

## POLICY BRIEF

### Enhancing Resilience in Pharmaceuticals Supply Chains

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*The United States and the European Union (EU) have recently launched various initiatives to manage their competition and enhance their cooperation on trade and technology issues. The Transatlantic Leadership Network's Trade and Technology Working Group addresses these topics in its work, including recommendations for more effective action. This policy brief recommends ways for the two parties to enhance pharmaceuticals supply chain resilience and competitiveness. One companion piece addresses broader supply chain issues, with recommendations for U.S.-EU action; another focuses more specifically on semiconductor supply chains. I thank Working Group colleagues for our discussions on these issues; I take responsibility for the recommendations offered here. All products from the TLN Working Group may be found at <https://www.transatlantic.org/transatlantic-technology-and-trade-working-group/>.*

#### Introduction

Until the mid-1990s, the United States, Europe and Japan produced 90% of the world's active pharmaceutical ingredients (API)—the key ingredients for antibiotics and many other common medicines such as painkillers. That situation began to change as companies, prioritizing efficiencies and cost savings over resiliency and security of supply, created extended value chains for medical ingredients and supplies that rendered them extraordinarily dependent on China and India.

Today, China provides between 80% and 90% of the global supply of active ingredients for antibiotics, and China and India are the source of about 75% of the APIs and 40% of finished medications imported by the United States. China accounts for 95% of U.S. imports of ibuprofen, 91% of U.S. imports of hydrocortisone, 70% of U.S. imports of acetaminophen, up to 45% of U.S. imports of penicillin, and 43% of U.S. imports of heparin.<sup>1</sup>

The generic drug business, which accounts for more than 90% of all prescriptions in the United States, Germany and many other developed countries, turned to India, which has become the world's largest manufacturer of generic drugs. Its nickname is "pharmacy to the world." Most countries around the globe import most of their generics, including antibiotics, from India. India, in turn, imports some 70% of its active ingredients from China.<sup>2</sup>

The shift to low-cost suppliers was so complete that for 17 years the United States was home to no single large-scale antibiotic producer, until USAntibiotics recently reopened a manufacturing facility in Tennessee.<sup>3</sup> The U.S. remains reliant on imported antibiotics to address a wide range of infections that are threats to human life, from pneumonia and sexually-transmitted diseases to strep throat and even anthrax. After the anthrax attacks on Capitol Hill and elsewhere in 2001, the U.S. government had to turn to a European company to buy 20 million doses of the recommended treatment for anthrax exposure,

doxycycline. That company, in turn, had to buy the chemical starting material from China. Two decades later, the United States is still reliant on doxycycline imports from China.<sup>4</sup>

The situation is similar in Europe. Its last acetaminophen (paracetamol) manufacturing plant closed in 2008. Its last large-scale antibiotics plant is located in the Austrian town of Kundl, and the only site in the Western world that produces ascorbic acid, better known as Vitamin C, is in the Scottish hamlet of Dalry.<sup>5</sup> Europe was becoming equally dependent on China for heparin until several tainted heparin products imported from China and other countries forced European countries to manufacture their own heparin products. Overall, upward of 80% of chemicals used to make drugs sold in Europe now originate from China and India.<sup>6</sup>

The complex nature of pharmaceutical value chains can obscure these deep and often asymmetric entanglements. The “trade in tasks” nature of these supply chains often means that China provides APIs, largely to India, which then processes intermediate elements for generic drugs, which may be assembled in final form in places like Italy or Ireland, and then exported elsewhere in Europe or to the United States. This can confound traditional trade measurements. In 2019, for example, official statistics show that 73% of U.S. imports of pharmaceutical products came from Europe, while 61% of imported APIs came from European sources. The United States actually sourced 40% more of its imported APIs from Ireland than it did from China. Yet the ingredients and intermediate tasks that resulted in those European exports were predominantly sourced from China and India.<sup>7</sup>

These entanglements enmesh most of the world. At least three WHO-identified essential medicines—capreomycin and streptomycin for the treatment of *Mycobacterium tuberculosis*, and sulfadiazine, used to treat chancroid and trachoma—rely on API manufacturers based solely in China. Africa is extraordinarily dependent on external suppliers; effectively all APIs and 80-90% of its finished medicines are imported, mostly from India.<sup>8</sup>

The pandemic exposed these dependencies when factory shutdowns in China slashed API exports to India, which relies on China for about 70% of its supply of APIs and is almost 100% dependent on China for some well-known drugs, such as paracetamol, amoxicillin and ibuprofen. The Indian government responded by financing indigenous production of bulk drugs and 53 priority APIs. It restricted exports of API and medication to Europe and the United States, leading to critical drug shortages.<sup>9</sup> Dependencies extended beyond drugs to medical supplies. Europeans and Americans were stunned to find how dependent they were on other countries, particularly China, for personal protective equipment (PPE), especially medical masks. By late April 2020, more than 80 countries had introduced export curbs or restrictions on medical supplies related to COVID-19. Shortages caused European countries, U.S. states and individual hospitals to bid against each other.<sup>10</sup>

### *Chinese Dependencies on the United States and Europe*

These dependencies are not simply one-way. China also relies on the United States and major European countries for some of its medicines. In 2019, Germany was the largest source of China's medicine imports, followed by France, the United States, Italy and Sweden. The United States and Europe are the world's predominant sources of pharmaceutical innovation, including new cancer drugs, next-generation biopharmaceuticals and tests that determine which patients will benefit from those drugs. China, in turn, is facing a crisis of non-communicable diseases, including cancer, cardiovascular diseases, and diabetes. The medicines it needs are often found in the West.

China is highly reliant on U.S. cancer drugs in particular. Of those launched world-wide from 2013 to 2017, 51 of 54 were available within two years in the United States. Only two were available in China. Cancer survival in China is only half that in the United States. Beijing is aware; it omitted U.S. cancer drugs from tariffs placed on other medications in 2019.<sup>11</sup>

In short, pharmaceutical supply chains have entangled countries around the world in a web of asymmetric interdependencies that may limit short-term temptations toward instrumentalizing health in geopolitical competition, even as it sparks longer-term efforts to unwind such dependencies.

## **Recommendations**

**Improve transparency throughout the pharmaceuticals supply chain.** Although pharmaceuticals are among the most regulated industries in the United States and the EU, pharmaceutical supply chains remain relatively opaque, especially with regard to the origins of API within generic drugs, which account for the vast majority of pharmaceuticals consumed on both sides of the Atlantic. Many foreign API manufacturers that ship their drug to another foreign country to be incorporated into a finished product that is ultimately imported into the United States or the EU do not register their establishments with relevant U.S. or EU member state health authorities. The two parties should coordinate action to track pharmaceutical production by facility, track API sourcing, and require API and finished dosage from sources can be identified on labeling for all pharmaceuticals sold in both jurisdictions.<sup>12</sup>

**Improve quality management.** Unlike the auto or aerospace industries, where quality management systems have been a key ingredient of success, many pharmaceutical firms have been slow to adopt such measures. Doing so promises to improve reliability of supplies, and ensuring that high standards are maintained throughout the pharmaceutical supply chain. The U.S. FDA has urged a focus on such efforts; they are more likely to be realized if the United States and the EU convey a single message about their importance to the pharmaceutical industry.<sup>13</sup>

**Facilitate advanced manufacturing to promote diversification and redundancy.** Traditional pharmaceutical manufacturing technologies make it difficult for U.S. or European manufacturers to offset the labor and other cost advantages of companies in third countries. Greater transatlantic research and development cooperation on advanced manufacturing technologies, which for example could enable continuous manufacturing instead of traditional batch manufacturing, could help domestic manufacturers compensate for cost disadvantages by offering more effective and higher-quality products with lower environmental footprints, increasing their resilience and reducing dependence on third-country sources of APIs. U.S. FDA is already engaged with European and other international counterparts in harmonizing requirements to spur advanced manufacturing.<sup>14</sup> Early work indicates barriers to be overcome include conflicting incentives for the industry, logistical hurdles, and shortage of relevant expertise. The TTC Working Group could accelerate efforts to address these challenges.

**Accelerate capacity for on-demand manufacturing capabilities for APIs and finished drug products.** Advances in science and technologies have now given us the ability to generate rapid-reaction capabilities to produce and deliver vaccines and medicines at scale on short notice. This has the potential to boost domestic pharmaceutical manufacturing in ways that could revolutionize pharmaceutical supply chains. Enhanced scientific collaboration on these novel approaches can accelerate these opportunities.<sup>15</sup>

**Cooperate to establish virtual stockpiles of APIs and other critical materials necessary to produce essential medicines.** A virtual stockpile would involve contracts with API and drug suppliers to support surge capacity rather than keeping APIs and drugs physically stockpiled, which could lead to waste and stress supply chains. U.S. and European countries are each seeking to establish something along these lines. While each party is likely to prioritize domestic suppliers as far as possible, additional contracts and other arrangements could be arranged with transatlantic suppliers to fill in gaps as possible. U.S.-EU efforts should include a review of regulatory procedures that could permit rapid-reaction and deployment across jurisdictions. One early action suggested by the U.S. FDA is development of a centralized API supplier database, which would enable manufacturers to identify alternative sources of APIs easily, and to shift

suppliers in the event of disruption. Another action is to work together, and with other international partners, to map a critical-drug supply chain that is redundant, diverse, includes sufficient onshoring, production in geographically accessible locations, and production by allies.<sup>16</sup>

## Notes

- <sup>1</sup> White House, “Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth,” June 2021, <https://www.whitehouse.gov/wp-content/uploads/2021/06/100-day-supply-chain-review-report.pdf>; Stephen Ezell, “Faulty Prescription: Why a ‘Buy American’ Approach for Drugs and Medical Products Is the Wrong Solution,” International Information Technology and Innovation Foundation (ITIF), June 15, 2020, <https://itif.org/publications/2020/06/15/faulty-prescription-why-buy-american-approach-drugs-and-medical-products/>; Mordor Intelligence, Active Pharmaceutical Ingredients (API) Market – Growth, Trends, COVID-19 and Forecasts (2021 - 2026), <https://www.mordorintelligence.com/industry-reports/global-active-pharmaceutical-ingredients-api-market>; Rosemary Gibson, “Exploring the Growing U.S. Reliance on China’s Biotech and Pharmaceutical Products,” Testimony Before the U.S.-China Economic and Security Review Commission, July 31, 2019, <https://www.uscc.gov/sites/default/files/RosemaryGibsonTestimonyUSCCJuly152019.pdf>; Florence Schulz, “Europe’s dependence on medicine imports,” Euractiv, March 16, 2020, <https://www.euractiv.com/section/health-consumers/news/europes-dependence-on-medicine-imports/>; Rory Horner, “The world needs pharmaceuticals from China and India to beat coronavirus,” The Conversation, May 25, 2020, <https://medicalxpress.com/news/2020-05-world-pharmaceuticals-china-india-coronavirus.html>; Martijn Rasser, “Pandemic Problem: America’s Supply Chains Are Dangerously Brittle,” National Interest, March 17, 2020, <https://nationalinterest.org/feature/pandemic-problem-americas-supply-chains-are-dangerously-brittle-134022>.
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- <sup>5</sup> Michael McCoy, “Sandoz to shore up Europe’s last antibiotics facility,” Chemical and Engineering News, June 30, 2020, <https://cen.acs.org/pharmaceuticals/pharmaceutical-chemicals/Sandoz-shore-Europes-last-antibiotics/98/i30>; DSM, “Committing to Quality and Sustainability with Quali@-C,” <https://www.dsm.com/human-nutrition/en/talking-nutrition/committing-to-quality-and-sustainability-with-quali-c.html>.
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- <sup>12</sup> White House.
- <sup>13</sup> White House.
- <sup>14</sup> White House.
- <sup>15</sup> See Daniel Hamilton and Tara O’Toole, “New security alliances: Facing up to the bioterror threat,” *New York Times*, Jan. 31, 2005, <https://www.nytimes.com/2005/01/31/opinion/new-security-alliances-facing-up-to-the-bioterror-threat.html>; Daniel S. Hamilton & Bradley T. Smith, “Atlantic Storm,” *EMBO Reports*, Vol. 7, No. 1, January 2006, <https://www.embopress.org/doi/epdf/10.1038/sj.embor.7400606>.
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