A Non-Profit Approach to Address Foreign Dependence of Generic Drugs

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Abstract: The COVID-19 pandemic has revealed the vulnerability of the US generic drug supply chain to foreign production. Many policies have been proposed to mitigate this vulnerability. In this article, we argue that nonprofit drug manufacturers have the potential to make important contributions.

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The COVID-19 pandemic has exposed US dependence on foreign countries for generic drugs.[1] Although such reliance can lead to lower manufacturing or procurement costs, it increases supply chain vulnerability of US medical products and poses substantial national security risks, especially during global crises.[2] For example, amid the pandemic, production disruptions and local medical needs in China, a dominant supplier of generic drugs and active pharmaceutical ingredients, reportedly caused shortages of generic antibiotics needed to treat COVID-19-related secondary bacterial infections, such as azithromycin, ciprofloxacin, and piperacillin/taobactam.[3] In March 2020, China's official news agency threatened a ban on exports of these and other medical products to United States.[4]

In 2001, China joined the World Trade Organization and gained access to global markets. Since then, generic drug companies have shifted much of their manufacturing from the United States to China, motivated by China's low costs.[5] Today, China produces 9% of all generic drugs in the US market, while India, which produces 25% of all generic drugs in the US market, relies heavily on China for pharmaceutical ingredients.[6] Approximately 90% of pharmaceutical ingredients used for essential generic drugs treating

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serious coronavirus infections in United States are made in China.[7]

In the wake of COVID-19, several bills have been introduced in Congress to address this foreign dependence (Table). Overall, they have three main objectives: (1) to provide funding to encourage domestic production of generic drugs, (2) to improve the transparency of the generic drug supply chain information and assess its vulnerability, and (3) to require that critical drugs purchased by Strategic National Stockpile be "Made in America." The Trump Administration has also invoked the Defense Production Act to fund some companies' effort to establish domestic manufacturing facilities for generic drugs and active pharmaceutical ingredients, and mandated that essential generic drugs purchased by the federal government be produced domestically.[8] These initiatives aim to diminish the cost differential between domestic and overseas production and reflect an opportunity to transform the US supply chain.

Amid the pandemic, production disruptions and local medical needs in China, a dominant supplier of generic drugs and active pharmaceutical ingredients, reportedly caused shortages of generic antibiotics needed to treat COVID-19-related secondary bacterial infections, such as azithromycin, ciprofloxacin, and piperacillin/taobactam. In March 2020, China's official news agency threatened a ban on exports of these and other medical products to the Uniteds States.

While public attention has been focused on responses from for-profit companies, non-profit manufacturers may actually be better positioned to play an important role in bringing production back to the US. Manufacturing drugs requires considerable upfront capital investment and has a large fixed overhead cost, leading to high operating risks. When demand is low, manufacturers are likely to generate significant losses. Even with healthy demand, the profit margin for generic manufacturing is often thin, since the price needs to be competitive to the prices of overseas suppliers. However, for-profit entities must generate sufficient profits to reward investors, who would otherwise seek alternative investment options. For-profit entities, therefore, have a relatively high cost of capital and are often not likely to find the combination of a high operating risk and a thin profit margin attractive.

By contrast, non-profit entities have no equity investors; their initial capital usually comes from philanthropy; and they face no pressure to earn profits for the purpose of attracting and retaining investors.[9] They may directly contract with health systems, insurance companies, and pharmacies — independent of pharmacy benefit managers or group purchasing organizations. Non-profit entities can also accommodate fully transparent cost-plus pricing model and multi-year purchasing, which ensures demand and reduces revenue volatility and operating risks. Except in highly regulated environments such as defense and public utilities, such a model is generally unattractive to for-profit drug manufacturers due to its revenue-restricting nature.

The market for non-profits can be substantial if the federal, state, and local governments decide to purchase generic drugs that are "Made in America." Potential purchasers include government strategic stockpiles, the Department of Defense, the Veterans Administration, the Bureau of Indian Affairs, federally qualified health centers, government employees, Medicare and Medicaid, and prisons. On September 28, 2020, California Governor Gavin Newsom signed SB 852 into law, which requires the California Health and Human Services Agency to establish partnerships with drug manufacturers to produce or distribute more affordable generic prescription drugs, including at least one form of insulin.[10] Some other states are considering a similar approach or have expressed interest in purchasing drugs produced or distributed under this law from California.

These public programs would offer a continuous and stable demand for generic drugs. Multi-year contracting would ensure a large scale of production and allow the manufacturer to obtain a low fixed cost for each drug unit, making it possible to achieve the lowest possible price that is competitive with the prices of international suppliers and attractive to health systems, insurance companies, and pharmacies. The initial multi-million capital investment necessary could come from philanthropies, government grants, and/or loans. In addition to improving the supply chain resil-

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Table

Recently Introduced Legislation to Address Drug Supply Chain Vulnerability

Introduced Legislation	Co-Sponsors	Summary
House of Representatives		
Commission on America's Medical Security Act	David Roe [R-TN] Paul Ruiz [D-CA] Lauren Underwood [D-IL]	The Department of Health and Human Services (HHS) would report on the security of the medical product supply chain.
Medical Supplies for Pandemics Act	Susan Brooks [R-IN] Debbie Dingell [D-MI] Eliot Engel [D-NY] Sheila Jackson Lee [D-TX] David McKinley [R-WV] Eleanor Norton [D-DC] Pete Olson [R-TX] Elissa Slotkin [D-MI] Fred Upton [R-MI] Jefferson Van Drew [R-NJ] Jackie Walorski [R-IN]	HHS would incentivize manufactures to increase emergency stocks and diversity geographic production. HHS would also buy, lease, or enter into joint venture to produce medical supplies and work with distributors to refresh and replenish medical supplies.
Strengthening America's Strategic National Stockpile Act	Susan Brooks [R-IN] Michael Burgess [R-TX] G. K. Butterfield [D-NC] Earl Carter [R-GA] Gilbert Cisneros [D-CA] Diana DeGette [D-CO] Debbie Dingell [D-MI] Anna Eshoo [D-CA] Brian Fitzpatrick [R-PA] Greg Gianforte [R-MT] Richard Hudson [R-NC] Ben Lujan [D-NM] Tom Malinowski [D-NJ] David McKinley [R-WV] Joe Neguse [D-CO] Kim Schrier [D-WA] Elissa Slotkin [D-MI] Darren Soto [D-FL] Fred Upton [R-MI] Jefferson Van Drew [R-NJ] Jackie Walorski [R-IN]	The annual authorized funding for the Strategic National Stockpile would increase from $610 million to $705 million from fiscal years 2020 through 2023. The Strategic National Stockpile would partner with manufactures to build domestic production capacity and sell items to other federal agencies. HHS would ensure the effective functioning of the stockpile contents, improve financial security, report on requests and the response, and establish transparent process for distribution. A $500 million pilot program would be established to support state efforts to expand and maintain their own stockpile.
Senate		
Pharmaceutical Accountability, Responsibility, and Transparency Act	Gary Peters [D-MI]	Reporting requirement would be expanded for critical manufacturing data.
Help Onshore Manufacturing Efficiencies for Drugs and Devices Act	Gary Peters [D-MI]	HHS would establish a new agency to facilitate the investment to create domestic manufacturing capacity.
United States Pharmaceutical Supply Chain Review Act	Marco Rubio [R-FL] Elizabeth Warren [D-MA]	The Federal Trade Commission would report on foreign investment in the U.S pharmaceutical industry.
Pharmaceutical Supply Chain Defense and Enhancement Act	Marco Rubio [R-FL] Elizabeth Warren [D-MA]	$1 billion a year for 5 years would be provided to update domestic manufacturing capacity of critical drugs. DoD, VA, HHS, and Bureau of Prisons would purchase domestically made drugs.

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iency and national health security, the establishment of domestic drug production would also create jobs and skilled human capital.

This business approach — featuring a low cost of capital, a competitive and transparent cost-plus pricing model, and a multi-year purchase agreement — is based on the successful entry of a non-profit manufacturer in the generic drug market recently. Civica Rx was established in 2018 by large health systems and philanthropies to address the lack of affordability and access to generic drugs in the U.S. market.[11] Since July 2020, Civica Rx has been providing more than 40 generic drugs to its institutional partners (health systems, insurance companies, and pharmacies), constituting approximately one-third of the U.S. inpatient generic drug market. Civica Rx has also formed an outpatient generic drug subsidiary — in partnership with insurance companies — that will provide affordable medications to more than 100 million beneficiaries.

The purpose of establishing Civica Rx was to address the market failures for generic drugs by promoting competition with for-profit companies. Its initial performance suggests that non-profit generic manufacturers can offer competitive pricing and generate value for their institutional partners and the patients they serve. Non-profits are also well positioned to address the supply chain vulnerability of generic drugs. With strong and transparent governance structure to ensure the alignment between business operations and their charitable mission, non-profit drug manufacturers have the potential to compete with for-profit entities to improve domestic production, reduce foreign dependency, and enhance national health security.

Note

Mr. Liljenquist is Senior Vice President and Chief Strategy Officer of Intermountain Healthcare and the Chairman of Civica Rx, a non-profit drug manufacturer; Dr. Anderson reports grants from Arnold Ventures during the conduct of the study; Dr. Sarpatwari reports grants from Arnold Ventures and the Open Society Foundations during the writing of the work, and personal fees from West Health outside the submitted work. Dr. Bai received funding from Arnold Ventures and consulting fee from Council for Informed Drug Spending Analysis.

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