to distribute the product. Additional packaging and labeling are then added to the product container and the product moves through the distribution channels. The end pharmaceutical product must then be prescribed by an authorized provider who specifies how the product is to be used to deliver the active ingredient to the site of clinical activity in a specific patient.

Securing and assuring the reliability of the upstream drug supply chain must include a market-wide view back to the origin of the pharmaceutical product. One can ask: "Who is the manufacturer of a pharmaceutical product?" and "What determines the Country of Origin (COO)?" An answer to these questions should consider the source of the API, at a minimum, if not also the sources for KSMs and intermediates.

Supply chain purchasers, health providers, and even at times consumers, should know the 'Country of Origin' (COO) of a pharmaceutical product to assess the risk of not having the API and related finished products when needed. 'Country of Origin' of a pharmaceutical product should not be simply defined by where the components are assembled, as is done for some types of consumer products (*e.g.*, cars). Instead, 'Country of Origin' for the API in a pharmaceutical product (COOAPI) should be defined as the location "where the API is physically made". Additionally, there is value in also designating the 'Country of Origin' for the finished dosage form (COOFDF), that is, the location "where the FDF is physically made". Both types of COO (*i.e.*, API and FDF) should be transparent to policymakers, purchasers, providers, pharmacists, and patients.

Identifying and Measuring Dependence And Risk in the Upstream Supply Chain

Dependence is the state of relying upon another person, source, or condition to properly function. So, what does it mean to say that the U.S. drug supply is dependent upon foreign sources? Dependence upon foreign sources implies that the U.S. drug supply market relies upon outside sources beyond its control for critical steps in the upstream supply chain, such as access to KSMs, intermediates, and APIs, in order to assure that pharmaceutical products will be available in the market when needed. While there may be some unused capacity in the U.S. for manufacturing finished dosage forms,[16] that capacity alone cannot produce pharmaceutical products when the necessary ingredients (KSMs and APIs) are not available. Merely having excess capacity in finish-and-fill facilities for prescription drugs is not sufficient to prevent shortages when demand spikes or supply is disrupted. That is, if one does not have the necessary KSMs and API that can deliver the desired therapeutic effect to the patient, a tablet made without the active pharmaceutical ingredient is no better than a placebo.

The U.S. drug supply can be described as being dependent when any necessary step in the upstream drug supply chain, or a functional alternative, is not available in a timely manner. A basic principle in economics holds that “the market is self-clearing”, meaning that the market is able to efficiently and automatically adjust prices and volumes to match supply and demand in the long-run. This principle works well in many markets and it may apply at times in healthcare markets; however, when there is a shortage or absence of a critical drug that is needed by one or more specific patients, those patients may suffer severe consequences or even die if the product is not available immediately or in the short-run.

For a specific pharmaceutical product, one measure of dependence is assessed by identifying the number and location of alternative sources for the API—the core ingredient in a pharmaceutical product. When an API is only produced at one factory in the world—no matter where it is located--there is dependence. If the one factory is in a location that is subject to external conditions (*e.g.*, weather, geopolitical pressures, trade barriers, logistics and transportation issues, or other conditions) which increase the likelihood that it cannot, or does not, deliver the API to meet demand, the ‘risk’ and consequence of dependence will increase the likelihood of a drug shortage.

For example, from the U.S. perspective, if there is one factory that is in the U.S. (*e.g.*, North Carolina), there would be less risk of trade barriers than if that one factory was in Beijing, China. The factory in North Carolina vs. the one in Beijing, China would be expected to have less risk of failure to supply the market due to trade barriers, or geopolitical pressures, or logistics and transportation issues). Also, even when there are several alternative API sources in the market, the risk of dependence and subsequent drug shortages would be expected to increase with the degree of concentration as measured by unit volume market share. For an API that has 10 active producers in the market with one of those producers holding a 50% market share, there would be more dependence and a higher risk of drug shortages than if all 10 active producers each held a 10% market share. If the one producer with a 50% market share is no longer able to produce, and the other 9 producers are operating at an efficient level they may not have the capacity to meet the spike in demand from loss of supply for 50% of the market. If one has a market-wide view of all producers and their relative market shares and production capacities, analytics can be used to identify pharmaceutical products that have a higher level of dependence for various reasons and a greater likelihood of drug shortages in the market. The U.S. government does not have a market-wide view of all API producers and their locations, as well as related characteristics, to assess the level of dependence and the relative risk of drug shortages.

How complete is U.S. government data collection on the pharmaceutical supply chain, particularly for monitoring vulnerabilities related to China?

Dependence of the U.S. drug supply may occur at several critical chokepoints in the upstream supply chain and for a variety of reasons.[17] In order to monitor the state of the U.S. prescription drug supply and its vulnerabilities, some entity in the U.S. government should develop and maintain a comprehensive, integrated, and market-wide view of the U.S. and global upstream drug supply chains. Although this task is conceptually feasible, there is no focal point in the U.S. government with the responsibility, authority, appropriation, and access to the necessary data to accomplish this task on an ongoing and prospective basis. The U.S. government does not have a market-wide database of the upstream U.S. drug supply and its supply chain dependencies. Such a database could be built and applied to resolve and prevent drug shortages and to strengthen the security and resilience of the U.S. drug supply.

The U.S. federal government should develop a database and analytic capability to identify and predict potential market disruptions, failures, and solutions related to drug shortages and other distortions in the market that may jeopardize public health and national security. An example of this type of national data system can be found as part of the New Zealand federal government system known as MedSafe. The MedSafe agency collects data on the upstream supply chain for each drug product on the market in the country.[18] This information (at the NDC equivalent level) includes the name and location of the API and FDF manufacturers and other information, in addition to the drug product sponsor and marketer in the country. New Zealand has demonstrated the feasibility and utility of a market-wide drug product database with details on the upstream supply chain and they maintain the database on an ongoing basis. The public transparency of this information does not appear to have commercially harmed the manufacturers or marketers of drug products in New Zealand. Many of the same corporate entities marketing drugs in New Zealand are marketing the same, or very similar, drugs in the United States and they often use the same supply chain sources.

There have been at least two private efforts at developing a U.S. drug supply map: (1) the Resilient Drug Supply Project (RDSP) at the University of Minnesota developed in 2018,[19] and (2) the Medicines Supply Map (MSM) at the United States Pharmacopeial Convention (MSM-USP) internally developed in 2018 and made public in 2022.[20] The annual cost of maintaining these databases is estimated to be very modest at about $15 million to $20 million per year. While these drug supply maps have demonstrated proof of concept and feasibility for such a database; they both are based on publicly and commercially available data as well as some private or confidential data, but they do not have complete access to various government datasets. Also, they have not been interfaced with all relevant government agencies to facilitate efficient updating of datasets or to allow government access to, and use of, the data.

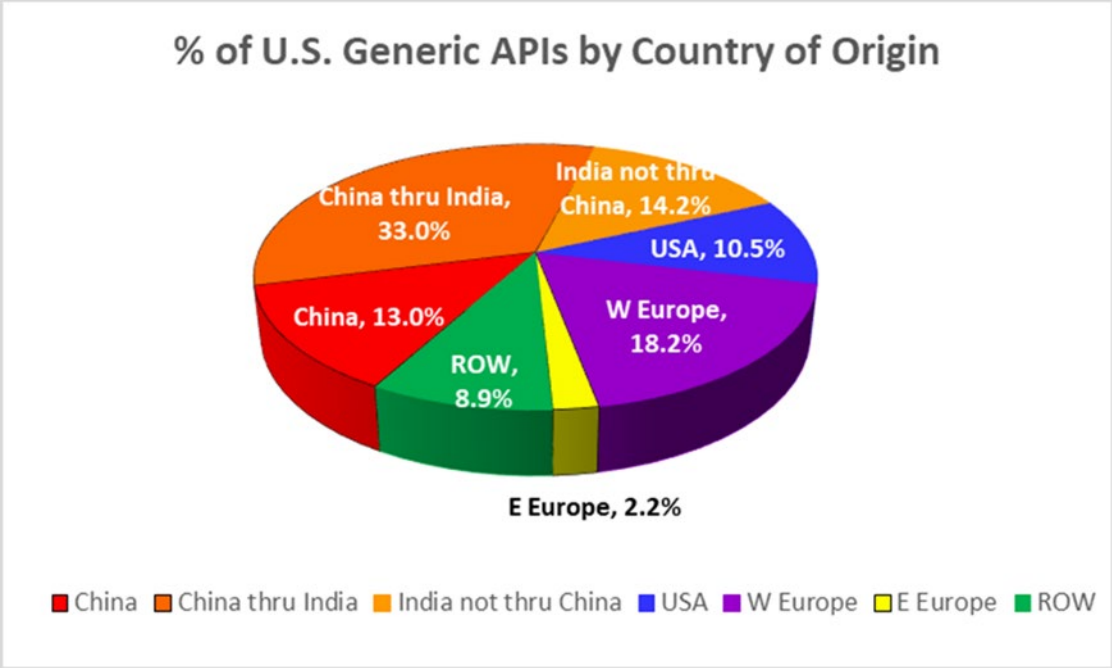
The U.S. government's data collection on the pharmaceutical supply chain, particularly in relation to monitoring vulnerabilities associated with China, or any other type of vulnerability, is a critical issue for ensuring the resilience and security of the U.S. healthcare system. While private data sources such as the RDSP and the MSM-USP have demonstrated proof of concept and feasibility of a comprehensive U.S. drug supply map, the federal government has not taken steps to develop such a market-wide upstream database. Although the U.S. government collects data on individual drug products for regulatory purposes, the data is generally not structured to permit systematic, market-wide assessment of the drug supply chain within a given agency, let alone across agencies. Among the agencies that have data related to a pharmaceutical product's supply chain are: the U.S. Food and Drug Administration (FDA); Department of Commerce; the Centers for Disease Control and Prevention (CDC); the Bureau of Customs and Border Patrol (BCP) (import and export data); Department of Health and Human Services (DHHS), Asst. Secretary for Preparedness and Response (ASPR); Department of Homeland Security (DHS); the Drug Enforcement Administration (DEA); the Federal Trade Commission (FTC); Department of Defense (DOD); Veterans Administration (VA); and others. Data collection remains fragmented and is not conducive for use to monitor the upstream drug supply chain, in general, let alone for vulnerabilities related to China.

At present, the government's use of its databases for supply chain assessment and addressing drug shortages is limited primarily to event management and response tasks rather than preventive and predictive tasks related to the drug supply chain. This data approach will not support identification and pre-emptive resolution of systemic vulnerabilities in the U.S. upstream drug supply chain.

Describe U.S. dependence on China for active pharmaceutical ingredients (APIs) and key starting materials (KSMs), both directly and through third countries.

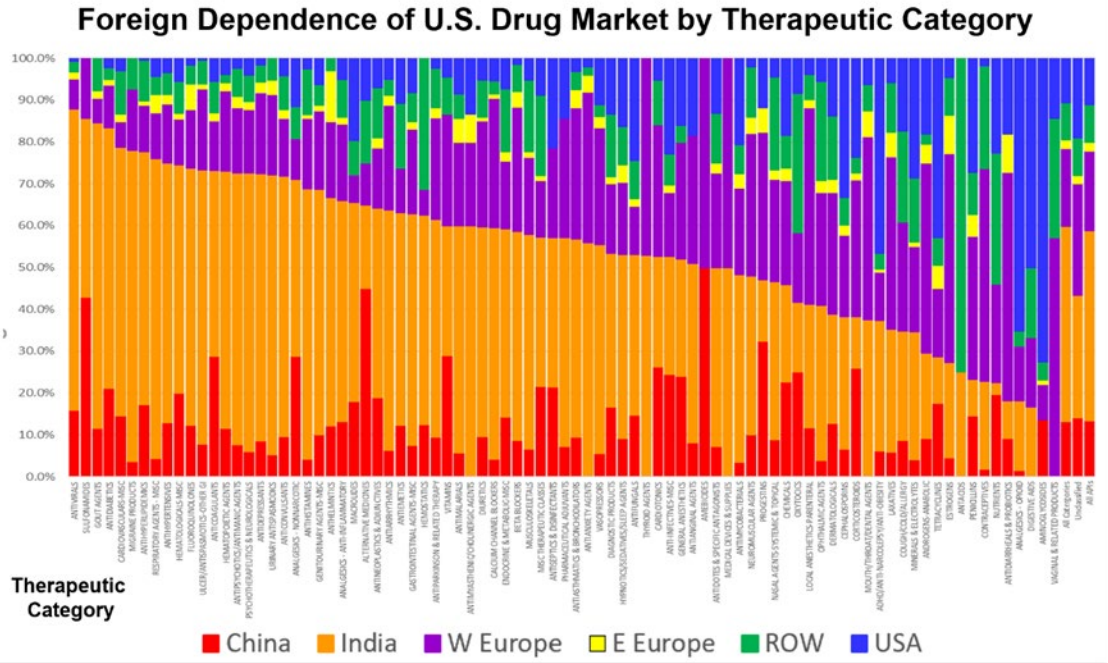
First, the U.S. imports about 47.2% of its generic drug products based on unit volume) from India and about 13.0% from China (Figure 2). The foreign dependence of the U.S. market by share of APIs and country of origin in various therapeutic categories is shown (Figure 3.). Note that more than one-half of the therapeutic categories get more than one-half of their APIs from India or China. Obviously, India appears as the most dominant country, although about 70% of APIs attributed to India are actually API that India gets from China. Both the Indian pharmaceutical industry and the Indian government acknowledge that Indian pharmaceutical firms rely on China for about 65%-70% of their KSM, intermediate, and API sourcing. After adjusting for India's secondary dependence on China for KSM, INT, and API sourcing, it is estimated that 46.0% of U.S. daily doses of generics have source materials from China. Thus, the U.S. generic drug supply chain is heavily dependent upon China for Key Starting Materials (KSMs), Intermediates (INTs), and Active Pharmaceutical Ingredients (APIs). This is a critical issue for health and national security reasons since it affects the production and availability of essential medicines.

Figure 2.



Source: Analysis by Resilient Drug Supply Project, University of Minnesota, based on data from FDA Drug Master Files, CGI Cortellis, and other sources, 2022.

Figure 3.



Source: Analysis by Resilient Drug Supply Project, University of Minnesota, based on data from FDA Drug Master Files, CGI Cortellis, and other sources, 2022.

APIs are the biologically active components in pharmaceutical products that provide the intended therapeutic effect. Not only is the U.S. heavily reliant on China for the production of the APIs, but it also relies on China for KSMs and the precursors or intermediate chemicals used in synthesis of APIs. China also produces a significant portion of the world's KSMs and INTs. Certain bulk chemicals and solvents are critical for drug formulations and are largely produced in China. For example, acetone and acetic acid are key chemicals used in various drug synthesis processes.

China is a dominant global player in the production of APIs and is reported to produce about 40-50% of global APIs. China directly supplies some finished dosage form manufacturers in the U.S., but it also supplies manufacturers in India, Italy, Europe and the rest of the world. Key reasons for China's dominance as a KSM, INT, and API supplier include: cost advantages, scale and infrastructure, regulatory environment, subsidization, and government policy. China has a lower manufacturing cost burden compared to the U.S. and Europe including labor and raw materials making Chinese-produced APIs more cost-effective than APIs from U.S. pharmaceutical companies. China has a well-established, large-scale infrastructure for API production with multiple manufacturers in large government-subsidized industrial parks. The regulatory environment in China has less stringent requirements than the U.S. or Europe which makes it easier for companies to scale up pharmaceutical production. This is especially important since pharmaceutical manufacturing is known as one of the 'dirtiest' industrial processes.[21]

China's dominance in the API production space has raised concerns about the vulnerability of the U.S. pharmaceutical supply chain. Issues like geopolitical tensions, trade disputes, transportation logistics, and pandemics (*e.g.*, COVID-19) have disrupted global supply chains, highlighting risks to U.S. drug availability. In the event of supply chain disruptions, the U.S. could face shortages of critical medications.

How did China become so dominant in the pharmaceutical supply chain?

China and India are dominant players in the global pharmaceutical market. China has become known as the "*pharmaceutical ingredients factory to the world*" because it supplies KSMs, intermediates, APIs, and other chemicals used in pharmaceutical production to India and to many other countries.[22] Similarly, India's role in the global pharmaceutical market is so dominant that it refers to itself as the "*pharmacy to the world*."[23] The geographic proximity of China and India have facilitated the intertwined nature of their respective roles in production of APIs and finished generic products.

Prior to the 1970s, most pharmaceutical products in the United States were made domestically. Beginning in the 1970s, a substantial part of the U.S. pharmaceutical manufacturing industry moved from the mainland to Puerto Rico in response to tax incentives and research credits.[24] In the 1980s, pharmaceutical manufacturing moved to Western Europe and Eastern Europe. By the late 1980s, drug production was growing in emerging and developing countries, and especially in India and China. The journey of

China toward dominance in production of pharmaceutical materials (*i.e*., fine chemicals, KSMs, Intermediates, and APIs) emerged in response to China's industrial development strategy which initially focused on basic chemical production.[25] Gradually China built expertise in producing pharmaceutical intermediates and then full-scale API manufacturing. The government's five-year plans consistently prioritized pharmaceutical manufacturing as a strategic industry by providing favorable policies, infrastructure development, and financial incentives. In the early 2000s, China joined the World Trade Organization which accelerated the growth of its API manufacturing industry. By producing high-volume, low-margin APIs for widely-used medications, the Chinese firms were able to capture domestic market share as well as a growing share of the market in the U.S. and Europe. China gradually captured significant market share in the West and eventually came to have a dominant position, especially in API production. China was able to build manufacturing scale while they developed technical expertise and later pivoted to more complex API molecules and biological production.

China's role as a dominant force in the pharmaceutical market took several decades to build. China had a strategic industrial policy that prioritized pharmaceutical production of Key Starting Materials (KSMs), Intermediates (INTs), and Active Pharmaceutical Ingredients (APIs). Their prominent role evolved due to China's strategic economic investments, regulatory flexibility, lower labor costs, economy of scale production, subsidized manufacturing infrastructure, global trade practices, and other factors.

China's government has had a strategic industrial policy to boost economic growth in the critical pharmaceutical manufacturing sector. The government has made substantial state-sponsored investments to support the pharmaceutical industry through subsidies, tax incentives, and low-interest loans to build infrastructure and expand production capacity. These investments encouraged development of an industry capable of producing large quantities of KSMs, APIs, and finished generic drugs, not just for the enormous domestic market in China, but also for the global market. China's 'Made in China 2025' plan set goals to become a global leader in pharmaceuticals, by increasing production capacity, improving manufacturing standards, and supporting domestic API producers.[26]

Two significant contributors to China's dominance were low labor costs and economies of scale in manufacturing. Chinese manufacturers have been able to produce APIs and generic drugs at costs far lower than the U.S. or Europe. China's low wages and large labor pool allowed manufacturers to keep costs down. This is particularly important for API production, where the cost of raw materials and labor are significant factors. China's vast industrial capacity allows for mass production of APIs, leading to economies of scale that further reduce the cost of production.

China has invested heavily in developing its manufacturing infrastructure, including state-of-the-art factories, transportation networks, and logistics systems, creating effective hubs for global supply chains. China's pharmaceutical industry is concentrated

in key regions, such as Zhejiang, Shandong, and Jiangsu, where numerous API manufacturers are located in close proximity to one another. These industrial clusters allow for streamlined production, lower transportation costs, and easier access to raw materials. China's vast network of ports, airports, and railways also plays a major role in reducing the cost and time needed to export APIs and other pharmaceutical products globally.

China's regulatory environment has been conducive to the growth of its pharmaceutical manufacturing industry. Historically, the Chinese regulatory system for pharmaceuticals has been less stringent than those for the U.S. or Europe, allowing manufacturers to ramp up production more quickly and without having to meet the same level of standards required in more developed markets. While Good Manufacturing Practice (GMP) regulations are improving and have become somewhat stricter in China, they still present a comparative advantage in cost. A favorable intellectual property (IP) landscape in China encouraged foreign companies to off-load production to Chinese firms without stringent IP oversight in manufacturing processes which allowed Chinese manufacturers to ramp up production faster and with lower costs.

China's pharmaceutical sector has a heavy emphasis on API production, bulk chemicals, and generic drugs, partly because of the large domestic market for pharmaceuticals. The Chinese government's focus on access to affordable healthcare spurred large-scale production of APIs, which in turn enabled Chinese manufacturers to become suppliers to global markets. Chinese companies have developed significant expertise in manufacturing APIs and key intermediates for common medications, such as antibiotics, cardiovascular agents, pain relievers, and other drugs. This helped China develop and manage vertical integration of the pharmaceutical supply chain.

China's global market presence in pharmaceuticals has been bolstered by trade practices that prioritize cost advantages and the ability to offer bulk quantities at low prices. China participates in the World Trade Organization (WTO) which has enabled its pharmaceutical companies to better access global markets, including U.S. trade agreements and export incentives that favor exporting bulk APIs and generics. Many Chinese pharmaceutical manufacturers have established relationships with international clients in the U.S., Europe, and developing countries because it was cheaper to buy from Chinese manufacturers than to produce domestically. The U.S. has been outsourcing API manufacturing to China for several decades and China has become the global go-to sourcing hub for API production.

China's dominance in the global pharmaceutical supply chain is the result of a combination of government policies, cost advantages, advanced manufacturing capabilities, and strategic focus on generics and APIs. While the country has improved its regulatory standards and manufacturing practices in recent years, the economic drivers and strategic government initiatives from the past few decades have positioned China as the key player in this sector. Its ability to produce high-quality APIs at competitive

prices, coupled with its vast manufacturing infrastructure and logistics networks, ensure its continued dominance in the global pharmaceutical supply chain.

Are there distortive, coercive, or protectionist policies in drug manufacturing or upstream in fine chemicals that contributed to its market position?

China has employed several distortive, coercive, and protectionist policies that have contributed to its dominant position in the global pharmaceutical and fine chemicals manufacturing markets. These policies and practices have included: (1) coercive trade practices and intellectual property violations; (2) state-subsidized and preferential financing; (3) export-driven policy and "dumping" of pharmaceuticals; (4) protectionist measures and import substitution; and (5) environmental and safety regulations. These efforts have facilitated China's dominance in the production of Active Pharmaceutical Ingredients (APIs) and fine chemicals and have had a substantial impact on the upstream pharmaceutical supply chain. While these strategies have helped build China's pharmaceutical manufacturing base, they have also raised concerns among its trading partners, including the United States and the European Union, who accuse China of unfair trade practices that distort global markets.

China has been accused of using coercive trade practices to strengthen its position in manufacturing of pharmaceuticals and fine chemicals. For example, the forced and unfair transfer of intellectual property (IP) has been a major point of contention.[27] Foreign companies that wish to enter China's market often face requirements to transfer technology and manufacturing processes to local Chinese partners. This practice has been particularly significant in the pharmaceutical and chemical sectors, where foreign firms are forced to share proprietary drug formulas, process and production methods, and intellectual property with Chinese companies in exchange for access to the domestic market. This tactic has allowed Chinese firms to rapidly enhance their manufacturing capabilities creating an unfair playing field for foreign pharmaceutical companies, and allowing local firms to leapfrog into international markets with fewer R&D costs.

There have been numerous allegations that Chinese companies engage in IP theft by copying patented drug formulations or processes and by producing unauthorized and counterfeit products. The Chinese government has been criticized for not enforcing intellectual property rights adequately, leading to market distortions that favor local companies over foreign competitors.[28] These practices undermine the value of intellectual property owned by global pharmaceutical companies, further distorting competition in global markets.

China's government has provided significant subsidies, low-interest loans, and tax incentives to its domestic pharmaceutical and fine chemical manufacturers.[29] These forms of financial support distort market competition by giving Chinese companies an unfair advantage over foreign competitors. Direct subsidies to lower production costs for APIs and generic drugs have allowed Chinese firms to offer products at much lower prices

than competitors in the U.S. or Europe. By reducing the operational costs of Chinese manufacturers, these subsidies make it difficult for Western companies to compete on price. The Chinese government has also made it easier for pharmaceutical and chemical companies to access cheap capital through state-owned banks. These financial institutions provide favorable lending terms, allowing Chinese companies to expand production and capacity at an accelerated rate. This access to capital allows Chinese companies to outcompete foreign firms that do not have similar financial advantages.

China has been accused of dumping pharmaceutical products and fine chemicals in global markets at below-market prices, a practice that undercuts competitors and can drive foreign firms out of business.[30] By artificially lowering the prices of APIs, Chinese companies often flood international markets with cheap products. This practice has been particularly evident in the generic drug sector, where Chinese manufacturers can offer products at a fraction of the price charged by Western companies, due to their lower production costs. The result is that Chinese firms gain significant global market share which fosters dependence, while foreign companies struggle to compete. The Chinese government also supports pharmaceutical and chemical exports through tax rebates, export subsidies, and reduced customs duties on raw materials. These incentives further incentivize Chinese companies to expand export volumes to markets like the U.S., the EU, and developing countries.

China has used protectionist policies to shield its domestic pharmaceutical and fine chemical industries from foreign competition; thus, encouraging self-reliance and bolstering domestic producers. China has actively pursued import substitution strategies by promoting local production of drugs and APIs that were previously imported.[31] The government has pushed for self-sufficiency in critical medicines and fine chemicals to reduce dependency on foreign suppliers. This has been achieved through subsidies and tariff barriers that make it more expensive for foreign competitors to enter the market. In some cases, China has implemented non-tariff barriers to protect its domestic market from foreign imports, including stringent regulatory approval processes, which delay or prevent foreign drugs from entering the market. These measures protect domestic manufacturers and give them time to scale up their production capabilities.

China's relaxed environmental and safety standards for production of pharmaceuticals and fine chemicals, compared to the U.S. and Europe, have significantly lower production costs giving its companies an edge in global markets. In contrast, Western companies face higher production costs due to more stringent environmental laws.[32] Another factor is that China's labor laws are often less strictly enforced compared to the U.S. and Europe, reducing labor costs and enabling pharmaceutical manufacturers to achieve lower production costs.

China's rise to dominance in the pharmaceutical and fine chemicals industries has been facilitated by a combination of coercive trade practices, subsidized manufacturing, export-driven policies, and protectionist measures. These policies have allowed China to

undermine foreign competitors by distorting market dynamics, from intellectual property theft and forced technology transfers to dumping cheap products in global markets. While these strategies have supported China's industrial growth, they have sparked significant tensions with its trading partners, particularly the U.S. and EU, who view such practices as unfair and market-distorting.

What is China's global market share for KSMs and APIs?

China is the world's largest supplier of pharmaceutical raw materials and it currently dominates the KSM and API markets, with an estimated 60-70% in KSMs and 40-80% share in APIs depending upon the therapeutic category.[33] The API market consists of two main categories: innovative (patented) APIs and generic APIs. The innovative API market segment was $147.45 billion in 2024, while the generic API market segment accounted for $78.69 billion.[34] In 2023, China held about 80% of the global generic API market. China's total API sales are expected to grow from $247.8 billion in 2024 to $347.9 billion by 2029, at a CAGR of 5.90%.[35]

Clearly, "China has established itself as the undisputed powerhouse in the global API market, particularly dominating the generic drug segment."[36] APIs can also be classified as synthetic (chemical) APIs or biotech (biologic) APIs. Synthetic APIs in 2023 were valued at $181.3 billion (about 73% of the market), while biotech APIs had a value of $66.5 billion; however, biotech APIs are growing at a faster rate (7.4% CAGR through 2029).[37] The distinction between synthetic and biotech APIs is particularly important since China has traditionally excelled in synthetic API production, although now it is actively expanding into the biotechnology API market. Several reports have estimated that China's share of global API production ranges from 40% (up to 80% or more in some key therapeutic categories like antibiotics, antidiabetics, and cardiovascular drugs). The country's dominance in API production is largely driven by low production costs, economies of scale, and state-driven industrial policies.

China is estimated to supply over 60% of global KSM manufacturing[38] and about 70% of global production of intermediate chemicals.[39] China's control over KSM production is particularly significant because these chemicals are integral to the manufacturing of a wide range of pharmaceutical products. KSMs produced by China are typically used to produce APIs for generic drugs, particularly in therapeutic areas such as antibiotics, oncology, cardiovascular, and neurology. China offers lower labor costs and has developed a massive manufacturing infrastructure for bulk chemical (KSM) production. Major U.S. and European pharmaceutical companies (*e.g.*, Pfizer and Merck) source a significant percentage of their APIs from China. Such globalized sourcing strategies have supported China's KSM and API growth.

Many Chinese companies make KSMs and subsequently convert them into APIs. This vertical integration by making generic drugs from raw materials (KSMs) to finished APIs has facilitated Chinese firms' dominance in the global market. Chinese companies

produce KSMs for both domestic and international pharmaceutical companies. Many U.S. and European pharmaceutical companies have outsourced much of their KSM and API production to Chinese manufacturers. China's market share in KSMs and APIs extends beyond production to exertion of influence over global supply chains in both developed countries (*i.e.*, the U.S. and Europe) as well as developing countries including Africa and Latin America.

The COVID-19 pandemic underscored the vulnerability of relying heavily on China for pharmaceutical supplies. In early 2020, COVID-19-related disruptions to manufacturing in China led to shortages of critical KSMs and APIs globally, sparking renewed concerns over supply chain resilience.[40] Disruptions to global pharmaceutical supply chains during the COVID-19 pandemic, focused attention on China's dominance in KSM and API production and how that led to significant vulnerabilities such as drug shortages.

As demand for generic drugs continues to rise globally, particularly in low- and middle-income countries, China's position as the low-cost leader in KSM and API production will likely remain strong or even grow in the short to medium term. While China's dominance in these markets is clear, the country's future success may depend on its ability to meet rising global standards for production quality, safety, and environmental sustainability. Some efforts to improve regulatory compliance and adopt green chemistry practices are underway.[41]

China currently dominates the global pharmaceutical KSM and API markets. This dominance has been driven by favorable Chinese government policies, subsidized cost advantages, vertical integration, and the massive scale of production. The impact of this dominance was made more visible during the COVID-19 pandemic, when global pharmaceutical supply chains faced significant vulnerabilities due to dependence on Chinese suppliers. As the demand for generics and active pharmaceutical ingredients continues to rise worldwide, China's market position in pharmaceutical raw materials (KSMs and APIs) is likely to remain strong.

To what degree are APIs ostensibly sourced from third countries actually reliant on Chinese inputs to the supply chain?

The global pharmaceutical supply chain is extensively intertwined, with China playing a pivotal role not only in the direct export of active pharmaceutical ingredients (APIs), but also in supplying key starting materials (KSMs), intermediates and other chemicals to most major pharmaceutical-producing countries. This layered dependency means that even when APIs are sourced from countries like India, the U.S., Italy, Spain, or other European nations, they often rely on Chinese inputs at earlier stages of their production.

APIs produced anywhere in the world often have indirect dependence upon third countries, and particularly China, for KSMs and intermediates. Indian industry sources indicate that approximately 70% of India's APIs are sourced from China.[42] India and its

dependence on China for APIs, KSMs, and intermediate source material is the most extensive example of this third country reliance phenomenon, although it is not the only example (*e.g.*, European countries). Before 1991, Indian manufacturers imported only 0.3% of its API from China, and by 2019 the share imported from China had increased to 68%.[43] Because of China's dominance, India has given up manufacturing APIs in favor of Chinese API for molecules such as ascorbic acid, aspartame, and antibiotics, like rifampicin, doxycycline, tazobactam acid and even steroids.[44] China API prices have also driven India to stop production of intermediaries such as atorvastatin, chloroquine, gabapentin, ciprofloxacin, cephalosporins, CoQ10, and immune-suppressants, and others.[45] The majority of reagents required for manufacturing APIs in India are imported from China.[46]

European countries (*e.g.*, Italy, Spain, Portugal, and Germany) account for 30% of the world's API production. These European firms are significantly dependent on Asian countries for their pharmaceutical inputs, with 74% of Europe's API precursor imports coming from Asia and 70% of that supply is from China.[47] This means that more than one-half (51.8%) of Europe's API precursors are sourced from China. Thus, Europe has substantial indirect reliance on Chinese pharmaceutical inputs. In the 1970s and 1980s, Europe made the most of its own APIs and precursors, especially in Italy, Spain, and Portugal. At that time, Europe was only 30% to 40% dependent on other countries, while today it's almost 80%.[48] The U.S. has also experienced a similar loss in API production capacity and increased dependence upon India and China sources for pharmaceutical inputs.

Many medications produced in India with Chinese-sourced materials are exported worldwide, including to the U.S. and Europe. The intertwined nature of the pharmaceutical supply chains in India and China means that disruptions in China can have cascading effects globally. For instance, during the COVID-19 pandemic, China's stringent lockdown measures led to significant shortages of essential drugs in Europe and the U.S., highlighting the vulnerabilities when supply sources are highly concentrated geographically.

While many pharmaceutical products are made with APIs labeled as originating from the U.S. or European countries; however, the underlying supply chain often traces back to China, especially when considering KSMs, intermediates, catalysts, reagents, enzymes, solvents, and other chemicals.[49] This deep-rooted and hidden dependence on China underscores the need for diversified sourcing strategies and increased transparency in the pharmaceutical manufacturing process to bolster global health security.

Constant pressure on the price of generic medicines in developed markets (*i.e.*, the U.S. and Europe) pushed producers to use the cheapest APIs they could find. These cheap APIs were bought in Asia or in Europe with Asian precursors. Chinese API suppliers offer products that are about 40% cheaper than those produced in Europe and

15% cheaper than those produced in India.[50] This significant cost difference has led many global pharmaceutical companies to APIs and KSMs from China. Besides the price, there was a different climate for environmental awareness and safety regulations in Asia than in Europe, creating an uneven playing field that disadvantaged EU companies. It became nearly impossible to continue the European production of pharmaceutical precursors.

When European pharmaceutical manufacturers were asked to identify solutions to the China dominance issue, they recommended: (1) take action considering the whole European market; (2) set criteria to identify the most critical or strategic APIs and precursors; (3) support investments into new APIs with the highest quality standards; (4) implement rules supporting European production and include criteria other than the lowest price; (5) promote re-shoring of production to Europe.[51] Three European consumer companies (*i.e.*, Adidas, Volvo, and Burberry) that used to produce their products in China have now shifted production back to Europe—a decision with impact, that has been proven to be possible.

For which critical pharmaceutical inputs is China the sole or a dominant producer?

China is the dominant producer of certain pharmaceutical inputs or active ingredients including APIs, KSMs, and other essential raw materials for a number of pharmaceutical products. This dominant, or near-monopolistic, position is particularly important for certain categories of products that are critical care and essential drugs such as antibiotics, heparin, insulin, steroids and hormones (KSMs), vitamins (*e.g.*, Vitamin C), statins, enzymes, fermentation-based APIs and intermediates, and pharmaceutical-grade sodium bicarbonate.[52]

The heavy dependence of India on China for APIs, KSMs, and other pharmaceutical materials is reflected in both industry and regulatory data. The Indian pharmaceutical industry in 2020 reported 36 molecules for which India had nearly two-thirds to 100% dependence on China for APIs or KSMs (see Appendix A).[53] There were 19 molecules on the list that reported 100% dependence on China for APIs or KSMs. Additionally, the University of Minnesota RDSP analyzed all current U.S. drug master files (DMFs) by molecule and location of the factory.[54] There were 66 API molecules that only had factories in China and there were 148 API molecules that had more than 50% of their DMF factory locations in China (see Appendix B). The world appears to be solely or predominantly dependent upon China for these 148 API molecules. If China were to stop making or stop shipping these molecules to India, or other countries, these 148 API molecules would not be available, at least in the short-run (1-2 years), for making finished dosage form drug products for the U.S. or anywhere else. Additionally, the U.S. FDA determined that among the WHO Essential Medicines there were three molecules (*i.e.*, capreomycin, streptomycin, and sulfadiazine) whose API was manufactured only in China.[55]

Antibiotics. Specific types of antibiotics, or their essential components and precursors, are produced almost exclusively in China including penicillin, tetracycline, and cephalosporins. Around 70-80% of the world's antibiotic APIs are produced in China including more than 70% of the global production of APIs key ingredients like penicillin G and amoxicillin.[56] The global antibiotic supply chain relies heavily on Chinese manufacturers, especially for tetracycline and cephalosporins, which are essential for treating bacterial infections.[57] China is the dominant global supplier of many antibiotic APIs including penicillin, tetracycline, cephalosporins, azithromycin, levofloxacin, ciprofloxacin, doxycycline, gentamicin, chloramphenicol, and erythromycin. These antibiotics are used in a wide range of medicines, including both branded and generic products. The Chinese government provides subsidies and tax incentives to local manufacturers of antibiotics, further boosting the country's market share in global production.

Heparin. Heparin is produced with animal tissues (from pigs) and China is the primary supplier of these porcine inputs needed for heparin production. China has built a highly specialized and cost-efficient heparin manufacturing infrastructure, making it the lowest-cost producer globally. China controls about 80% of the global production of heparin.[58] This gives Chinese companies a competitive advantage in sourcing the raw materials needed for heparin production. The heparin supply chain is extremely concentrated, with a small number of Chinese manufacturers producing the majority of unfractionated heparin and low-molecular-weight heparin (LMWH), which are key treatments used for anticoagulation therapy. This critical anticoagulant is used to prevent blood clots, including for patients undergoing surgery or dialysis.

Insulin. Novo Nordisk (Denmark) and Sanofi (France) are the two largest players in the global branded insulin market; however, Chinese manufacturers produce a significant share of generic insulin used especially for low- and middle-income countries, particularly in Asia and Africa. China's pharmaceutical companies (including state-owned enterprises) produce a significant percentage of the world's generic insulin. China has invested heavily in insulin production to meet the rising domestic demand for diabetes treatment within the country. Chinese insulin manufacturers benefit from lower production costs, which allows them to offer more affordable insulin, particularly in generic and biosimilar forms. China accounts for a growing share of the global generic insulin analog market, driven by domestic demand and increasing export volumes to developing countries.

Sodium Bicarbonate. Pharmaceutical-grade sodium bicarbonate (*i.e*., baking soda) is used as an excipient and as an active ingredient in various pharmaceutical formulations, including antacids and intravenous solutions. China is a near-monopolistic producer of pharmaceutical-grade sodium bicarbonate, and produces nearly 100% of the world's pharmaceutical-grade supply. Sodium bicarbonate is crucial in pharmaceutical formulations, and its use in cardiac arrest as well as in dialysis solutions make the threat of shortages a major risk for critical care patients in the healthcare system. When China

possesses a near monopoly for a critical drug like sodium bicarbonate, it becomes a significant risk to global supply chains in case of disruptions for any reason. China's massive production capacity in fine chemicals, including sodium bicarbonate, has made it a global leader in this sector.

Vitamin C. The U.S. is a significant importer of Vitamin C (ascorbic acid), with nearly all of the Vitamin C used in the U.S. pharmaceutical and supplement market being sourced from China. China produces about 80% of the world's supply of Vitamin C. The Chinese government has historically supported the Vitamin C manufacturing industry with subsidies to keep costs low and production high.

China holds a dominant, or near-monopolistic, position for several critical pharmaceutical products and their inputs, including antibiotics (penicillin and tetracyclines), heparin, insulin, pharmaceutical-grade sodium bicarbonate, and Vitamin C. China's dominance is driven by its low-cost manufacturing, large-scale production capabilities, state subsidization, and market efficiencies. However, this concentration of production in one country raises significant supply chain risks, as evidenced during events like the COVID-19 pandemic, which exposed vulnerabilities in global pharmaceutical supply chains. If trade and tariff issues escalate, China could leverage its dominant position in the upstream supply chain for certain pharmaceuticals to punish its competitors by significantly raising price or by withholding supply of these pharmaceuticals.

Which essential medications rely most heavily on Chinese inputs?

There are many drug categories that depend on KSMs, INTs, and APIs from China, although this dependence is particularly high (*i.e.*, greater than 50%) for antibiotics (*e.g.*, penicillins, cephalosporins, and tetracyclines); cancer drugs (*e.g.*, chemotherapy agents such as paclitaxel); cardiovascular drugs (*e.g.*, valsartan, losartan, and others); psychiatric drugs; heart disease drugs; blood thinners (*e.g.*, heparin); cancer medicines, and painkillers (*e.g.*, acetaminophen and ibuprofen). India, and secondarily the U.S., is very dependent upon China for the 36 API molecules listed in Appendix C.

Which of these materials would cause the most severe public health impacts if supply chains were disrupted?

The public health impact of pharmaceutical supply chain disruptions depends on a number of factors such as: (1) the number of persons needing a particular product; (2) the severity of the condition being treated; (3) the relative availability, effectiveness, and safety of alternative therapies; (4) the consequences of not treating a condition, if no alternative is available; (5) the duration of the shortage of a given pharmaceutical; and (6) other factors. Disruptions in the supply chains of critical pharmaceuticals can have profound impacts on public health. Among the pharmaceuticals where China holds a dominant or near-monopolistic position, some would cause severe public health consequences if their supply were interrupted. The most critical of these are heparin,

metformin, insulin, cancer drugs, contrast media, other China-dependent drugs, antibiotics, and trade barrier drugs. These pharmaceuticals include essential medicines for treating common, yet life-threatening conditions, and any disruption in their availability could lead to a widespread public health crisis.

Heparin and Deaths. Heparin is a critical anticoagulant used to prevent blood clots, which can lead to stroke, heart attack, and other life-threatening conditions. Heparin is essential for patients undergoing surgeries, dialysis, or certain cancer treatments. A disruption in heparin supply could have immediate and devastating effects, particularly for hospitalized patients or for those with chronic conditions requiring regular treatments (*e.g.*, dialysis patients). Emergency surgeries, cardiovascular procedures, and dialysis would be severely impacted, as alternative anticoagulants may not be available or as effective in treating such conditions. Since China produces more than 80% of the world's heparin supply, any interruption would significantly impact global healthcare systems. The impact may be even more severe in developing countries where healthcare access to alternatives is more limited. In addition to the severe consequences from not having heparin, heparin that does not meet the high standard for purity, quality, and freedom from adulteration is also a serious threat.

In fact, in 2007 and 2008, China-sourced heparin that was adulterated in the upstream supply chain entered the U.S. market and caused adverse effects for hundreds of Americans and resulted in 80 or more deaths.[59] Heparin is used by more than 10 million patients annually and most of the world's heparin is produced in China.[60] Farmers with large pig farms harvest pig intestines for their ingredients, and then consolidators collect them and sell them to API manufacturers who process the heparin for export. Baxter Healthcare, the major U.S. manufacturer of heparin, made its heparin API by using crude material from Scientific Protein Laboratories–Changzhou, China. Evidence indicates that the contaminant, identified as over-sulfated chondroitin sulfate (OSCS), was most likely introduced upstream from the Chinese API producer.[61] The FDA has suggested that this adulteration was an economically motivated act.[62] The OSCS, which closely resembles heparin in both chemical structure and anti-coagulant (blood-thinning) properties,[63] costs nearly 100 times less to produce than heparin[64] and is so similar to the actual drug that it was undetected by the USP standards test.[65] Overall, the FDA worked with 16 drug and device firms "to recall at least 11 drug products and 72 medical device products as a result of the heparin crisis."[66] There were also news reports of heparin products being recalled in Australia, Denmark, France, Germany, Italy, Japan, Sweden, and Switzerland.[67] There were a number of oversight failures by the manufacturer and the FDA that enabled this disaster: Baxter did not conduct an audit of the plant making the heparin API; the FDA did not conduct a pre-approval inspection of the API producer; an FDA inspection after the incident found manufacturing quality issues and insufficient quality controls for incoming materials; investigators from Baxter and the FDA were sent to China to evaluate the situation and they were both denied access; the API producer in China was not registered with the Chinese FDA and did not have any oversight.[68] This

event exposed the vulnerability of the upstream supply chain to lack of oversight in the production of the raw material from a single source from a single country.

Insulin and Emergency Rooms. Diabetes affects millions of people worldwide and disruptions in insulin supply would lead to immediate health crises for diabetic patients. People with Type 1 diabetes, who require insulin for survival, would be at serious risk of diabetic ketoacidosis (DKA) or other consequences if there was no insulin for whatever reason. Based on the severity of consequences from not getting needed treatment, absence of insulin in the market would have a severe impact and could increase emergency room visits and even deaths. Fortunately, there are three major branded producers of insulin analogs (*i.e.*, Novo Nordisk (Denmark), Lilly (U.S.), and Sanofi (France)) in Europe and the U.S. It is not clear if, and what share of, their pharmaceutical API and key starting materials may come from China. China has at least 8 firms producing insulin APIs. China is active in the market for low-cost insulins and biosimilars and holds a growing share of that market. The Chinese manufacturers produce a significant share of generic insulins used especially for low- and middle-income countries, particularly in Asia and Africa. As noted earlier, China's pharmaceutical companies (including state-owned enterprises) produce a significant percentage of the world's generic insulin analogs. China has invested heavily in insulin production to meet the rising domestic demand for diabetes treatment within the country. Chinese insulin manufacturers benefit from lower production costs, which allows them to offer more affordable insulin, particularly in generic and biosimilar forms. China accounts for a growing share of the global insulin analog market, driven by domestic demand and increasing export volumes to developing countries. China is a key supplier of generic and biosimilar insulin analogs, and disruptions in its supply would create a massive gap in access, especially for low-income countries that rely on affordable insulin. A disruption in production and in China's upstream supply chain in the global generic insulin market could lead to a public health emergency and could cause catastrophic health outcomes for millions of people with diabetes globally.

Metformin and NDMA. Metformin is the first line of oral drug therapy for nearly 30 million patients with Type 2 diabetes in the U.S.[69] With over 86 million prescriptions in 2022, metformin was the second most prescribed drug in the U.S. and was being used by about 19.5 million patients.[70] As of 2024, China is the major global producer of metformin API, with over 80% of the global market share.[71] In March 2025, prices for metformin hydrochloride in China surged due to tight supply and elevated production costs, highlighting the potential risks associated with heavy reliance on a single country for essential pharmaceutical ingredients.[72] Given that metformin is the first-line oral therapy for Type 2 diabetes and is prescribed to millions of patients in America and worldwide, the heavy dependence on Chinese manufacturing for API emphasizes the need for diversified, redundant, and resilient pharmaceutical supply chains. Absence of a commonly-used, critical chronic drug (*i.e.*, metformin) would cause disruption of care for millions of patients and could lead to an overwhelming increase in demand for primary

care physician visits to get an alternate therapy, increased ER visits to manage symptoms from lack of therapy, or even, in a few cases, hospital admissions.

Unfortunately, in the past several years (2020-2023) there have been more than 281 recalls of metformin hydrochloride extended-release tablets in the U.S. market due to contamination with N-nitrosodimethylamine (NDMA), a human carcinogen.[73] These recalls covered millions of metformin doses from thousands of lots across 5 or 6 manufacturers and about 20 distributors. At this point, most of the recalls of metformin have been primarily for extended-release tablets, and not immediate release tablets. The metformin FDF manufacturers were from India, although the API was mostly from China. The first prescription drug with recalls due to NDMA contamination was valsartan and that adulteration was traced back to an API manufacturer (*i.e.*, Zhejiang Huahai Pharmaceutical Co. Ltd) in China.[74] If all metformin tablets were recalled for the 19.5 million patients using them, the healthcare system would be overwhelmed with patients making physician visits to get their prescription changed to a new medication. Actually, another medication (*i.e.*, ranitidine) was completely recalled from the market on April 1, 2020 because of NDMA contamination.[75] Ranitidine can be NDMA-contaminated in at least two ways: (1) during the manufacturing process, or (2) as the ranitidine molecule degrades over time. NDMA in ranitidine was enough of a concern that all ranitidine products have been removed from the market.[76] At least ten drugs have had recalls due to NDMA in the past few years including: metformin, ranitidine[77], valsartan[78], losartan, irbesartan, varenicline[79], rifampin[80], rifapentine, nizatidine, and sitagliptin.[81] These NDMA contamination cases raise a number of critical issues: (1) Are there other drugs with NDMA that have not yet been found? (2) Are there other contaminants with serious impact that have not yet been detected? (3) How should the standards for purity be revised to screen for NDMA or other contaminants that may be present? and, (4) How will the health system respond if a critical and/or widely used drug is recalled due to NDMA adulteration? A wide-spread recall of a major drug could overwhelm the healthcare system and cause a dramatic increase in expenditures for primary care to find alternate therapies. Even more concerning would be intentional sabotage of a popular oral solid medication with a contaminant that is not easily detectable, and which causes serious health and economic consequences.

Cancer Medicines and Children. Vincristine is a critical chemotherapy drug that "has been included in nearly every treatment protocol for childhood cancer, as well as some adult cancers, for the past five decades."[82] A critical shortage of vincristine emerged when: (1) Teva with a 3% market share made a business decision to discontinue the drug; and (2) Pfizer (*aka* Hospira) with a 97% market share encountered quality control problems and had to temporarily stop production.[83] The result was an acute shortage of vincristine beginning in July 2019 and continuing through the end of 2019.[84] Children with cancer had to go without life-saving treatments because of a market failure and poor quality control and production. The consequences were as serious as they get—life and death. This drug shortage reminds us that a sole source generic drug product is at high risk of causing a shortage if anything happens to disrupt the upstream supply chain.

Other cancer drugs for children, and adults, have been in shortage including: methotrexate, carboplatin, cisplatin, nelarabine, leucovorin, and others. Cisplatin and carboplatin, for example, are essential platinum-based chemotherapies that had shortages in late 2022 due to shutdown of a manufacturing facility in India which supplied a significant portion of the U.S. market. Approximately 75% of the 20 most essential pediatric cancer drugs have experienced shortages in the past five years. Pediatric oncology drugs are 90% more likely to be in shortage compared to other medications. Pediatric cancer drug shortages tend to last about 33% longer than those affecting adult medications. Among the underlying causes are economic factors (*e.g.*, older generics with low profit margins, less attractive for manufacturers to produce); manufacturing challenges with quality control issues and limited production capacities; and supply chain vulnerabilities due to dependence on a limited number of manufacturers and global supply chain complexities. The proposed Pediatric Cancer Drug Supply Act seeks to establish a six-month reserve of critical pediatric cancer drugs to ensure consistent availability. Pediatric drug shortages have led to treatment delays, substitutions with less effective therapies, increased relapse rates, and, in some cases, preventable deaths.

Contrast Media and Hospital Productivity. Iodinated contrast media (ICM) are drugs that are used for critical diagnostic purposes. The role of ICMs in conjunction with computed tomography (CT) in emergency departments (ED) is indispensable in facilitating timely and precise diagnostic evaluations in emergent situations such as active bleeding, trauma, infections, inflammatory processes, coronary artery disease, stroke, pulmonary embolism, tumors, and other urgent situations. Most hospitals in the U.S. relied on the GE Healthcare-produced ICM products such as Omnipaque (iohexol) and Visipaque (iodixanol) and other products. These ICM products were made at the GE Healthcare plant in Shanghai, China, which supplied about 80% of the global market for ICM. GE Healthcare also had a smaller production plant in Ireland.[85]

As the COVID-19 pandemic progressed, several variants emerged and caused regional outbreaks. The Omicron variant began an outbreak in Shanghai, China in late February of 2022. The Chinese government put a travel restriction in place for Shanghai and started mandatory PCR testing for COVID. By March 15, international travel into the city was restricted. On April 1 Shanghai initiated closing certain zones and restricted travel in the city and by April 5 the lockdown was expanded to cover the entire city of 25 million. As a result of the 'lockdown' policies put in place, businesses and factories in Shanghai were shut down and stopped operation abruptly, including the factory for GE Healthcare which made ICM for 80% of the global market. This lockdown continued until June 1, when restrictions began to ease in some areas, although closure remained in select areas past June 7 and until August 7, 2022.[86]

U.S. hospitals served by GE Healthcare were warned in April 2022 of a limit on order fulfillment due to a shortage of both Omnipaque (Iohexol) and Visipaque (Iodixanol). Hospitals in Canada and Australia had similar limitations. By May 2022, GE began to

reopen the Shanghai plant by following local COVID-19 work protocols, enabling more workers to return back, and boosting output at the Shanghai plant from 0% to 60%. Production levels increased steadily back to baseline, finally achieving normal supply levels in February 2023.[87] GE Healthcare's other factory in Ireland, and other smaller producers, "did not have the capacity to scale up production at such short notice to meet the global demand."[88]

When ICM production was halted due to the COVID-19 lockdown in Shanghai, the combination of "Just-in-Time inventory management and lean production strategies that afforded competitive pricing … led to a massive disruption in the global supply of ICM…"[89] "During the shortage, providers were forced to conserve ICM supplies, which often meant prioritizing patients and limiting imaging services with contrast media to medical emergencies only."[90] One article observed that: "The iodinated contrast scarcity underscored the need for cooperation among healthcare systems, hospitals, and manufacturers to tackle weaknesses in the supply chain and formulate backup strategies, which can be applied to future supply shortages…"[91] This episode taught us some important lessons when it comes to critical medical supplies: "Diversification is essential, even if it is costly, and healthcare services must consider self-sufficiency in the face of vulnerable global supply chains, whether it be through local production or amassing sufficient stockpiles."[92]

Antibiotics, Morbidity, and Resistance. Antibiotics including penicillin, tetracycline, and cephalosporins are foundational for treating bacterial infections. China produces about 70-80% of the world's penicillin APIs, as well as a large share of tetracyclines and cephalosporins. Disruptions could therefore severely impact the ability to treat common and life-threatening infections like pneumonia, sepsis, meningitis, and urinary tract infections. A disruption in the supply of antibiotics would have devastating public health consequences. The rise of antibiotic-resistant bacteria would be exacerbated if first-line antibiotics like penicillin were not available. Routine use of second-line antibiotics due to disruptions in antibiotic supply could lead to an increase in antibiotic resistance, hospital-acquired infections, and treatment failures. There is a potential for global health crises if the supply of critical antibiotics like penicillin is disrupted, with implications for both common and serious infections.

Disruptions in the supply chains of heparin, insulin, metformin, pediatric cancer drugs, and antibiotic APIs would have severe public health impacts, leading to widespread morbidity and mortality. Heparin and insulin are particularly critical for acute medical emergencies, while antibiotic APIs are vital for treating common and life-threatening infections. The dependency on China for these critical pharmaceutical materials increases the vulnerability of global health systems to disruptions in the drug supply.

How could China leverage its position in pharmaceutical supply chains for economic or strategic advantage?

China's dominance as a major producer at the core of upstream global pharmaceutical supply chains provides it with significant economic and strategic leverage. By controlling critical components like Key Starting Materials (KSMs), Active Pharmaceutical Ingredients (APIs), and Finished Dosage Forms (FDFs) of essential drugs (*e.g.*, antibiotics, insulin, metformin, heparin, and cancer drugs), China has the ability to influence global health markets and prices, negotiate trade terms, and impact global health security. This leverage can be used for economic or strategic gain in several ways.

China's Economic Leverage. China's domestic market size provides it with an inherent economy of scale for the volume consumed of most goods including essential pharmaceuticals. Therefore, any pharmaceutical production for export to other markets is already at marginal cost levels, delivering a substantial competitive advantage to China from lower prices. In addition, the cost of labor and the cost of environmental mitigation in China are lower than in Western markets such as Europe or the United States. China's inherent economic advantages in pharmaceutical production provide it with the opportunity to engage in price manipulation, dumping, and market dominance.

China's role in the pharmaceutical supply sector is heavily intertwined with its neighbor, India. These two economies now have more than one-third of the world's 8.2 billion people with populations of 1.46 billion in India and 1.41 billion in China. The influence and leverage of China from its pharmaceutical sector is often masked because it can exert much of its power through its impact on India, which depends on China for about 70% of its pharmaceutical materials (*i.e.*, KSMs, APIs, and FDFs) needed to support India's position in the global pharmaceutical market. But for China, India would not have its dominant position in global pharmaceuticals. Its role in global pharmaceutical supply chains enables China to influence the economics of the global drug market through direct and indirect price manipulation and subsidization of production costs. China's dominance in producing essential pharmaceutical ingredients allows it to dictate market prices for these materials. For example, intentional or unintentional disruptions in China's supply of penicillin or heparin or metformin could lead to imposed price hikes due to limited global supply, giving China the opportunity to further increase prices or to demand more favorable terms for export and trade. This leverage could be applied to relations with other strong economies such as Europe or the United States, because these economies often do not have an alternative source of production for many critical pharmaceutical products, at least in the short-run—5 to 10 years.

China's government subsidizes the pharmaceutical sector in various ways including funding infrastructure costs, reduced labor and environmental cost, transportation and shipping costs, and favorable access to capital; thus, enabling Chinese companies to outbid international firms by offering lower prices. By offering low-cost APIs and finished drugs, China can make its products more attractive to developing nations, allied countries, and Chinese-dependent countries (*i.e.*, India); and, potentially drive out international and domestic competitors.

China's Trade Leverage. Countries that rely heavily on Chinese pharmaceutical products (*e.g.*, many African and Asian nations) could be forced into favorable trade agreements or loans in exchange for continued access to vital medications. China could also use its position to expand its influence in international trade talks, leveraging its supply of critical drugs or raw pharmaceutical materials as bargaining chips. China could restrict the export of certain APIs, critical drugs, or other medical supplies, as seen during the COVID-19 pandemic. By controlling exports of key ingredients or finished medications, China could pressure other nations to align with its political or economic priorities.

China could leverage through investment and foreign aid tactics. China could invest in pharmaceutical production infrastructure in strategic regions (such as Africa or Latin America), building local production capabilities, or create economic dependencies. Through Belt and Road Initiative (BRI) projects, China could offer pharmaceutical infrastructure development in exchange for access to local markets or natural resources. In addition to direct investments, China could provide aid and humanitarian assistance. China could use its pharmaceutical exports as part of foreign aid packages; thereby gaining goodwill and political leverage. For example, offering generic insulin, HIV medicines, or antibiotics at low prices in developing countries would foster stronger economic and political ties.

China's Strategic Leverage. China's position in the pharmaceutical supply chain also provides substantial strategic leverage that extends beyond economics into geopolitical influence and global health security. China could hold leverage over health security and biosecurity through influence over global health systems. China's control over essential medicines and raw materials means it could withhold supply in the event of a geopolitical conflict or trade dispute, impacting the ability of countries to access life-saving treatments. This is especially relevant for countries that are heavily reliant on China for antibiotics, insulin, or heparin. During public health crises, such as the COVID-19 pandemic, China demonstrated its ability to dictate allocation of supply for domestic use rather than meeting global commercial trade obligations. If there were a similar situation involving pharmaceutical ingredients, China could control access to essential medicines, positioning itself as an indispensable partner in global health governance.

China's Soft Power and Global Influence. Through initiatives like China's "health silk road", China could use its dominance in pharmaceuticals as a form of soft power. For example, by providing essential medicines or vaccine access to developing countries at lower prices or priority access, China could increase its influence in these regions, establishing itself as a key player in global health governance. China could use its position in the pharmaceutical supply chain to foster alliances that build trust in the developing world, offering affordable medicines in exchange for economic or political support on global platforms such as the UN or WHO. This type of influence extends China's geopolitical footprint, particularly in Africa, Asia, and Latin America, where many countries rely on Chinese imports.

China's Technology and Intellectual Property Leverage. By developing, or appropriating, intellectual property (IP) and pharmaceutical innovation, China could develop new drugs or other IP and sell it through state-owned firms in the U.S. market. With its own IP, China can apply patents and for FDA approval of pharmaceutical products in the U.S. market. Once, new IP-based drugs are approved in the U.S. market, China would have control over pricing of the finished product in the U.S. and the government programs (*i.e*., Medicare and Medicaid) would, in most cases, be required to cover these new drugs or biological products at whatever price the Chinese state-owned firms wanted to charge. Basically, the Chinese state-owned firms can recover revenue from the U.S. public programs to pay for their research and development costs as well as attractive profits, all at the U.S. taxpayers' expense.

With the continuing trend of biosimilar drugs and generic medicines, China could also position itself as a leader in the generic pharmaceutical industry. As it becomes a hub for biosimilar production, it can exert significant influence over the global pricing of these products. And, it can develop evergreen versions of biosimilar or generic drugs that use devices (*i.e.*, auto-injectors, inhalers, etc.) or other technology to extend the intellectual property rights associated with otherwise off-patent, life-saving drug molecules.

As China strengthens its role in the pharmaceutical industry, it could shape development of global pharmaceutical standards and pharmaceutical regulations through the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and other venues, including those related to drug approval and patent protection, aligning them more closely to its own domestic view of appropriate standards. Along with support leveraged from its allies and other economically and technologically dependent nations it could further consolidate China's influence over global pharmaceutical markets.

China's Geopolitical Power and Supply Chain Leverage. China could use supply chain disruption as a geopolitical strategy. China has demonstrated its ability to use trade restrictions or export bans as a strategic tool. In times of conflict or tension, China could leverage its control over pharmaceutical raw materials to create supply chain disruptions in countries that oppose its political or economic interests. For example, China could limit the availability of critical APIs to domestic manufacturers, forcing foreign manufacturers to rely on Chinese suppliers or to compromise on trade terms.

The U.S. and E.U. are both heavily dependent on China for pharmaceutical ingredients. China could use this dependence as a tool of leverage in broader geopolitical negotiations. For instance, if relations between China and the U.S. were to become contentious, China could threaten to cut off key supplies of certain drug molecules, thereby severely disrupting healthcare access in the U.S. and its allies. This could cause public health harm, as well as economic harm, to U.S. citizens.

Potential Leverage Scenarios. Scenarios that could exaggerate or accentuate China's use of its leverage from the pharmaceutical market include heightened geopolitical conflict such as trade tensions or a new global health crisis or pandemic. If geopolitical conflict or trade tensions between China and the U.S. escalate, China could reduce or suspend the export of critical APIs and medications (*e.g.*, heparin, insulin, antibiotics). This would create an immediate health crisis in the U.S. healthcare system, as these materials are crucial for treating serious and widespread conditions. This could force the U.S. to reconsider its economic and political stance toward China, potentially offering concessions in trade or diplomacy.

In the event of a new global health crisis or another pandemic requiring massive medical supplies, China could control access to key pharmaceutical materials, including vaccines, antiviral treatments, or other critical APIs. By prioritizing certain markets (*e.g.*, China-aligned developing nations) and restricting supply to others (*e.g.*, the E.U. and the U.S.), China could expand its global influence through the provision of essential medicines in exchange for political support or economic advantages.

China's dominance in upstream pharmaceutical supply chains gives it significant economic and strategic leverage that can be used to influence global markets, shape health policies, and advance geopolitical interests. The ability to control or disrupt access to critical pharmaceutical inputs like insulin, heparin, cancer medicines, and antibiotics allows China to play a central role in global health security and economic negotiations. In many ways, China's strength in pharmaceuticals is masked by its intertwined and stealthy position supporting the pharmaceutical industry of India. Whether by controlling prices, leveraging supply chains during crises, or engaging in health diplomacy, China can use its pharmaceutical power to enhance its global influence and political leverage.

What is the worst-case scenario, and how would the United States be impacted?

Impactful scenarios regarding U.S. dependence on China for pharmaceuticals can occur for a number of reasons including economic factors, natural or man-made disasters, or geopolitical hostilities and trade issues. Determining which scenario is the worst case involves weighing several factors including: (1) the type of harm (*i.e.*, economic, physical health, or psychological health), (2) the number of people or drug products involved or harmed, and (3) the severity of harm.

Economic Scenarios. With respect to economic harm, there are several ways that U.S. dependence on China for pharmaceuticals could have an impact. First, for a specific drug molecule where China is the dominant (>40% to 79% of units) or sole producer (80% to 100% of units), China could leverage their market position to raise the price of a specific drug or set of drugs. The amount of the price increase will influence the impact with increases ranging from 5% to 50% or as much as 100%, 1,000%, or even 10,000% or more. Even if the price gets so high that a U.S. firm considers market entry to counterbalance the high price, it may take one to three years or more, and considerable

expense, for a new or alternative production site to be established. Obviously, if several, or all drugs, have their price raised, the impact would be greater (*i.e*., worse) than for one drug. If the drug products whose prices are raised are for a symptomatic condition like allergies, the severity may not be as severe compared to the effect if the drug is for a critical chronic condition like diabetes, epilepsy, or cancer where the health impact will be much more severe.

China is increasingly partnering with, or creating their own, biotech firms and conducting research and development to introduce IP-protected products of their own. When a Chinese state-owned firm prepares an IP-protected finished product and obtains U.S. FDA approval to market it, they will be able to establish the price of this new product, at their own discretion, as is the practice in the U.S. market. Also, once a new product is approved by FDA, that product is usually required to be covered by the U.S. government programs (*i.e*., Medicare and Medicaid) at the price set by the manufacturer with no negotiation or oversight. Chinese state-owned firms operating in this U.S. market will be able to leverage their IP-protected position to set and raise the price of their product, at will, with little or no accountability. Essentially, this means that a Chinese state-owned firm whose product is on the U.S. market can set a price with a gross margin of 70% to 95% or more. The Chinese-owned drug firm can raise the price at will and whenever they want. Thus, the Chinese firm would be able to cover the costs of its research and development program and to reap generous profits without effective economic market competition—all funded on the backs of American taxpayers. This situation would be the equivalent of writing ‘blank checks’ to the Chinese government. Biological products can earn $100s of millions to billions of dollars per year in the U.S. market alone. In terms of pure economic harm, this constitutes a worst-case scenario.

Natural and Man-Made Disaster Scenarios. Natural disasters include events like earthquakes, tornados, hurricanes, cyclones, typhoons, tidal waves, fires, floods, heat waves, and other events. Man-made disasters include many things that can go wrong such as quality issues at the factory, transportation and shipping delays, strikes, port closures, hijacking, robbery, and other events. Most of these events can happen in the upstream supply chain including at production facilities anywhere in the world; and, production facilities can become compromised and lose their ability to produce pharmaceutical materials. When production and output at a manufacturing plant is reduced, there will be a reduced supply of the pharmaceutical material (*i.e.*, KSM, API, or FDF) available in the market. At times, there may be enough product in inventory, or in a reserve, to buffer the supply needed to meet the market demand. Although at other times the inventory may be depleted and the supply may fall short of the demand and result in a drug shortage. These natural or man-made disasters may occur at facilities in China or India or elsewhere. When a disaster affects a facility that is supplying a product to the U.S. market, there is likely to be a drug shortage until the plant can be repaired or restored and put back into production or until the precipitating event is resolved. If there are one or more other firms in the market making the same or a similar pharmaceutical product, these other firms may be able to increase production to meet the surge in market demand.

When a production facility is impacted by a natural or man-made disaster, there may be one or more pharmaceutical products affected. Some factories may be sole-product operations, although most facilities have multiple products made at the site. Depending upon the inventory on hand, usually about two weeks to two months supply, the market can continue until the inventory supplies are depleted. The likelihood of a drug shortage developing after a plant experiences an event is often related to the size of each product's market share. Products with larger (>30%, and especially >50%) market shares being produced at the affected plant are more likely to have a shortage, because it is more difficult for the market to make up the quantity of supply lost. Also, products that may be made at only one plant in the world, which becomes compromised, are more likely to result in a drug shortage. When a drug product does have a shortage, it is not unusual to see the price go up due, in part, to the limited supply. A drug shortage may last a few months to years with the average shortage in 2023 lasting about 3 years.[93] Shortages mean that the pharmacy does not have the product; the prescriber must identify and prescribe an alternate product, if there is one; and the patient must go back to the prescriber to get an alternate less effective product or nothing at all.

Adulteration of Pharmaceutical Products Scenarios. Adulteration of drug products in any way, and for any reasons is not appropriate or acceptable in the market. Sometimes a change in the process for making a drug molecule or the drug product formulation results in the product being contaminated with an adulterant. Such was the case with the presence of NDMA—a probable carcinogen—that was first found in valsartan tablets in 2018. Unfortunately, the standards for checking the purity of valsartan did not detect the presence of the NDMA. Since finding the NDMA-adulterated valsartan, the products for at least ten other drug molecules have been found to have NDMA contamination. Two drug products with NDMA contamination have been completely withdrawn from the U.S. market. The FDA has been investigating to find the root cause of NDMA presence in various drug products. The undetected presence of a contaminant such as NDMA in a number of different unrelated drug products raises concern about the safety and purity of the U.S. drug supply. We don't know how many other drug products on the market may have NDMA contamination. And, we don't know if there are other undetected and unknown contaminants in drug products widely used in the U.S. market. Undetected, unintentional adulterants, such as NDMA, in a prescription drug is an unacceptable scenario.

Another example of an adulterated drug was the heparin incident in 2007 and 2008. In that case, heparin API material was contaminated with over-sulfated chondroitin sulfate (OSCS) by a Chinese processor in the upstream supply chain. The OSCS substituted for heparin was substantially cheaper (1/100th the cost) than the heparin it replaced and the processor was cutting corners for economic gain. The contaminant caused a number of serious adverse effects including many patient deaths. The FDA has characterized this incident as an intentional 'economically motivated act'.[94] The OSCS, which closely resembles heparin in both chemical structure and anti-coagulant (blood-

thinning) properties,[95] costs nearly 100 times less to produce than heparin[96] and is so similar to the actual drug that it was undetected by the USP standards test.[97] Intentional contamination of a drug product that can lead to widespread economic and clinical effects is an even worse and unacceptable scenario.

Perhaps the worst worst-case scenario for adulteration would be the intentional contamination of a widely used prescription drug with a harmful, yet undetectable contaminant. Someone working at, or with access to, a pharmaceutical plant in China, or elsewhere, and who wants to do harm to Americans could put an undetectable contaminant in the drug formulation that will cause serious consequences, or even death. If put in a widely used drug formulation such as metformin, which is used by about 20 million patients each day of every year, the harm would overwhelm the healthcare system's resources. This drug product would pass the usual standards for purity and quality, and get into the downstream distribution system eventually reaching patients. These 'poison pills' could be widely distributed and used by thousands, or even millions, of patients before the problem is identified and addressed. This 'stealthy', undetectable and adulterated widely used drug would be a worst-case scenario in terms of both clinical and economic harm. Also, an event of this type would likely have a psychological impact on the public and it may undermine the inherent trust, in general, that Americans have in the medications that they use every day.

Trade Tensions and Geopolitical Hostilities Scenarios. A worst-case scenario in terms of trade tensions or geopolitical hostilities and U.S. reliance on China for pharmaceutical supply chains would involve a complete disruption, or significant restriction, of critical pharmaceutical ingredients (APIs) and finished drugs that are directly supplied by China. Such an action could be taken in response to a dispute between China and the United States and could be driven by a range of geopolitical tensions, trade disputes, or even strategic use of pharmaceutical supply chains as leverage. Recall that about 13.3% of all generic drug doses taken by Americans are imported directly from China. A supply chain disruption of this magnitude could have severe public health and economic consequences for the United States.

However, there is an even worse scenario involving trade tensions or geopolitical hostilities. In this scenario the dispute would be between China and India, and may or may not even involve the United States. If there was a dispute between China and India and China implemented a complete disruption, or significant restriction, on pharmaceutical ingredients (APIs) that it supplied to India, it could disrupt the generic finished dosage form drug supply from India to the United States. In this case, recall that finished drug products supplied by India account for about one-half of all generic drug doses taken by Americans every day. A supply chain disruption of this magnitude could have extremely severe public health and economic consequences for the United States. This would be the worst of the worst-case scenarios.

Absence of each critical chronic drug that causes disruption of care for a chronic disease like diabetes, asthma, or epilepsy would lead to increased demand for physician visits, ER visits, and hospital admissions. If even one critical chronic drug, let alone many drugs, is completely blocked from access in the U.S. market, it would overwhelm the healthcare system, clinically and economically, and cause a dramatic impact on the health of Americans.

That's the bad news; the good news is that India serves as a buffer between the U.S. and China. This buffer means that China and the U.S. do not directly have trade deals for most of the Chinese ingredients incorporated by Indian drug manufacturers in the finished products that are shipped to the U.S. Even though a large share of the generic drugs used by Americans have chemicals and active ingredients that are dependent upon China, those pharmaceutical materials pass from China to India, before the final product is exported to the U.S. There is no practical way for China to block their ingredients being used to make drug products for America without China blocking all pharmaceutical ingredients being passed first to India. In general, only the pharmaceutical ingredients and products shipped directly from China to the U.S. would be subject to tariffs or export controls by China.

Which countries offer viable alternatives to Chinese APIs and KSMs?

China is the dominant supplier of KSMs and APIs and India is the dominant supplier of FDFs to the United States. India is very heavily dependent upon China for KSMs and APIs. However, the strong dependency on China and India are a concern to policy makers, healthcare professionals, and patients in the U.S. The U.S. needs to develop resiliency, diversity, redundancy, and efficiency in its upstream supply chain. The question arises: What countries are viable alternatives to facilitate development of resiliency in the upstream medicines supply chain as the U.S. moves away from dependence upon China and India. This question is especially important in light of current geopolitical and trade tensions between the U.S. and China.

Re-Shoring to the U.S. Making the U.S. medicines supply chain more secure and resilient should include not only production in the United States (re-shoring), but also production in other Western hemisphere countries such as Canada and Mexico (near-shoring) and Brazil and Argentina (friend-shoring). The U.S. should bring some pharmaceutical manufacturing back to the United States, or at least closer to U.S. borders.[98] Production of the most critical medications in the United States will strengthen and protect the U.S. drug supply chain. However, it may not be wise to make all prescription drug products in the United States for both geographic diversity and cost reasons. Geographic concentration, even in the U.S., can make pharmaceutical production vulnerable to a natural disaster, a localized health emergency, or transportation and logistics problems. For example, in 2017 Hurricane Maria devastated Puerto Rico and disrupted the flow of large volume intravenous fluids throughout the

United States[99] because one plant in Puerto Rico had 60% of the U.S. market share of large volume intravenous fluids.

When moving manufacturing operations to the United States, keeping the cost of pharmaceuticals affordable is important. Manufacturing and labor costs for making an API may be 15% to 40% more in the United States than in India or China.[100] These costs may include capital costs for purchasing land and building new and updated manufacturing facilities, as well as developing and maintaining a high-quality workforce. Some of these increased costs can be offset by federal investments, particularly for manufacturers of drugs with low-profit margins such as sterile injectable generic pharmaceuticals. Other costs can be offset by employing advanced technologies with continuous flow chemistry-based manufacturing that can reduce costs and environmental impact.[101] Finally, near-shoring or friend-shoring of pharmaceutical production for other drug products can be done in other Western hemisphere markets with lower labor and environmental costs such as Canada, Mexico, Brazil, or Argentina. Both on-shoring and near-shoring can help to keep pharmaceuticals safe and affordable in the United States, while being made in the U.S. or in neighboring and friendly countries.

Resilience of the medicines supply chain needs to include geographic diversity and redundancy in sourcing of pharmaceutical products. Geographic diversity involves making the same drug in more than one location so that if something happens to one locality, it will not affect all producers of the drug product. Redundancy is concerned with purchasers having more than one source of supply from which they can buy the drug product. Since the U.S. market needs to diversify its dependence on China and India, it needs to find, encourage, and support production at other locations. One option is to get products made in Europe, when possible, although Europe is also heavily dependent upon China and India for their drug supply. There is some pharmaceutical production in the United States and Canada, but not sufficient variety of the drugs needed or enough quantity to meet the total needs of the U.S. market. There is an important need to encourage and develop additional pharmaceutical production (KSMs, APIs, and FDFs) in the Western hemisphere.

One of the key factors that has enabled China and India to become the world's dominant players in pharmaceutical production is the need to meet the domestic pharmaceutical demand of their respective populations. China has 1.41 people and India has 1.46 billion people—each accounting for have more than 17% of the world's 8.2 billion people and collectively they hold 35% of all people on earth. In contrast, all countries in the Western hemisphere have about 1.06 billion people, or 12.9% of the world's population. Even if the U.S. partnered with the entire Western hemisphere, the scale from this population is only about 75% of China's population alone. Other than Canada, the U.S. imports very little of its pharmaceutical production from within the Western Hemisphere. There are a number of countries in the Western hemisphere that could serve as additional and alternative sources of pharmaceutical production or consumption

including: Mexico, Brazil, Argentina, Colombia, Chile, Peru, Guatemala, Dominican Republic, Paraguay, Costa Rica, and Panama.

What factors make a country a strong partner for producing KSMs, APIs, and/or FDFs for the U.S. market? Based on the experience of China and India, a country should have: (1) a large domestic market; (2) an existing pharmaceutical manufacturing sector; (3) relatively low labor costs; (4) relatively low environmental regulation barriers; and (5) geographic proximity to the U.S.

Near-shoring from Canada. The population of Canada was 41.5 million in 2024, the sixth largest country in the Western hemisphere. In 2024, the total trade between the United States and Canada was $762.1 billion with $394.4 billion in U.S. exports to Canada and $412.7 billion in U.S. imports from Canada, resulting in a U.S. trade deficit of about $63.3 billion. As of 2024, the United States and Canada maintained one of the world's most robust bilateral trade relationships. In early 2025, trade relations experienced strains due to the imposition of a 25% tariff by the U.S. administration on most Canadian imports. This move affected various sectors, including agriculture and manufacturing, and raised questions about the stability of the U.S.-Canada trade relationship. Canada has a substantial pharmaceutical manufacturing sector with over 700 pharmaceutical manufacturing companies and about 45% of these are situated in Ontario, a central hub for pharmaceutical production. Prominent domestic pharmaceutical manufacturers in Canada include Apotex Inc. and Bausch Health Companies Inc. Canada's pharmaceutical industry has a combination of domestic and international companies, contributing to its role as a key player in the global pharmaceutical sector.

Near-shoring from Mexico. The United States and Mexico have a long history of trade including at least 70 years in the manufacturing and distribution of pharmaceutical products.[102] In 2021, the RDSP performed a strategic examination of the pharmaceutical trade between the U.S. and Mexico to identify approaches to strengthen the resilience of supply chains for critical U.S. drug products (see Appendix D).[103] That analysis reviewed Mexico’s capability as a strategic partner in the production of pharmaceutical products for export to the United States. Mexico has a population of 131.7 million—3rd largest in the Western hemisphere—and is geographically adjacent to the U.S. Mexico is well-positioned to increase its production and export of pharmaceuticals to the U.S. in a way that would benefit both countries. With proper support and incentives from both Mexico and the U.S., both governments can strengthen and ensure the stability of their drug supply chains for critical and essential medications needed by their respective populations.

Friend-shoring from Brazil. The population of Brazil was 212.6 million in 2024, the 2nd largest country in the Western hemisphere. There has been a robust trade relationship between Brazil and the United States with a positive balance of trade for the U.S. in 2024. Brazil is the ninth-largest trading partner with the U.S. and the U.S. exports pharmaceuticals (*i.e.*, branded products) to Brazil. In 2022, there were 341 companies

engaged in pharmaceutical manufacturing with 246 of Brazilian origin and 95 as subsidiaries of international firms. These companies include large-scale manufacturers, contract development and manufacturing organizations (CDMOs), and specialized producers of active pharmaceutical ingredients (APIs), generics, and biosimilars. The pharmaceutical manufacturing sector in Brazil is predominantly concentrated in the state of São Paulo in the Southeast region of the country which serves as the primary industrial hub. Brazil appears to be a viable candidate to partner with the U.S. for production of APIs and FDFs to strengthen the resilience of the U.S. medicines supply chain.

Friend-shoring from Argentina. The population of Argentina was 46.3 million in 2024, the 5th largest country in the Western hemisphere. In 2024, the total trade between the United States and Argentina was $16.3 billion with $9.2 billion in U.S. exports to Argentina and $7.1 billion in U.S. imports from Argentina, resulting in a U.S. trade surplus of about $2.1 billion. The trade relationship between the two countries encompasses a variety of goods including machinery, agricultural products, and energy resources and the level of bilateral trade has remained substantial. As of 2024, Argentina's pharmaceutical manufacturing sector had 230 pharmaceutical plants, with 182 of these facilities owned by national companies and there were about 40 public laboratories. The Argentinian pharmaceutical industry has a significant presence in the domestic market. Notably, only two of the top ten pharmaceutical companies in Argentina—Sanofi and Bayer—are foreign multinationals. Argentina's pharmaceutical sector is a significant contributor to the national economy, accounting for about 5% of the total industrial production. The industry employs around 43,000 individuals and exports over $800 million worth of pharmaceutical products annually, primarily to neighboring Latin American countries. Argentina also has a robust biotechnology sector, with approximately 65 biotech companies that have strengths in developing generics and biosimilars. Overall, Argentina's pharmaceutical industry has a strong domestic manufacturing base, significant employment, and a growing presence in international markets. Argentina appears to be a viable candidate to partner with the U.S. for production of APIs, FDFs and biosimilars in order to strengthen the resilience of the U.S. medicines supply chain.

Friend-shoring from Colombia. The population of Colombia was 53.3 million in 2024, the 4th largest country in the Western hemisphere. In 2024, the total trade between the United States and Colombia was $36.7 billion with $19.0 billion in U.S. exports to Colombia and $17.7 billion in U.S. imports from Colombia, resulting in a U.S. trade surplus of about $1.43 billion. In early 2025, trade relations experienced strains and have affected various sectors, including agriculture and textiles. There are concerns about the stability of the U.S.-Colombia Free Trade Agreement. Colombia's pharmaceutical industry has a combination of domestic and international companies, and plays a key role in Latin America's healthcare sector with over 100 pharmaceutical manufacturing companies and about two-thirds of those situated in the Bogotá region, the central hub for pharmaceutical production. Colombia's pharmaceutical industry currently exports $547 million worth of pharmaceutical products, ranking it 48th globally among pharmaceutical exporters. In July 2024, President Gustavo Petro signed Law 2386, declaring the pharmaceutical sector as

strategic and the law aims to promote technological development, innovation, and pharmaceutical production within the country. Colombia's pharmaceutical industry is characterized by a robust manufacturing base, a mix of domestic and international players, and a supportive regulatory environment. These factors, combined with strategic legislation and a strong healthcare infrastructure, position Colombia as a key player in the Latin American pharmaceutical landscape.

Friend-shoring from Chile. The population of Chile was 19.7 million in 2024, the 9th largest country in the Western hemisphere. In 2024, the total trade between the United States and Chile was $36.6 billion with $18.2 billion in U.S. exports to Chile and $16.5 billion in U.S. imports from Chile, resulting in a U.S. trade surplus of about $1.7 billion. The United States exported a diverse array of goods to Chile, including pharmaceuticals. Chile's exports to the United States included copper, fresh fruits, wine and seafood. In early 2025, trade relations experienced strains and there have been questions about the stability of the U.S.-Chile Free Trade Agreement, although both nations continue to engage in diplomatic efforts to maintain and strengthen their economic ties. As of 2023, Chile's pharmaceutical manufacturing sector had about 27 production laboratories for APIs, FDFs, and pharmaceutical raw materials. The majority of these manufacturing facilities are concentrated in the Santiago Metropolitan Region, benefiting from the area's advanced infrastructure and regulatory support. Chile's pharmaceutical manufacturing capacity is modest compared to larger Latin American countries, although it meets domestic demand and serves as a strategic base for regional operations and exports in Latin America.

Choosing Medicines Supply Partners for the United States. Developing new medicines supply partners for the United States will be an important step in assuring the resilience of the U.S. medicines supply chain. After considering possible countries that could serve as a pharmaceutical supply partner for the U.S., the countries of Canada and Mexico are the two leading candidates for near-shoring. Canada is an English-speaking country that has a history of pharmaceutical production (*i.e*., especially FDFs) and trade with the U.S. and it has been one of the United States' closest allies since World War II. Mexico is a Spanish-speaking country that has a long history of trade with the U.S. including at least 70 years in the manufacturing and distribution of pharmaceutical products (*i.e.*, APIs and some FDFs). Both Canada and Mexico share a substantial border with the U.S. and have efficient road and rail transportation that will not require air or sea transport. In the interest of geographic diversity in the U.S. supply chain, other potential partnerships in pharmaceutical production should be considered such as friend-shoring from Brazil and Argentina. Both countries have experienced pharmaceutical manufacturing sectors with a large labor force and experience in trade with the U.S. Other Latin American countries that may play some role in pharmaceutical supply for the U.S. include Peru, Dominican Republic, Costa Rica, and Panama.

What specific drugs or inputs should be prioritized for reshoring or friend-shoring based on both criticality and feasibility?

Prioritization of Drugs for Reshoring and Friend-Shoring. When considering the reshoring and friend-shoring of pharmaceutical manufacturing and critical inputs, it is essential to focus on both criticality (*i.e.*, public health importance) and feasibility (*i.e.*, technical, economic, and logistical practicality). Below are key categories of drugs and inputs that should be prioritized for reshoring and friend-shoring. Ideally, identification of the prioritized drugs to re-shore, near-shore and friend-shore should be done with a comprehensive drug database for the U.S. and global markets. Specific criteria should be established for prioritizing the drugs to be preferentially made as part of the medicines supply chain resilience and security effort. In this testimony, three lists of at-risk and priority drugs have been identified and can serve as a starting point until a more comprehensive analysis can be done. Those lists are: (1) Appendix A. APIs & Therapeutic Use by India % Dependence on China with 36 molecules identified; (2) Appendix B. # of API Producers with U.S. Drug Master File by Molecule or Molecule-Salt: API-Molecule Concentration in China—based on percent of API factories for a molecule that are in China with 148 molecules identified; and (3) Appendix C. List of 53 APIs Specified by Indian Government for Its Incentive Scheme—to stimulate production of APIs that are not produced in India or are in short supply with 53 molecules identified. Across all three of these lists, there were 206 unique molecules.

The Commission is mandated to make policy recommendations to Congress based on its hearings and other research. What are your recommendations for Congressional action related to the topic of your testimony?

Prescription drugs account for more than 3.3% of the U.S. gross domestic product and they contribute to the health and well-being of American citizens as well as the strength and readiness of the U.S. military. A major disruption in the upstream supply chain for pharmaceuticals could have a substantial impact on the U.S. economy, the health of its population, and the readiness and effectiveness of its military. Despite the significant role of pharmaceuticals in the economy, health care, and national security, there is no coordinated and integrated industrial policy process at the federal level in the United States. It would be short-sighted to think that the decades long development of dominance by China, and India, in the pharmaceutical market for active pharmaceutical ingredients and finished dosage forms can be countered, or even reversed, with a simple, singular policy change. The U.S. will need to adopt and implement a constellation of policies and to make commitments to fund and implement them. The following policies are among the constellation of actions that would facilitate the U.S. in building a more resilient and secure U.S. drug supply.

Establish a Government-wide Focal Point for Industrial Pharmaceutical Policy.

- The U.S. should establish a government-wide national focal point for industrial pharmaceutical policy within the U.S. government.

This focal point should be an inter-agency entity that can communicate with all government bodies that have a role in the pharmaceutical market and policy space. This Industrial Pharmaceutical Policy Commission could be established as an independent Congressional Commission similar to the U.S.-China Economic and Security Review Commission or it could be housed in the Office of White House Policy or another suitable location in the federal government. This entity should be authorized to access all data related to pharmaceuticals that is obtained and held by the federal government. This data should be organized in an integrated database that can be accessed by various government bodies as authorized. This Policy Commission should have an appropriation for operation and it should include funds to acquire selected commercial databases in addition to compiling data from federal government databases.

The Pharmaceutical Industrial Policy Commission should be charged with:
(1) establishing policy related to the security and resilience of the U.S. medicines supply;
(2) coordinating inter-agency communication and work within the federal government;
(3) developing and maintaining a market-wide medicine supply map for the U.S.;
(4) tracking, mitigating and preventing drug shortages;
(5) managing a national critical drug reserve and stockpile;
(6) leading public health initiatives involving the resilience of the U.S. medicines supply;
(7) providing support to the Department of Homeland Security on national security issues;
(8) interacting with international efforts to manage the medicine supply.

Develop and Maintain a Market-wide Medicines Supply Map.

- The U.S. should develop and maintain a market-wide medicines supply map.

The U.S. should develop and maintain a centralized system to effectively map, track, predict, and respond to drug shortages and vulnerabilities. Note that even the FDA reports difficulties monitoring the production, quality, and distribution of active pharmaceutical ingredients (APIs) in foreign countries, especially in locations such as China and India—the primary source of drugs used in the U.S. market. The upstream drug supply chain in the U.S. should be mapped in order to identify vulnerabilities, to prevent disruptions, and to prepare coordinated responses.

A medicine supply map should be developed within the federal government for use in assuring a secure and resilient medicine supply in the United States. This medicine supply map should be market-wide and include all prescription drug products and related information. This effort should have authorization to use government data related to pharmaceuticals from any government source. An appropriation should be established for the medicines supply map with funding of $15 million to $20 million per year. In addition

to using authorized data from the federal government, this database may acquire and use select commercial and private databases. An ongoing research program should be established and funded ($25 million per year) to study drug supply resilience and security including approaches to predict, prevent, and resolve drug shortages.

The federal medicines supply map should collaborate with the United States Pharmacopeial Convention Inc and its Medicines Supply Map and with the University of Minnesota's Resilient Drug Supply Project. The market-wide medicines supply map should focus on the upstream drug supply chain. The medicines supply map should routinely monitor trends and vulnerabilities of the U.S. drug supply including the role of China, India, the European Union, and other related activities.

There is a need for an international global system for addressing drug shortages and their causes so that preemptive action can be taken to prevent future drug shortages. The U.S. medicine supply map effort should be coordinated with similar efforts by the European Union, the New Zealand MedSafe database, and other international groups. Comprehensive information on drug supply and drug shortages is needed to provide awareness of vulnerabilities that is timely and transparent enough to predict and respond to drug shortages before the public faces real and significant consequences.

Disclose 'Country of Origin' for Pharmaceutical Products and Make It Transparent.

- The U.S. should require disclosure of the Country of Origin for pharmaceutical products marketed in the United States.

The term 'Country of Origin for Active Pharmaceutical Ingredient' (COOAPI) should be defined in statutes and regulations of the United States. And, the term 'Country of Origin for Finished Dosage Form' (COOFDF) should be defined in statutes and regulations of the United States. All marketed prescription drug products in the United States should be required to report to the FDA the COOAPI and the COOFDF for each drug product at the 11-digit NDC level. This data should be shared with the federal medicines supply map group and with researchers under appropriate access and use terms. The conditions for disclosure, reporting, and use of this information should be defined in statutes and regulations.

Facilitate and Fund a National Pharmaceutical Reserve.

- The U.S. should establish and maintain a Strategic Pharmaceutical Reserve for national emergencies and for coordination with state pharmaceutical reserve programs.

A strategic national reserve for critical drug products should be established to help manage and mitigate surges of drug demand, especially when driven by specific disaster events. A list of critical drugs to be maintained in the reserve should developed with appropriate criteria. The strategic reserve will be a hybrid virtual stockpile approach to

increase inventory of critical drugs, but still keep the stock fresh and in-date by rotating stock at a major wholesaler that has specific inventory held for the Strategic Reserve. The process for access to the Strategic reserve of critical drugs needs to be defined and the role of the Strategic National Reserve in collaborating with state emergency reserve systems needs to be defined.

Establish and Support Public Good Drug Product Designation.

- The U.S. should define criteria for designation of Public Good Drugs and should establish incentives to encourage Public Goods Drugs to remain in the U.S. market.

Lessons from the two decades of experience with tracking drug shortages have shown that there are market failures for some drug products and especially generic sterile injectables. Over time competition drives the price of these products below their marginal cost and manufacturers leave the market because they are not able to sustain the cost. Many of these drug products that are frequently in shortage are critical and essential drug products that are clearly needed in the market. The term 'Public Good Drug' should be defined and criteria should be established for designating public good drugs. Incentives should be established to keep these drugs and their manufacturers in the market.

Develop a Program to Encourage Re-shoring & Near-shoring of Production.

- The U.S. should provide incentives for Re-shoring and near-shoring production of active pharmaceutical ingredients (API) and finished dosage forms (FDF) in the United States and in the Western hemisphere.

The terms 're-shoring' and 'near shoring' should be defined and incentives should be provided to encourage production of APIs, and FDFs in the Western hemisphere. Types of incentives should be explored and established to bring about increased production of pharmaceuticals (API and FDF) in the Western hemisphere. Set goals (30% by unit volume) for the share of dollars and the share of units to be produced in the Western hemisphere.

Track Reserve Capacity for Pharmaceutical Production in the United States.

- The U.S. should establish a process to track reserve capacity for pharmaceutical production and to access that reserve capacity for drug shortages and other emergencies.

There are pharmaceutical manufacturers in the United States who claim to have excess capacity for production of API and FDF products. A process to survey U.S. manufacturers to determine the amount and type of excess capacity should be developed. Strategic plans should be developed for how this excess capacity can be accessed and put to use to resolve drug shortages and to meet excess demand.

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Appendix A

APIs & Therapeutic Use by India % Dependence on China

(*India's Dependence on China for API or KSMs in 2020*)

Item #	APIs	Therapeutic Class/Use	Dependence on China (%)
1	Oxytetracycline	Antibiotic	100
2	Tetracycline	Antibiotic	100
3	Azithromycin	Antibiotic	100
4	Norfloxacin	Antibiotic	100
5	Ofloxacin	Antibiotic	100
6	Aspirin	Pain management	100
7	Metformin	Anti-diabetic	100
8	Ampicillin	Antibiotic	100
9	Levofloxacin	Antibiotic	*100*
10	Atorvastatin	Anti-cholesterol	*100*
11	Chloroquine	Anti-malarial	*100*
12	Montelukast	Asthma treatment	*100*
13	Telmisartan	Anti-hypertensive	*100*
14	Cephalosporins	Antibiotic	*100*
15	Olmesartan	Anti-hypertensive	*100*
16	Penicillin G	Antibiotic	*100*
17	Streptomycin	TB treatment	*100*
18	Ranitidine	Anti-histamine	*100*
19	Ambroxol	Respiratory disease	*100*
20	Metronidazole	Anti-diarrheal	99
21	Neomycin	Antibiotic	98
22	Ciprofloxacin	Antibiotic	97
23	Rifampicin (rifampin)	TB treatment	97
24	Amoxicillin	Antibiotic	93
25	Doxycycline	Antibiotic	91
26	Paracetamol	Analgesic & antipyretic	90
27	Gabapentin	Antibiotic	89
28	Gentamicin	Anxiety drug	86
29	Vitamin C	Antibiotic	81
30	Chloramphenicol	Antibiotic	78
31	Vitamin B6	Vitamin	77
32	Vitamin B1	Vitamin	75
33	Ibuprofen	Pain Management	75
34	Heparin	Anti-coagulant	72
35	Vitamin B12	Vitamin	68
36	Erythromycin	Antibiotic	63

Source: Table 8. Important APIs and Therapeutic Use
Active Pharmaceutical Ingredients: Status, Issues, Technology Readiness and Challenges
Technology Information Forecasting & Assessment Council, July 2020, pp. 20-21
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-Status%2C%20Issues%2C%20Technology%20Readiness%20and%20Challenges_0.pdf

Appendix B

of API Producers with U.S. Drug Master File by Molecule or Molecule-Salt:

API-Molecule Concentration in China

Item #	Molecule-Salt	Total # of DMFs	China # of DMFs	% of DMFs in China
1	fidaxomicin	2	2	100%
2	iodixanol	1	1	100%
3	dalbavancin	3	3	100%
4	insulin aspart	1	1	100%
5	hyoscyamine	1	1	100%
6	vitamin a	2	2	100%
7	degarelix	2	2	100%
8	salicylic acid	1	1	100%
9	ziconotide	1	1	100%
10	anidulafungin	1	1	100%
11	telavancin	1	1	100%
12	tinidazole	1	1	100%
13	polycarbophil	1	1	100%
14	cobamamide	1	1	100%
15	miglitol	1	1	100%
16	trypsin	2	2	100%
17	doxapram	1	1	100%
18	cortisone	1	1	100%
19	pimobendan	1	1	100%
20	chloroxylenol	2	2	100%
21	ethiodized oil	1	1	100%
22	peppermint	1	1	100%
23	acetylglucosamine (N-)	1	1	100%
24	androstenedione	1	1	100%
25	ansamitocin	1	1	100%
26	cefcapene pivoxil HCl	1	1	100%
27	cefmetazole sodium	1	1	100%
28	cefoperazone sodium	1	1	100%
29	cefsulodin	1	1	100%
30	chlortetracycline HCl	2	2	100%
31	chymotrypsin	3	3	100%
32	cytisine	1	1	100%
33	diphenidol HCl	1	1	100%
34	dipyrone sodium	1	1	100%
35	dirithromycin	1	1	100%
36	dyphylline	1	1	100%
37	ethacridine lactate	1	1	100%
38	flunixin meglumine	1	1	100%
39	flupirtine maleate	1	1	100%
40	fosfestrol	1	1	100%
41	gimeracil	1	1	100%
42	huperazine A	1	1	100%
43	hydrotalcite	1	1	100%
44	inamrinone	1	1	100%
45	ipragliflozin	1	1	100%
46	laropiprant	1	1	100%
47	methionine (d-)	1	1	100%
48	mosapride citrate	1	1	100%
49	moxidectin	3	3	100%
50	nadroparin calcium	1	1	100%

of API Producers with U.S. Drug Master File by Molecule or Molecule-Salt:

API-Molecule Concentration in China

Item #	Molecule-Salt	Total # of DMFs	China # of DMFs	% of DMFs in China
51	nitrofurazone	2	2	100%
52	omarigliptin	1	1	100%
53	oteracil potassium	1	1	100%
54	pentoxyverine citrate	1	1	100%
55	pleuromulin	2	2	100%
56	pneumocandin	3	3	100%
57	poliglusam	1	1	100%
58	promestriene	1	1	100%
59	rutin	1	1	100%
60	spectinomycin HCl	1	1	100%
61	sulfadimethoxine	2	2	100%
62	sulfadimethoxine sodium	1	1	100%
63	sulfamethazine sodium	1	1	100%
64	thiostrepton	1	1	100%
65	tibolone	1	1	100%
66	unithiol	1	1	100%
67	lincomycin	8	7	88%
68	enoxaparin sodium	13	10	77%
69	daptomycin	12	9	75%
70	caffeine	4	3	75%
71	povidone	4	3	75%
72	mevastatin	4	3	75%
73	spironolactone	7	5	71%
74	acarbose	7	5	71%
75	prednisone	10	7	70%
76	lanreotide	3	2	67%
77	cyanocobalamin	3	2	67%
78	sevoflurane	3	2	67%
79	alanine	3	2	67%
80	glucosamine	6	4	67%
81	mifepristone	3	2	67%
82	estrone	3	2	67%
83	fusidate sodium	3	2	67%
84	fusidic acid	3	2	67%
85	chondroitinsulfuric acid	11	7	64%
86	tazobactam	13	8	62%
87	piperacillin	15	9	60%
88	thiamine	5	3	60%
89	isosorbide-5-mononitrate	5	3	60%
90	choriogonadotropin alfa	5	3	60%
91	megestrol	7	4	57%
92	fludarabine	7	4	57%
93	prasterone	7	4	57%
94	liraglutide	16	9	56%
95	eptifibatide	11	6	55%
96	somatropin	2	1	50%
97	estrogenic sub,conjugated	2	1	50%
98	iohexol	2	1	50%
99	albumin	6	3	50%
100	pyridoxine	2	1	50%

of API Producers with U.S. Drug Master File by Molecule or Molecule-Salt:

API-Molecule Concentration in China

Item #	Molecule-Salt	Total # of DMFs	China # of DMFs	% of DMFs in China
101	folic acid	4	2	50%
102	teduglutide	2	1	50%
103	selenous acid	2	1	50%
104	ruxolitinib	2	1	50%
105	ceftaroline fosamil	2	1	50%
106	mycophenolic acid	8	4	50%
107	desflurane	2	1	50%
108	lysine	2	1	50%
109	methionine	2	1	50%
110	proline	2	1	50%
111	spinosad	2	1	50%
112	ergocalciferol	4	2	50%
113	idelalisib	2	1	50%
114	dobutamine	4	2	50%
115	fosphenytoin	4	2	50%
116	captopril	6	3	50%
117	secnidazole	2	1	50%
118	cidofovir	2	1	50%
119	isoflurane	4	2	50%
120	flumazenil	4	2	50%
121	omacetaxine mepesuccinate	4	2	50%
122	dalteparin sodium	2	1	50%
123	vinorelbine	6	3	50%
124	mitoxantrone	2	1	50%
125	iopromide	2	1	50%
126	dimenhydrinate	2	1	50%
127	ingenol mebutate	2	1	50%
128	rifamycin	8	4	50%
129	betahistine	2	1	50%
130	mitotane	2	1	50%
131	nesiritide	2	1	50%
132	cefditoren pivoxil	2	1	50%
133	colistimethate sodium	4	2	50%
134	croscarmellose sodium	2	1	50%
135	dexibuprofen	2	1	50%
136	flumethasone	4	2	50%
137	gestodene	2	1	50%
138	idebenone	2	1	50%
139	levocarnitine	2	1	50%
140	menotropin (FSH; LH)	2	1	50%
141	methyl salicylate	2	1	50%
142	procaine HCl	2	1	50%
143	sodium ascorbate	2	1	50%
144	sodium monofluorophosphate	2	1	50%
145	sodium tetradecyl sulfate	2	1	50%
146	tocopherol (alpha-)	2	1	50%
147	trimebutine maleate	2	1	50%
148	vildagliptin	10	5	50%

Source: Resilient Drug Supply Project, PRIME Institute & CIDRAP, University of Minnesota
Based on data from U.S. FDA Drug Master Files and from Cortellis Generic Intelligence

Appendix C

List of 53 APIs Specified by Indian Government for Its Incentive Scheme*

Item #	Molecule-Salt
1	Amoxicillin
2	Cephalexin
3	Cefoperazone
4	Cefixime
5	Tetracycline
6	Potassium clavulanate
7	Oxytetracycline
8	Doxycycline
9	Gentamycin
10	Neomycin
11	Betamethasone base
12	Piperacillin tazobactam
13	Acyclovir
14	Lopinavir
15	Ritonavir
16	Sulfadiazine
17	Levofloxacin
18	Ceftriaxone sodium sterile
19	Telmisartan
20	Losartan
21	Valsartan
22	Olmesartan
23	Atorvastatin
24	Streptomycin sulphate sterile
25	Gabapentin
26	Levodopa
27	Carbidopa
28	Artemisinin
29	Ofloxacin
30	Dexamethasone base
31	Clarithromycin
32	Rifampicin
33	Azithromycin
34	Ciprofloxacin
35	Norfloxacin
36	Clindamycin hydrochloride
37	Vitamin B1
38	Vitamin B6
39	Paracetamol (acetaminophen)
40	Diclofenac sodium
41	Aspirin
42	Clindamycin phosphate
43	Metronidazole
44	Tinidazole
45	Ornidazole
46	Prednisolone
47	Carbamazepine
48	Erythromycin stearate/estolate
49	Metformin
50	Sulbactam
51	Meropenem
52	Levetiracetam
53	Oxcarbazepine

* A high-level Indian government committee's recommendations to the Department of Pharmaceuticals (DoP) as a finalized list of 53 APIs. The APIs chosen: (1) are not produced domestically (in India), or (2) are in short supply, or (3) are essential to treat highly prevalent diseases in India like diabetes, tuberculosis and cardiovascular problems, or (4) are in high demand like antibiotics and vitamins. Among these molecules are some APIs exclusively imported from China such as ciprofloxacin, potassium clavulanate, ceftriaxone sodium sterile, vancomycin, gentamycin, piperacillin tazobactam and meropenem.

Source: Vibha Ravi. COVID-19 Lesson: India Earmarks $1.3bn To Reduce Dependence On China: Lopinavir, Ritonavir On List Of 53 Incentivized APIs. Pink Sheet, March 27, 2020. Accessed on May 23, 2025 at: https://insights.citeline.com/PS141939/COVID19-Lesson-India-Earmarks-13bn-To-Reduce-Dependence-On-China/

Appendix D

White Paper: Ensuring a Resilient Mexican & U.S. Drug Supply

By Stephen W. Schondelmeyer, M. Fabiana Jorge, David Margraf, and James Seifert
Resilient Drug Supply Project, University of Minnesota
August 30, 2021

Overview

Mexico and the United States have a long history of trade including at least 70 years in the manufacturing and distribution of pharmaceutical products.[1] The purpose of this document is to provide an overview of Mexico's capability as a strategic partner in the production of pharmaceutical products for export to the United States. A strategic examination of the pharmaceutical trade between the U.S. and Mexico is warranted as part of the overall examination of the resilience of supply chains for critical U.S. drug products. During the COVID-19 era (Jan. 1, 2020-present), the United States has realized that there are potential and real vulnerabilities in the supply chain for pharmaceuticals that need to be examined and made more resilient. Clearly, the COVID-19 pandemic has challenged global pharmaceutical supply chains and some supply chains have been disrupted in ways that led to drug shortages and absence of critically needed care. Both the public and the private sectors are working together to understand these vulnerabilities, to re-design and re-align supply chains, and to ensure supply chain resilience and long-term stability.

This White Paper explores issues of potential coordination and collaboration between the U.S. and Mexico with respect to efficient production of high-quality prescription pharmaceuticals to meet the needs of the public in both countries and elsewhere. First, a brief background is provided on the size and scope of the Mexican pharmaceutical market. Next, capacity for production of prescription pharmaceuticals and their predecessors (i.e., active pharmaceutical ingredients (API)) are assessed. The status and potential for import and export of pharmaceuticals between the U.S. and Mexico are reviewed. The benefits of increased cooperation and trade of pharmaceuticals between the U.S. and Mexico are outlined. Finally, issues related to implementation of increased trade of pharmaceuticals between the U.S. and Mexico are identified.

Mexico's Healthcare & Pharmaceutical Markets

Mexico is a Spanish-speaking country with a population of 126 million people in 2021. The Mexican federal government implemented a universal health care system in 2012 that included several federal government-run networks as well as private sector providers and insurers. Mexican states provide some additional healthcare services and the Mexican Armed Forces have their own healthcare system. The López Obrador Administration worked to combine three federal programs into a single national healthcare system in an effort to reduce staff and costs. Also, the Administration made significant changes in the procurement process "to reduce alleged widespread corruption and to force reductions in cost of drugs, devices, supplies, and services."[2] The procurement changes led to major revisions in the distribution system for pharmaceuticals and

[1] KPMG, The Mexican Pharmaceutical Industry, News, 2017, p.16.
[2] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services.

medical supply items that have resulted in product shortages. While these changes were intended to lower costs for medications and devices in the healthcare sector, they may have driven the system toward lower-cost and lower-quality producers.

Mexico is the eleventh largest pharmaceutical market in the world and is second, only to Brazil, in Latin America. In 2019, Mexico's pharmaceutical market reached about $11.8 billion (USD) total sales.[3] Pharmaceutical sales in Mexico are projected to grow at a compound annual growth rate of 2.4% over the next eight years and are expected to reach $13.8 billion (USD) by 2027. Generic sales for the public sector in 2018 were US$3.08 billion and are expected to show continued growth reaching US$9.0 billion by 2027.[4] By value, 51% of the total Mexican pharmaceutical market is patented brand name prescription drugs, generic prescription drugs are 35%, and OTC (or non-prescription) drugs are 14%.[5] Generic prescription drugs account for about 80% of the unit volume of the Mexican pharmaceutical market[6], while patented brand name prescription drugs account for about 14% of the volume and OTC drugs represent about 6% of the volume.[7] The government has a role in acquisition of approximately 27% of the total pharmaceutical market value.[8] Pharmaceuticals accounted for 14.5% of Mexican healthcare spending in 2018 and 0.86% of the Gross Domestic Product (GDP).[9] Annual per capita spending on pharmaceuticals was US$79.

Mexico: Pharmaceutical Manufacturers & Production

There are more than 400 hundred pharmaceutical companies registered in Mexico with various levels of operation (i.e., API manufacture, FDA manufacture, packaging, labeling, and analytical services).[10] Among these firms are subsidiaries from 20 of the world's top 25 largest multinational pharmaceutical companies who account for the largest share by monetary value of pharmaceutical production in Mexico (e.g., Sanofi, Bayer, Pfizer, Novartis, J&J, and GSK). However, there are many successful Mexican-based companies. Four of the top ten spots based on 2020 pharmaceutical sales in Mexico are held by Mexican-based manufacturers (e.g., Pisa, Sanfer, Senosiain, and Siegfried Rhein).[11]

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[3] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services; data presented in this report was from the Global Trade Atlas, CANIFARMA, AFAMELA, AESGP, Fitch Solutions.

[4] BMI Pharmaceuticals & Healthcare Report, Mexico Pharmaceuticals & Healthcare report, Mexico Generic Drug Market Forecast – Industry Forecast, March 6, 2019.

[5] Fitch Solutions estimate forecasted above 35% (35.6%) for 2018. BMI Pharmaceuticals & Healthcare Report, Mexico Pharmaceuticals & Healthcare Report, Mexico Generic Drug Market Forecast – Industry Forecast, March 6, 2019.

[6] COFEPRIS

[7] BMI Pharmaceutical & Health Report, Mexico Pharmaceuticals & Healthcare Regulatory Review – Regulatory Overview, March 6, 2019.

[8] KPMG, The Mexican Pharmaceutical Industry footnote 8 (original source: II Statistic Abstract, Canifarma, 2015 (www.canfarma.org.mx)).

[9] BMI Pharmaceutical and Healthcare Report, Mexico Pharmaceuticals & Healthcare Report, Market Overview, March 6, 2019.

[10] https://www.saintytec.com/pharmaceutical-companies-mexico/

[11] IQVIA, Feb. 2020; PharmaBoardroom,com, Top 10 Pharma Companies in Mexico, May 14, 2020, https://pharmaboardroom.com/articles/top-10-pharma-companies-in-mexico/

(1) Sanofi Corp.
(2) Bayer Corp
(3) Pisa
(4) Pfizer Corp
(5) Sanfer Corp
(6) Novartis Corp
(7) Senosiain
(8) Siegfied Rhein
(9) Johnson & Johnson Co
(10) GlaxoSmithKline Co

Briefly, the four Top 10 Mexican-owned pharmaceutical companies are:

 # 3: Pisa; Laboratorios Pisa, S.A. de C.V. (Guadalajara, Jalisco, Mexico). Pisa was founded in 1945 and is involved in the manufacturing and development of pharmaceutical drugs for human health and animal health.

 # 5: Sanfer; Sanfer Mexico (Boulevard Adolfo López Mateos 314, Alvaro Obregon, Tlacopac, 01049 Ciudad de México). Sanfer was established in 1941 and is a leader in the Mexican pharmaceutical market offering a comprehensive range of products including cardiology, infectious disease, etc.

 # 7: Senosiain; Senosiain Laboratories S.A. de C.V. (Andrés Bello 45, Polanco, Chapultepec, Miguel Hidalgo, 11560 Ciudad de México, CDMX, Mexico). Senosiain is dedicated to developing, manufacturing, and marketing innovative pharmaceutical products in Mexico and in other Latin American countries.

 # 8: Siegfried Rhein; Siegfried Rhein (Torre D, Piso 12, Antonio Dovali Jaime 70, Zedec Sta Fé, Álvaro Obregón, 01210 Ciudad de México, CDMX, Mexico). Siegfried Rhein was founded in 1973 and is dedicated to manufacture, fabricate and market nutritional materials, pain killers, urinary system agents, and hygienic products.

Prior to 2010, the Mexican government would only allow pharmaceutical companies to market their drug in Mexico if they produced the drug product locally. Elimination of the manufacturing plant requirement for those selling in Mexico led to an increase in the presence of the large multi-national pharmaceutical companies, although some dropped or did not have local manufacturing facilities.[12] However, weakening of the peso in recent years has negatively affected these multinational companies and the market value in dollars contracted from 2014 to 2016 but since that time modest growth has returned.[13]

The pharmaceutical industry directly employs over 79,000 people in Mexico (1.6% of the manufacturing sector) and that indirectly generates over 300,000 additional jobs.[14] There are approximately 400 pharmaceutical manufacturing facilities in Mexico. These manufacturing facilities are concentrated in certain geographic regions with Mexico City and the state of Jalisco representing 86% of the total pharmaceutical production.[15] Other regions with substantial pharmaceutical manufacturing include the states of México, Puebla and Morelos. More recently, Baja California has developed industrial and academic centers for biotechnology R&D and the federal government has published guidelines for approval of biological and bio-comparable medicines. Several multinational companies have made investments in biological product launches and Mexico expects growth in the biological sector. The COFEPRIS reported in 2019 that 70 originator biotech drugs and 13 biosimilars had received marketing approval in Mexico.[16]

[12] Business Monitor Online, Mexico Pharmaceuticals & Healthcare Competitive Landscape, August 19, 2019.
[13] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services.
[14] KPMG, The Mexican Pharmaceutical Industry (page 7).
[15] Instituto Nacional de Estadistica y Geografia – INEGI
[16] COFEPRIS is the Mexican Federal Commission for the Protection Against Sanitary Risks.

Mexico Pharmaceutical Imports. The Mexican market imported $2.5 billion (USD) or about 21% of total pharmaceutical consumption by monetary value during 2019.[17] The United States is the largest foreign supplier of pharmaceutical products to the Mexican market. In 2019, the United States exported $828 million (USD) to Mexico, accounting for one-third (33.6%) of the total pharmaceutical imports into Mexico.[18] The largest portion of the U.S. imports into Mexico are higher cost, patent-protected brand name drug products. Although imports from the United States declined by 21 percent in 2019 compared to 2018, the U.S. is still the major source for imported pharmaceuticals. The decrease of pharmaceutical imports by Mexico appears to be related to changes in the government procurement process such as increased market participation of low-cost generics, uncertain product approval and registration timings, continued issues in intellectual property protection, and the low value of the Mexican Peso against the U.S. Dollar.[19] In 2019, several *public health institutions in Mexico faced shortages of medicines due to issues resulting from the recent government procurement changes*.[20]

Mexico Pharmaceutical Exports. In 2019, Mexico exported $567 million and 85 million kilograms of pharmaceuticals to the United States. When ranked by value (US$), Mexico ranks as the 10th largest exporter to the U.S. However, when ranked by volume (Kg), Mexico ranks as the 3rd largest exporter to the U.S. behind only China and India. The U.S. market is already the largest recipient of Mexican exports. Other major recipients of pharmaceutical exports from Mexico are Venezuela, Panama, Brazil, and Columbia.[21] In 2019, Mexico exported a total of $1.77 billion (USD) worth of pharmaceutical products to any destination.[22] However, Mexico imported pharmaceutical products worth around $4.80 billion (USD)—about 2.7 times more than it exported. Consequently, *Mexico has a negative balance of trade with the U.S. for pharmaceutical products.*

Opportunity for Increased Exports from Mexico to the U.S.

Historically, Mexican manufacturers have been important producers of APIs both for domestic use and for export to other countries. However, the amount of API production decreased substantially after adoption of the TRIPS Agreement (1990s & early 2000s) due, in large part, to lower prices from Chinese producers supported by government strategy and subsidies. Mexican pharmaceutical manufacturers are still engaged in production of active pharmaceutical ingredients (API) and many hold FDA approved processes and facilities including 108 drug master files, 28 drug master files for reference, 18 certificates of suitability, and 12 GDUFA sites.[23] These are all facilities or processes reviewed by the FDA making them eligible to produce API for drug products to be sold in the U.S. market.[24] *Mexico has underutilized capacity for increased pharmaceutical exports to the U.S.*

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[17] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services.
[18] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services; data presented in this report was from the Global Trade Atlas, CANIFARMA, AFAMELA, AESGP, Fitch Solutions.
[19] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, p. 2; accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services
[20] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, p. 8; accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services
[21] ProMexico with information from Global Trade Atlas and KPMG.
[22] https://www.statista.com/statistics/478653/pharmaceutical-production-in-mexico/; July 1, 2021.
[23] thepharmaletter, PharmaBoardroom,com, Mexico Facts & Figures Snapshot, Nov. 30, 2016.
[24] thepharmaletter, PharmaBoardroom,com, Mexico Facts & Figures Snapshot, Nov. 30, 2016.

The Resilient Drug Supply Project reviewed its U.S. supply chain mapping database and found that there are 346 establishments in Mexico registered or listed with the FDA. These facilities can perform various operations such as manufacturing facilities (301 registered & 292 active), active pharmaceutical ingredient (API) manufacture (29 & 6), packaging (89 & 49), labeling (94 & 4), repackaging (20 & 6), relabeling (18 & 6), sterilization (4 & 3), and analysis (54 & 5). [25] Most of the Mexican facilities currently active in preparing pharmaceutical products for the U.S. market were making non-prescription (OTC) drug products, while only nine firms were making finished prescription drug products and six firms were making API for export to the U.S. market. Clearly, Mexico has manufacturing resources that are qualified and registered with the U.S. FDA, but are not fully exercising the opportunity to export to the U.S. market.[26] *There appears to be substantial room for growth in Mexican pharmaceutical exports to the U.S. market*.

Under current Mexican law, government purchasing rules provide preference to suppliers from countries with which Mexico has a free trade agreement. These rules provided preferential advantages to U.S. suppliers under the North American Free Trade Agreement (NAFTA) and now under the new United States–Mexico–Canada Agreement (USMCA). However, it is unclear how the Mexican Government will apply its new procurement rules for the healthcare sector to its trade and treaty obligations. The USMCA provisions took effect on July 1, 2020, and with regard to the healthcare sector, the agreement contains significant improvements and modernized approaches to rules of origin and intellectual property issues. For example, a Certificate of Origin is part of the new USMCA treaty that took effect on July 1, 2020. Only North American (Mexico, Canada, and U.S.) products are eligible for preferential tariff treatment.[27] For products to qualify as having a North American origin under USMCA, they must possess a minimum set of nine required data elements to receive USMCA beneficial treatment. A certificate of origin may be issued by the importer, exporter, or producer. Current t*rade agreements (i.e., the USMCA) among Mexico, Canada and the U.S. are favorable to increased exports from Mexico to the U.S.*

Benefits to the U.S. from Mexican Pharmaceutical Exports

Alternative Source of Pharmaceuticals. The COVID-19 pandemic has challenged global supply chains, in general, and, in particular, it has sensitized the United States to the heavy dependence it has on Asian countries and especially China and India. Currently, *U.S. policymakers are looking for alternative supply channels to decrease the U.S. dependence on China and India for critical and essential pharmaceuticals.* One solution is encouragement of re-shoring to the U.S. of pharmaceutical manufacturing for critical active pharmaceutical ingredients (API) and finished dose forms (FDF). In addition to increased U.S. production of pharmaceuticals, there is a need to develop geographically diverse supply chains that address environmental, economic, and geopolitical challenges.

Geographic Diversity of Supply Sources. Mexico can provide near-shoring of pharmaceutical production that can decrease the U.S. dependence on more distant Asian sources

[25] www.accessdata.fda.gov/cder/drls_reg.zip

[26] Data from the Drug Registration and Listing System (DRLS) found at www.accessdata.fda.gov/cder/drls_reg.zip and from the Structured Product Labeling database accessed through the National Library of Medicine Daily Med web site.

[27] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services.

such as China or India. Near-shoring in Mexico is a means to minimize over-concentration of production in Puerto Rico or the mainland of the United States.

Improved Logistics & Transportation. *Mexico is geographically nearby the U.S. and offers more efficient shipping and logistical access.* Mexico is strategically located at the southern edge of the United States where it shares a border with four states (i.e., Texas, New Mexico, Arizona and California). Mexico's proximity and physical border with the U.S. enable transportation and shipping routes by rail and road and entirely over land. This means that shipping of pharmaceuticals from Mexico can avoid more expensive and congested sea and air transport.

Lower Cost Production. *Mexico can produce pharmaceuticals at a cost that is 14.4% less than in the U.S.* By comparison, Canada can produce pharmaceuticals at a cost that is 4.6% less than the U.S. and in Italy, costs are about 1.9% less than in the U.S.[28]

Improved Inspection Access. Pharmaceutical production in Mexico would allow FDA to have improved access to manufacturing facilities for inspection and oversight. The FDA does have an office and staff based in Mexico, which would facilitate more frequent and efficient inspections for quality and Good Manufacturing Practices than can be achieved in Asian countries.

Benefits to Mexico from Pharmaceutical Exports to the U.S.

Economy of Scale Can Reduce Domestic Cost of Pharmaceuticals. One major goal of the Mexican administration has been a desire to reduce the cost of pharmaceuticals in order to improve access to critical medicines for the general population. The government of Mexico has expressed significant interest in expanding policies to promote generic pharmaceuticals in Mexico.[29] At the same time, Mexican pharmaceutical firms appear to have excess capacity and facilities that are, or could be, approved by the U.S. FDA, for production of prescription pharmaceuticals for export to the U.S. market. If Mexican pharmaceutical firms increased their production of prescription drugs for export to the U.S. market, it would facilitate improved economy of scale and reduction of the marginal cost of production. This would benefit the Mexican healthcare system with access to lower cost generic medicines to improve access for the population and lower costs to the government.

Jobs & Employment. *Increased pharmaceutical exports from Mexico to the U.S. could substantially increase jobs and reduce unemployment in Mexico.* With careful planning and cooperation between the U.S. and Mexico, Mexican exports of pharmaceuticals to the U.S. could increase by 2-fold to 10-fold over the next few years. This expansion of Mexican exports to the U.S. would benefit both countries.

Improved Balance of Trade with the U.S. *Currently, Mexico has a negative balance of trade on pharmaceuticals with the U.S.* The value of U.S. pharmaceutical imports to Mexico exceed the value of Mexican exports to the U.S. by a factor of 2.7 to 1. The potential increased production and export of pharmaceuticals from Mexico to the U.S. could balance out this trade deficit, or it could even move to a positive balance of trade.

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[28] PharmaBoardroom.com, Mexico: Healthcare & Life Sciences Review, Nov. 2015, p.39.

[29] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services..

Stable Industrial & Economic Growth. The López Obrador Administration took steps in June of 2019 to centralize public sector pharmaceutical purchases. The Government claimed this effort would reduce escalating wholesale costs and perceived corruption, as seen in previous administrations, allegedly driven by the pharmaceutical distributors in Mexico.[30] The Mexican government policies related to pharmaceutical purchases and prices have resulted in some uncertainty in the pharmaceutical production environment. This uncertainty makes local and foreign investment in Mexican pharmaceutical firms less attractive. With increased exports to the U.S. market, the revenue potential for Mexican pharmaceutical firms would be greatly increased and substantially more stable, thus attracting more investment and long-term stability.

Reduced Drug Shortages in Mexico. Changes and uncertainty in the government procurement policies in Mexico have led to widespread drug shortages in Mexico. [31] There does not appear to be any publicly available government tracking of drug shortages. Non-governmental groups have offered reports detailing the worsening drug shortage issues in Mexico, which stem from recent changes in Mexican regulations. A report by Cero Desabasto "Zero Shortage" (cerodesabasto.org) found in 2020 a 6% increase in prescriptions that could not be filled by the Mexican Social Security Institute (IMSS). IMSS provides health care to 51% of Mexicans. July 2021 saw protests over the lack of pediatric cancer medications in Mexico City.[32] These shortages have persisted for 2 years, which some feel are the result of Mexican President López Obrador's overhauling the pharmaceutical procurement process. Nevertheless, the results of such policies have caused shortages of drugs and supplies in the public healthcare sector and a perception of lack of transparency within the private sector companies that sell to the government.[33] Experts attribute the drug shortages to poor planning and misunderstanding of the complex nature of pharmaceutical procurement and distribution, and the shortage of materials caused by the COVID-19 pandemic.[34]

Challenges and Implementation Issues

Several issues need to be addressed to facilitate and enable a win-win strategy for increased pharmaceutical exports from Mexico to the United States. Among the important issues that will need attention are:

- Incentives for Mexican firms to develop finished prescription drug products and active pharmaceutical ingredients for the U.S. market;
- Infrastructure in Mexico to support pharmaceutical manufacturers such as manufacturing hub sites, free trade zones, and enhanced utility capacity;
- Establishment of physical security and cybersecurity for pharmaceutical production and transport operations;
- Clarification of the USMCA trade agreement terms and how they interact with the increased pharmaceutical exports from Mexico to the U.S.;

[30] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, p. 9; accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services.
[31] Agren D. Lack of medicines in Mexico. The Lancet. 2021;398(10297):289-290.
[32] Das M. Shortage of cancer drugs in Mexico. The Lancet Oncology. Published online July 2021:S1470204521004526.
[33] U.S. International Trade Administration, Mexico – Country Commercial Guide, Aug. 18, 2020, p. 10; accessed on Aug. 19, 2021 at: https://www.trade.gov/knowledge-product/mexico-k-healthcare-products-services.
[34] Agren D. Lack of medicines in Mexico. The Lancet. 2021;398(10297):289-290.

- Harmonization of U.S. FDA regulations with its Mexican counterpart to facilitate coordination and consistency in regulation of pharmaceutical production;
- Cooperation between the U.S. FDA and its Mexican counterpart to assure product quality oversight and facility inspections;
- Implementation of track and trace methods and other approaches to prevent introduction of counterfeit products into the U.S. pharmaceutical market;
- Adoption and enforcement of laws that prohibit and root out corruption in the production, procurement, and import-export process; and
- Investment in improved roads and railroads between Mexico and the U.S. to facilitate transport and import-export of pharmaceutical products.

Summary

The United States needs new strategically positioned sources of supply for critical pharmaceutical products. Some of the pharmaceutical supply chain concerns can be addressed by re-shoring pharmaceutical production to the United States. However, the U.S. could also benefit from 'near-shoring' opportunities that provide other geographically diverse supply chains with efficient production costs. Mexico is well-positioned to increase its production and export of prescription pharmaceuticals to the U.S. Internally, collaboration between the Mexican government and the Mexican pharmaceutical industry has evolved and appears to be favorable to a more visionary partnership to strategically prioritize the pharmaceutical market for expansion.[35] The USMCA free trade agreement is now in place and can facilitate cooperation between Mexico and the U.S. to increase production of pharmaceuticals in Mexico in a way that benefits both countries. With proper support and incentives from both Mexico and the U.S., both governments can strengthen and ensure the stability of their drug supply chains for critical and essential medications needed by their respective populations.

[35]KPMG, The Mexican Pharmaceutical Industry, News, 2017.