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RESEARCH NOTE

The Geography of Health: Onshoring Pharmaceutical Manufacturing to Address Supply Chain Challenges

Andrew D. Mitchell[†]

Faculty of Law, Monash University, Melbourne, Australia
Email: andrew.mitchell@monash.edu

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Abstract

This article examines shifts towards onshoring pharmaceutical manufacturing, a response to the vulnerabilities exposed by the COVID-19 pandemic in global supply chains. It delves into how globalization, public policy, and geopolitical tensions have shaped pharmaceutical markets, compelling nations to seek solutions that ensure reliable medicine access and reduce dependency on foreign supplies. The study highlights disparities in regulatory oversight and geographic concentration of production, which contribute to frequent shortages, particularly of generic medicines. The pandemic intensified these issues, prompting increased state interventions and heightening concerns over geopolitical risks. As a result, onshoring efforts, often encapsulated in local content measures, have expanded, and are now driven by both economic motives and imperatives of national security and public health.

Keywords: pharmaceutical onshoring; global supply chains; COVID-19; local content measures; generic medicines; national security; public health

1. Introduction

Government efforts to locate the production of pharmaceuticals within their territories have intensified since the COVID-19 pandemic. The US,[1] EU,[2] and Australia[3] have joined or are considering joining countries like China,[4] Indonesia,[5] Turkey,[6] India[7]

[†]PhD (Cantab), LLM (Harv), LLB (Hons), BCom (Hons) (Melb).

[1]See, e.g., Department of Health and Human Services et al., 'National Strategy for a Resilient Health Supply Chain' (July 2021), 31–32; Department of Health and Human Services, *One-Year Report in Response to Executive Order 14017* (February 2022), 7–8.

[2]See, e.g., European Commission, *Pharmaceutical Strategy for Europe* (25 November 2020, COM(2020) 761), 18; European Commission, *Vulnerabilities of the Global Supply Chains of Medicines* (Staff Working Document, 2022); European Commission, Addressing medicine shortages in the EU (24 October 2023, COM(2023) 672), 1, and 12–13.

[3]See, e.g., allocation of $ 1.5 billion in subsidies for promoting domestic manufacturing in the medical sector: Federal Register of Legislation – National Reconstruction Fund Corporation (Investment Mandate) Direction 2023. See also Anthony Albanese, 'Putting Australian Medical Manufacturers at the Front of the Queue' (Press Release, 30 January 2022).

[4]Congressional Research Service, *The Made in China 2025 Initiative: Economic Implications for the United States* (12 April 2019), 1–2; Geneva Network, *Localisation Barriers to Trade in the Biopharmaceutical Industry* (August 2023), 2–3; Mercator Institute for China Studies, *Investigating State Support for China's Medical Technology Companies* (November 2023), 17.

[5]CSIS, *Economic Impacts of Local Content Requirements in Indonesia* (CSIS Research Report, 2023), 33–34; M. Limenta and P. Harapan Lili Yan Ing, Indonesia's Local Content Requirements: Assessment with WTO Rules (ERIA Discussion Paper Series No. 414, 2022), 9–10.

[6]See Final Panel Report as issued to the parties in *Turkey – Certain Measures Concerning the Production, Importation and Marketing of Pharmaceutical Products* (*Turkey–Pharmaceutical Products (EU)*), attached to Türkiye's notice of recourse to arbitration (WT/DS583/12 and Add.1), para. 7.122.

[7]Ministry of Chemicals and Fertilizers, Order No. 31026/4/2018.

and Bangladesh[8] that use local content requirements and incentives to onshore pharmaceutical manufacturing.

Some pre-COVID policies to promote local content in pharmaceutical manufacturing had economic rationales, such as developing new industries or reducing trade deficits.[9] More recently, however, these policies have been justified in terms of public health, supply-chain resilience, geopolitical risk, and national security concerns.[10] Mitigating the risks associated with the *location* of pharmaceutical manufacturing is central to these justifications. For many governments, pharmaceutical and other medical supplies shortages during the COVID-19 pandemic underscored the risks of relying on foreign suppliers for critical products.[11] Local content requirements and incentives are thus intended to ameliorate these risks by bringing some pharmaceutical manufacturing back into a government's territory.

States' moves to onshore pharmaceutical manufacturing can be understood as a location-based solution to what is perceived to be a location-based problem. The fundamental public policy problem that onshoring pharmaceutical production seeks to address concerns reliable access to medicines and the perceived risk of shortages that could arise from dependence on imports.

In this article, I describe the nature of the pharmaceutical market and supply chains, sources of shortage-related risks, and the onshoring measures some States take to redress these. In short, concerns over the location of pharmaceutical manufacturing ultimately stem from the market's nature and how it has been shaped by globalization, public policy, and intensifying geopolitical tensions. The article then explores the legal ramifications and policy debates surrounding these measures, setting the stage for a comprehensive analysis of how globalization and public policy intertwine with the imperatives of national security and public health. This article focuses primarily on small-molecule drugs, which represent a significant part of the pharmaceutical market but differ substantially from biologics regarding production and supply chain challenges.

2. Contextual Background

The literature addressing medicine shortages is extensive and provides a multifaceted understanding of the underlying causes, regional variations, and global strategies for mitigation. This section grounds my analysis of onshoring pharmaceutical manufacturing within this established body of work, elucidating the complex interplay of factors that lead to shortages and the varying responses by different countries.

The literature on medicine shortages is extensive, with numerous studies identifying and analyzing the causes and consequences of these shortages across different regions. Acosta et al. comprehensively review the global perspectives on medicine shortages, outlining the various contributing factors and strategies different countries adopt to address these challenges. They emphasize the multifaceted nature of medicine shortages, which are influenced by regulatory, economic, and geopolitical factors.[12]

To address these shortages, various strategies have been implemented globally. These strategies include advance notice systems managed by regulatory authorities, special programs to track

[8]M. Rahman et al. (2021) 'Policy Space for Building Production Capabilities in the Pharmaceuticals Sector in Low- and Middle-Income Countries: Evidence from Bangladesh', *Journal of Globalization and Development* 12, 221, 238–240, and 246.

[9]See, e.g., Ministry of Chemicals and Fertilizers, supra n. 7; Panel Report, *Turkey–Pharmaceutical Products (EU)*, paras. 7.210.

[10]See generally section 6. 'Overview of Measures to Onshore Pharmaceutical Manufacturing' below.

[11]See, e.g., Department of Health and Human Services (2021), supra n. 1, 9; European Commission (2023), supra n. 2, 1.

[12]A. Acosta, E.P. Vanegas, J. Rovira, B. Godman, and T. Bochenek (2019) 'Medicine Shortages: Gaps between Countries and Global Perspectives', *Frontiers in Pharmacology* 10, 763. Other contributing factors include sudden disease outbreaks and manufacturing issues: K. Heiskanen, R. Ahonen, R. Kaneva, P. Karttunen, and J. Timonen (2017) 'The Reasons Behind Medicine Shortages from the Perspective of Pharmaceutical Companies and Pharmaceutical Wholesalers in Finland', *Plos One* 12(6).

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medicines, and interventions to enhance the efficiency of the medicine supply chain.[13] Proactive strategies, such as structural flexibility and early warning systems, have effectively mitigated shortages in the pharmaceutical supply chain.[14] Additionally, implementing dynamic surveillance, coordinated reactions, and integrated platforms for managing shortage data has shown progress in addressing medicine shortages.[15] De Weerdt et al. review the effectiveness of these strategies, ranging from regulatory adjustments to market incentives aimed at improving the availability of essential medicines. They highlight the need for proactive measures, such as mandatory reporting of production levels and maintaining national stockpiles, to prevent shortages.[16]

Various factors, including the need for supply chain resilience, public health security, and geopolitical considerations, have driven the shift towards onshoring pharmaceutical manufacturing. Studies like those by Pisano and Shih explore the implications of relocating manufacturing processes back to domestic territories, emphasizing this strategy's potential benefits and challenges.[17]

In summary, the existing literature provides a rich foundation for understanding the causes and impacts of medicine shortages and the strategies to mitigate them. Addressing these shortages requires regulatory flexibility, economic incentives, and enhanced supply chain management. This article builds upon these foundational works, aiming to integrate these global insights with an analysis of recent onshoring trends in pharmaceutical manufacturing. By situating the current study within this broader context, it seeks to contribute to ongoing debates in international economic relations and public health policy.

3. Features of the Pharmaceutical Market that Engender Shortages

In basic terms, the supply-chain for pharmaceuticals involves three stages.[18] First is the production of the main raw materials, active pharmaceutical ingredients ('APIs'), derived from key starting materials and intermediates. Second is manufacturing the finished dosage form ('FDF') pharmaceutical products, which typically comprise both APIs and inactive ingredients. Third is distribution. Through globalization, these stages have diffused around the world, particularly for generic pharmaceuticals, which account for perhaps 90% of prescribed medicines.[19]

As with many other manufacturing sectors, globalization in the pharmaceutical sector has been driven by cost and price. Purchasing decisions within health systems, often made by health system decision-makers rather than individual consumers, are influenced by a variety of factors including cost, availability, and regulatory approval, leading generally to a preference for cost-effective solutions.[20] The incentive for manufacturers of both APIs/inputs and finished pharmaceutical products is thus to compete on price and minimize production costs.[21] Manufacturing, in

[13]S. Iyengar, L. Hedman, G. Forte, and S. Hill (2016) 'Medicine Shortages: A Commentary on Causes and Mitigation Strategies', *BMC Medicine* 14, 124.

[14]E. Vann Yaroson, L. Breen, J. Hou, and J. Sowter (2023) 'Examining the Impact of Resilience Strategies in Mitigating Medicine Shortages in the United Kingdom's (UK) Pharmaceutical Supply Chain (PSC)', *Benchmarking: An International Journal* 31(3), 683.

[15]Z.X. Fan, T.T. Gao, Q. Sun, and Z.-U.-D. Babar, 'Whether Medicine Supply is Really Meeting Primary Health Care Needs – A Mixed-Methods Study in Shandong Province, China', *Global Health Research and Policy* (https://doi.org/10.21203/rs.3.rs-4121340/v1).

[16]E. De Weerdt, S. Simoens, M. Casteels, and I. Huys (2015) 'Toward a European Definition for a Drug Shortage: A Qualitative study', *Frontiers in Pharmacology* 6, 253.

[17]G. Pisano and W. Shih (2009) 'Restoring American Competitiveness', *Harvard Business Review* 87, 114–125.

[18]W.J. Hopp, L. Brown, and C. Shore (eds.) (2022) *Building Resilience into the Nation's Medical Product Supply Chains*. National Academic Press, 4.

[19]Ibid, 4–5; White House, '100-Day Reviews under Executive Order 14017' (June 2021), 208.

[20]Hopp, Brown, and Shore (eds.), supra n. 18, 14–15.

[21]American Medical Association (2023) *A Primer on the Medical Supply Chain*: CLRPD Report 02; White House (2021), supra n. 19, 208–209 and 226.

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turn, gravitates towards locations with the most competitive cost advantages.[22] In the pharmaceutical sector, significant cost elements include compliance costs for environmental and workplace safety liabilities linked to API/pharmaceutical production processes and the real estate costs associated with production processes requiring large factory sites, as well as labour and energy costs, tax rates, and other regulatory compliance costs.[23] On one estimate, the production of APIs would cost around 50% more in the US or EU than in India.[24] Labour costs alone for API manufacturing in India and China are estimated to be around one-tenth of the cost for a typical Western company.[25] The US has also claimed that countries like China and India have used unfair trade practices in the pharmaceutical sector that undercut competitors and unfairly captured market share.[26]

The result of these cost-driven shifts in pharmaceutical manufacturing is a high level of interdependence amongst major economies for supplies of finished pharmaceuticals, APIs, and related inputs and ingredients. In the EU, 80% of APIs for generic pharmaceuticals and 40% of finished pharmaceuticals are manufactured in China or India.[27] For the US, 87% of facilities manufacturing generic APIs and 63% of facilities manufacturing generic finished pharmaceuticals supplied in its market were located overseas in 2021.[28] For India, up to 80% of the APIs used in manufacturing finished pharmaceuticals are supplied from China.[29] Thus, although the US imports only 16% of APIs from China, the fact that it imports 40% of its generic finished pharmaceuticals from India makes it indirectly reliant on Chinese APIs.[30] These dependencies are less pronounced for pharmaceuticals under patent but tend to be even sharper for individual product lines of generics.[31] For instance, the APIs for at least three generic WHO-listed essential medicines are manufactured solely in China.[32]

The pharmaceutical supply chain has also evolved into a just-in-time model that reduces inventory costs for distribution points like hospitals and pharmacies by alleviating the need to stockpile.[33]

As mentioned, the downward price pressure is particularly pronounced for off-patent generic pharmaceuticals, for which increased competition drives prices towards production costs and leaves thin profit margins.[34] Generic price reductions can be greater than 95% compared to branded prices.[35] By contrast, patented pharmaceuticals typically yield significantly higher profit margins in the face of less competitive pressure.[36] This dynamic creates different incentives for

[22]J. Bumpas and E. Betsch (2011) 'Exploratory Study on Active Pharmaceutical Ingredient Manufacturing for Essential Medicines' (Working Paper No. 53075, World Bank), 12–13; Hopp, Brown, and Shore (eds.), supra n. 18, 5.

[23]American Medical Association, supra n. 21; Testimony of Dr Janet Woodcock (USFDA) before US Congress, 'Safeguarding Pharmaceutical Supply Chains in a Global Economy' (30 October 2019); White House (2021), supra n. 19, 208; M. Hall et al. (2021) 'Corporate Compliance, Professional Perspective – Potential Costs of Reshoring Pharmaceutical Manufacturing', *Bloomberg Law* (March).

[24]Bumpas and Betsch, supra n. 22, 12; US Food and Drug Administration, Pathway to Global Product Safety and Quality: Special Report (2019), 20. For the EU's estimate that the cost of APIs sourced in Asia would be 20% to 40% lower than those produced in the EU, see European Commission (2022), supra n. 2, 7.

[25]Bumpas and Betsch, supra n. 22, 12; US Food and Drug Administration, supra n. 24, 20.

[26]Department of Health and Human Services (2021), supra n. 1, 46; Department of Health and Human Services (2022), supra n. 1, 8; White House (2021), supra n. 19, 231.

[27]The Economist, Confront the Fragility of Medicine Supply Chains (Economist Group, 2021), 24.

[28]US Senate Committee on Homeland Security & Government Affairs, *Short Supply: The Health and National Security Risks of Drug Shortages* (Majority Staff Report, March 2023), 16.

[29]US–China Economic and Security Review Commission, Annual Report to Congress 2022 (November 2022), 307.

[30]White House (2021), supra n. 19, 230; US–China Economic and Security Review Commission, supra n. 29, 307.

[31]US–China Economic and Security Review Commission, supra n. 29, 306–307.

[32]Testimony of Dr Janet Woodcock, supra n. 23.

[33]American Medical Association, supra n. 21; Department of Health and Human Services (2021), supra n. 1, 9; Department of Health and Human Services (2022), supra n. 1, 7.

[34]White House (2021), supra n. 19, 226.

[35]Ibid., 225.

[36]P. Ellis, 'Where There's a Will: Economic Considerations in Reforming America's Medical Product Supply Chains' (Paper Commissioned by Committee on Security of America's Medical Product Supply Chain, 2021).

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the supply chains for off-patent generic pharmaceuticals on the one hand and patented pharmaceuticals on the other.[37]

The high-profit margins achieved by patented pharmaceuticals mean that manufacturers have more to lose if there is a disruption in their supply chain. This incentivizes them to avoid shortfalls and invest in the resilience of their supply chains.[38] By contrast, the thin profit margins on generic pharmaceuticals leave manufacturers with less to lose during a shortage, reducing the incentive to incur the additional cost of protecting supply chains.[39] For similar reasons, generic pharmaceutical manufacturers are more likely to discontinue less profitable product lines, leading to increasingly fewer sources of a given API or pharmaceutical over time.[40] Consequently, generic pharmaceuticals are far more prone to shortages.[41] Reliability of supply and avoiding shortages may be in the public interest, but manufacturers and suppliers that incur costs to strengthen supply chains are typically not rewarded with higher prices.[42]

A related aspect of the pharmaceutical market that can accentuate shortages pertains to barriers to entry for new suppliers. In principle, supply shortages should increase prices and incentivize new suppliers to add production. However, in the pharmaceutical sector, high investment costs and a need to obtain regulatory approval – together with potentially low returns on investment due to strong downward price pressures over the longer term – dampen what would otherwise be the normal market response.[43]

The upshot is that reliability in supply chains is not incentivized in generic pharmaceutical pricing, nor does the pharmaceutical sector typically respond to supply disruptions in the self-correcting way that one would usually expect. These features make shortages in the pharmaceutical sector more likely and more protracted.

4. Main Causes of Pharmaceutical Shortages

Pharmaceutical shortages have two principal drivers: surges in demand or constraints in supply.[44] Surges in demand typically arise from a natural or anthropogenic disaster or some other public health emergency such as a pandemic. Constraints in supply are primarily related to quality-control issues. These can range from minor label errors to contaminations in the production process.[45] Studies such as those by the US Food and Drug Administration and parallel findings from the European Medicines Agency show that quality-related issues are a significant contributor to pharmaceutical shortages globally, accounting for approximately 60% of cases in the US and similar trends observed in Europe.[46] However, supply shortages can also occur from natural or anthropogenic disasters that disrupt supply. For instance, China's zero-COVID policy impacted pharmaceutical supplies in various ways: certain manufacturing facilities were shut down, the port terminals through which supplies were shipped were temporarily closed, and foreign regulators were limited in their ability to inspect manufacturing facilities.[47] Another example is that in

[37]Hopp, Brown, and Shore (eds.), supra n. 18, 4; S. Colvill et al. (2021) 'Supporting Resilient Drug Supply Chains in the United States: Challenges and Potential Solutions' (Duke University, Margolis Center for Health Policy, July), 2 and 6.

[38]US Food and Drug Administration (2019) 'Drug Shortages: Root Causes and Potential Solutions' (Drug Shortages Task Force Report, 6, 21–25.

[39]Ellis, supra n. 36; US Food and Drug Administration, supra n. 38, 6 and 21.

[40]US Food and Drug Administration (2024) 'Frequently Asked Questions about Drug Shortages' (accessed 2024); US Food and Drug Administration, supra n. 38, 21–25.

[41]US Food and Drug Administration, US Food and Drug Administration, supra n. 38, 5–6.

[42]White House (2021), supra n. 19, 225; US Food and Drug Administration, supra n. 38, 22–25.

[43]White House (2021), supra n. 19, 225 (June 2021); US Food and Drug Administration, supra n. 38, 26–32.

[44]Hopp, Brown, and Shore (eds.), supra n. 18, 6–7; American Medical Association, supra n. 21.

[45]US Food and Drug Administration, supra n. 40.

[46]US Senate Committee on Homeland Security & Government Affairs, supra n. 28, 16.

[47]American Medical Association, supra n. 21; M. Egan, 'Bill Would Give Biden New Powers to Prepare for the Next Pandemic', CNN (22 June 2023); US–China Economic and Security Review Commission, supra n. 29, 145.

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2016, an explosion in China at the sole global manufacturing facility of the APIs for a critical antibiotic led to worldwide shortages.[48] Likewise, in 2007, an infectious disease amongst China's pig herds led to a shortage of anticoagulant heparin made from pig intestines, of which 80% was manufactured in China.[49] Additionally, supply chain disruptions can arise from governmental interventions restricting trade, such as India's export ban on APIs and certain pharmaceuticals at the onset of the COVID-19 pandemic.[50]

Supply chain disruptions, demand surges, and the resulting shortages in medical supplies were obvious during the COVID-19 pandemic. Still, it is important to recognize that these phenomena are neither new nor unusual.[51] Quality issues that represent most pharmaceutical shortages have been a recurrent feature of the globalized supply chain. In the US, for instance, new shortages of a given pharmaceutical product quadrupled from 66 in 2006 to 250 in 2011 and have since stabilized at around 50 new shortages each year through active management and pre-emptive mitigation measures.[52] Various tools have been used to pre-empt the risks of shortages, such as better supply forecasting through mandatory reporting of expected production levels, extending product expiration dates and expediting approvals for new production lines, and maintaining a national stockpile of key ingredients and essential medicines.[53] In other words, shortages have been managed as a *structural* problem in globalized pharmaceutical supply-chains, and taking steps to facilitate the resilience of these supply chains has long been recognized as a public health imperative.

A main impact of the COVID pandemic, therefore, was to expose the existing fragilities in the supply chain, such as low diversification in sources of supply and a lack of inventory through just-in-time delivery, which were, in turn, responsible for exacerbating the effects of the pandemic-related pressures on the supply chain.[54] That said, the COVID pandemic did give rise to a truly stunning and novel development: export bans and other trade measures imposed by governments to secure their supplies of critical medical products at the expense of others.[55] Within the first few months of the COVID pandemic, the WTO identified at least 80 countries that had imposed export prohibitions or restrictions to retain medical supplies for domestic use.[56] Early in the pandemic, India and China banned exports of certain APIs, leading to supply shortages and price surges.[57] Later in the pandemic, the US, EU, and India maintained various export vaccine restrictions.[58] Perhaps these trade-related facets of the pandemic, more than any others, have since prompted moves to onshore pharmaceutical manufacturing.

5. Onshoring Pharmaceutical Production: Finding the Problem to be Solved

As many have pointed out, the onshoring of pharmaceutical supply chains is not an obvious solution to the structural reasons for pharmaceutical shortages.[59] Achieving more reliable supply chains involves more diversified sources of supply, better quality assurance for manufacturing facilities, the development of scalability or contingent capacity to respond to demand surges,

[48]US–China Economic and Security Review Commission, supra n. 29, 228.

[49]American Medical Association, supra n. 21, 3.

[50]H. Ellis-Petersen, India Limits Medicine Exports after Supplies Hit by Coronavirus (5 March 2020) *The Guardian*.

[51]US Senate Committee on Homeland Security & Government Affairs, supra n. 28, 3.

[52]US Food and Drug Administration, *Drug Shortages CY 2022* (Report to Congress, 2023), 2–4.

[53]See generally US Food and Drug Administration, supra n. 52, 2–4; US Food and Drug Administration, supra n. 40.

[54]The Economist, supra n. 27, 16; Department of Health and Human Services (2021), supra n. 1, 9 and 26.

[55]Hopp, Brown, and Shore (eds.), supra n. 18, 19; C. Bown (2022) 'How COVID-19 Medical Supply Shortages Led to Extraordinary Trade and Industrial Policy', *Asian Economic Policy Review* 17, 114, 115.

[56]WTO Secretariat, Export Prohibitions and Restrictions (Information Note, 23 April 2020).

[57]Congressional Research Service, COVID-19: China Medical Supply Chains and Broader Trade Issues (CRS Report, 23 December 2020), 15–21; C. Thomas and N. Dasgupta, 'Global Supplier India Curbs Drug Exports as Coronavirus Fears Grow', *Reuters* (3 March 2020).

[58]Bown, supra n. 55, 352 and 354–356.

[59]See, e.g., Hopp, Brown, and Shore (eds.), supra n. 18, 6 and 18; Ellis, supra n. 36.

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and somehow rewarding supply chain resilience through price signals.[60] At first glance, these outcomes are not contingent on manufacturing being undertaken domestically as opposed to overseas. Additional capacity for supply, multiple manufacturers and suppliers for individual APIs and finished pharmaceuticals, and lower geographic concentration of manufacturing are not the inevitable corollaries of prioritizing domestic production over imports. As the US Department of Health and Human Services recognized, 'geographic location alone may not be a risk factor for shortage'.[61] On the contrary, onshoring is potentially counterproductive if it results in *higher* geographic concentration (i.e. domestic) and *fewer* supplier relationships.[62] Moreover, vulnerabilities will likely persist unless a pharmaceutical's whole supply chain is onshored. Still, the prohibitive cost of onshoring all aspects of production could crowd out the resources available for other aspects of public health.[63]

That said, it would be wrong to dismiss location-based considerations as irrelevant to reducing risks and promoting resilient supply chains. Greater geographical diversity in supply chains implies multiple dispersed manufacturing locations. Additionally, manufacturing within a regulator's jurisdiction will typically make it easier to inspect facilities and ensure quality control while affording regulators greater visibility over emerging supply disruptions through reporting and notification obligations.[64] In those ways, domestic production of APIs and pharmaceuticals can potentially be conducive to supply chain resilience as *part* of a greater effort towards supplier diversity and reduced dependence on a single region, source, or product.[65]

However, as a *standalone* policy response to pharmaceutical shortages, onshoring only makes sense when understood as a safeguard against the geopolitical risk that a foreign government could disrupt supply access. According to the US government's rationale, '[f]oreign sourcing makes the United States vulnerable to other countries' export restrictions and other trade-restrictive measures', which 'can disrupt the supply of critical public health supplies'.[66] This, in turn, leaves the US 'vulnerable to the geopolitical strategies of foreign governments'[67], with a particular concern over China's ability to 'weaponize' pharmaceutical supply chains.[68] The European Commission has likewise indicated concern about 'Europe's supply chains dependencies and the risk that economic dependency could be weaponized' and has explored onshoring pharmaceutical and API manufacturing in light of such risks.[69]

A geopolitical motivation for onshoring pharmaceutical and API manufacturing is not necessarily at odds with protecting public health. Instead, resilient pharmaceutical supply chains are themselves a facet of protecting public health.[70] Steps to mitigate the risks of supply chain disruptions can be understood as public health measures,[71] and as mentioned above, these steps can encompass location-based considerations such as discouraging high geographic concentration of production or promoting production in locations conducive to smooth regulatory oversight and quality assurance. Onshoring pharmaceutical and API manufacturing to obviate geopolitical risks can potentially be understood as part of safeguarding supply chains to protect

[60]White House (2021), supra n. 19, 208, 210–211, and 237.
[61]Ibid., 223.
[62]Hopp, Brown, and Shore (eds.), supra n. 18, 6 and 18; Hall et al., supra n. 23; Ellis, supra n. 36.
[63]Hopp, Brown, and Shore (eds.), supra n. 18, 6 and 18.
[64]Ibid., 5; B. Weinman et al. (2001) 'The American Medical Product Supply Chain: Will COVID-19 Drive Manufacturing Back Home?', *Food and Drug Law Journal* 76, 235, 241–244; Hall et al., supra n. 23; US Senate Committee on Homeland Security & Government Affairs, supra n. 28, 21–26.
[65]See, e.g., European Commission (2023), supra n. 2, 16–17; Department of Health and Human Services (2021), supra n. 1, 10.
[66]Department of Health and Human Services (2022), supra n. 1, 7.
[67]White House (2021), supra n. 19, 230.
[68]US–China Economic and Security Review Commission, supra n. 29, 309.
[69]European Commission (2022), supra n. 2, 12.
[70]Hopp, Brown, and Shore (eds.), supra n. 18, 2.
[71]Ibid., 14.

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public health.[72] It is noteworthy, however, that efforts to onshore pharmaceutical and API manufacturing are increasingly being framed in terms of national security interests. There are niche aspects of pharmaceutical supply chains with a clear nexus to national security, such as militaries' access to medical supplies or access to medical countermeasures in response to bioterror or biosecurity events.[73] However, a more general pursuit of self-sufficiency in pharmaceutical and API manufacturing to eliminate the geopolitical risks of reliance on foreign sources is emerging as a national security interest, particularly in the US political context.[74] For instance, US legislators proposing measures to onshore pharmaceutical manufacturing have made remarks such as '[t]he United States' overreliance on Communist China for vital medications poses a threat to national security'[75]; '[w]ith China spying on Americans, threatening an invasion of Taiwan, and ignoring human rights, it is clear America cannot continue to rely on them for lifesaving medications'[76]; '[i]f the COVID-19 pandemic taught us anything, it is that we cannot trust the CCP as a reliable source for any part of our supply chains, especially vital medical supplies including drugs, PPE, or medical equipment … [o]ur national security depends on it'.[77] Recent studies prepared for the US Congress seek to draw clear links between resilient pharmaceutical supply chains, public health, national security, and onshoring.[78] The EU has likewise discussed the prospect of onshoring aspects of pharmaceutical manufacturing to guard against the risk of other countries 'weaponizing' these supply chains and support its 'strategic autonomy' goal.[79]

6. Overview of Measures to Onshore Pharmaceutical Manufacturing

In response to their location-based concerns over pharmaceutical supply chains, several States have pursued location-based solutions for onshore pharmaceutical manufacturing, including local content requirements and incentives.

The US, in particular, is exploring or implementing a series of measures to onshore pharmaceutical manufacturing. The most recent and prominent of these efforts was President Biden's invocation of Title III of the Defence Production Act to enable investment in domestic manufacturing of pharmaceuticals and APIs deemed essential to national defence.[80] In general terms, Title III authorizes measures to incentivize and expand the domestic production and supply of critical materials and goods. The measures permitted under Title III include grants, subsidies, loans, loan guarantees, direct purchases and purchase commitments, and the authority to procure and install equipment in private industrial facilities.[81] These incentives can be linked to local

[72]See Testimony of Dr Janet Woodcock, supra n. 23: 'The security of the nation's drug supply rests on three main factors: freedom from dependence on foreign sources of API, the resilience of our domestic manufacturing base, and the reliability of the facilities that make products for the US market'.

[73]US Senate Committee on Homeland Security & Government Affairs, supra n. 28, 5 and 10.

[74]Testimony of Dr Janet Woodcock, supra n. 23.

[75]J. Tsirkin, 'Bipartisan Senate Bill Aims to Bolster Drug Supply Chain by Prioritizing US Manufacturing' (NBC News, 27 July 2023).

[76]Office of Congressman Matt Cartwright, 'ReCartwright Reintroduces Bipartisan Made in America Act' (Press Release, 26 April 2023).

[77]Office of Congressman Brad Schneider, 'Schneider, Steel Introduce Bipartisan, Bicameral Legislation to Secure Medical Supply Chains' (Media Release, 27 June 2023).

[78]US Senate Committee on Homeland Security & Government Affairs, supra n. 28, 5, 10, and 14; US–China Economic and Security Review Commission, supra n. 29, 21–22, 145, 306–307, 309, and 731; US–China Economic and Security Review Commission, Annual Report to Congress 2019 (November 2019), 248–251.

[79]European Commission (2023), supra n. 2, 1; European Commission (2020), supra n. 2, 18; European Commission, Frequently Asked Questions: Revision of the Pharmaceutical legislation (26 April 2023), question 11.

[80]White House, Presidential Determination No. 2024-03 (27 December 2023); White House, 'Fact Sheet: President Biden Announces New Actions to Strengthen America's Supply Chains, Lower Costs for Families, and Secure Key Sectors' (27 November 2023).

[81]Congressional Research Service, 'The Defense Production Act of 1950: History, Authorities, and Considerations for Congress' (CRS Report, 6 October 2023), 1.

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content considerations.[82] The invocation of Title III was the culmination of a years-long policy process that President Biden launched by remarking, '[w]e shouldn't have to rely on a foreign country – especially one that doesn't share our interests or our values – in order to protect and provide our people during a national emergency',[83] and which had endorsed the use of local content incentives to reshore pharmaceutical manufacturing.[84] The first action taken in this regard under Title III is a USD 35 million subsidy for the domestic production of key starting materials for sterile injectable medicines.[85] It is estimated that 90–95% of sterile injectable medicines currently used in the US rely on starting materials sourced from China and India.[86] It is unclear whether this funding will be explicitly conditioned upon manufacturers using US-made goods at some stage in the supply chain. Still, such conditions would accord with the overall objective of promoting US-made inputs in sterile injectable medicines.

In an unambiguous use of local content incentives for medical supplies, the US government adopted rules for Medicare reimbursements in 2023 that provide higher reimbursements for US-made surgical N95 respirators over foreign-sourced equivalents.[87] This was explained as part of '[s]ustaining a level of domestic production [of] surgical N95 respirators' despite the 'additional costs when purchasing domestic … surgical N95 respirators' incurred by hospitals.

A bipartisan legislative proposal currently under consideration in the US would likewise provide financial incentives under Medicare and Medicaid for using US-manufactured pharmaceuticals.[88] Specifically, the law would initiate a pilot programme aimed at onshoring pharmaceuticals with vulnerable supply chains by giving preference to US-manufactured equivalents through preferences such as bonus payments or higher reimbursements. Its sponsors explained that '[t]he Chinese Communist Party threatened to cut off America's access to vital drugs during the pandemic.'[89]

Another bipartisan legislative proposal currently under consideration would seek to onshore production of pharmaceuticals by providing a tax credit for pharmaceutical manufacturing operations in the US.[90] Its sponsors framed the initiative as a 'national security' measure to address vulnerabilities in pharmaceutical supply chains. They explained that '[w]e simply can no longer be dependent on our enemies for anything, especially essential medications and medical supplies. America must secure pharmaceutical independence.'[91] A similar but separate legislative proposal currently under consideration would likewise provide a tax credit to onshore pharmaceutical manufacturing.[92] It would link the tax credit amount to the extent of domestic content used in a US-based pharmaceutical manufacturing process.[93]

In India, local content requirements for government procurement of pharmaceuticals were adopted in 2019 as part of a broader 'Make in India' industrial policy. These require

[82]See, e.g., White House, Executive Order 13944 of 6 August 2020.

[83]White House, 'Remarks by President Biden at Signing of an Executive Order on Supply Chains' (24 February 2021).

[84]Department of Health and Human Services (2021), supra n. 1, 31–32 and 45–47; White House (2021), supra n. 19, 241–243.

[85]Department of Health and Human Services, 'Biden–Harris Administration Announces Actions to Bolster Medical Supply Chain' (Press Release, 27 November 2023).

[86]US Senate Committee on Homeland Security & Government Affairs, supra n. 28, 4.

[87]Centers for Medicare & Medicaid Services, CY 2023 Medicare Hospital Outpatient Prospective Payment System and Ambulatory Surgical Center Payment System Final Rule with Comment Period (1 November 2022).

[88]Office of Senator Smith, 'US Senators Tina Smith, Tom Cotton Reintroduce Bipartisan Legislation to Boost US Pharmaceutical Manufacturing' (Press Release, 15 November 2023).

[89]Ibid.

[90]Text – S.2082 – 117th Congress (2021–2022): MADE in America Act.

[91]Office of Congressman Carter, 'Carter, Soto, Cartwright, Miller Reintroduce Proposal to Encourage America's Pharmaceutical Independence from China' (Press Release, 26 April 2023).

[92]Office of Claudia Tenney, 'Congresswoman Tenney Introduces Bill to Promote Production of Generic Medicine in the United States' (Press Release, 28 October 2023).

[93]See 'Domestic Content Bonus Credit', BILLS-118hr6109ih.pdf (govinfo.gov).

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Indian-made pharmaceuticals to be made with 90% of Indian-sourced inputs by 2023 and foreign-made pharmaceuticals to be made with 30% of Indian-sourced inputs by 2023.[94] Subsequently, following the onset of the COVID pandemic, India sought to reduce its pharmaceutical sector's reliance on APIs imported from China by offering subsidies to firms that established production lines using minimum levels of domestically produced APIs.[95] The Indian government stated that 'in view of [the] changing geo-political scenario and recalibrated trade alignments, it is imperative that India become self-reliant in production of APIs'.[96] China's export ban on APIs early in the pandemic exposed India's dependence on China and its vulnerability to supply chain disruptions.[97]

Bangladesh has also sought to substitute imports of APIs with domestically made APIs through tax incentives for pharmaceutical manufacturers and a 20% cash incentive for API manufacturers that use at least 20% local content. This was reinforced in part by China's API export restrictions early in the pandemic, which created shortages in Bangladesh.[98]

In the European Union, efforts to onshore aspects of pharmaceutical manufacturing are less developed.[99] The European Commission has tacitly endorsed the concept of onshoring vulnerable elements of the supply chain,[100] and there is recognition that this would require governmental intervention.[101] Still, there are not yet concrete legislative or policy proposals. However, some EU member states have provided subsidies to onshore the production of at-risk APIs and other pharmaceuticals.[102]

Indonesia identified the health sector as a priority for local content in 2016, and has subsequently adopted requirements of 15% local content in manufacturing pharmaceuticals and 80% local content in manufacturing medical equipment.[103] The EU has also recently complained to the WTO about new Indonesian requirements on hospitals to purchase medical devices manufactured with at least 40% local content and a requirement that foreign pharmaceutical suppliers engage in some level of local manufacturing within five years of offering pharmaceuticals on the Indonesian market.[104] These requirements have been described as *de facto* obligatory to access the Indonesian market and to be eligible for government procurement.[105] According to the US, Indonesia's local content requirements aim to reduce the market share of imports (e.g. from 94% to 45% by 2035 for medical devices).[106] Indonesia, however, has contested this assertion and has instead argued that these requirements relate solely to government procurement and

[94]Ministry of Chemicals and Fertilizers, supra n. 7.

[95]Ministry of Chemicals and Fertilizers, Guidelines for the Production Linked Incentive Scheme; Ministry of Chemicals and Fertilizers, Approvals for PLI Scheme (Press Release).

[96]Ministry of Science and Technology, TIFAC releases report on Active Pharmaceutical Ingredients: 'Status, Issues, Technology Readiness and Challenges (Press Release).

[97]A. Altstedter, 'India to Spend $1.3 Billion to Boost Pharmaceutical Production', *Bloomberg* (22 March 2020).

[98]Rahman et al., supra n. 8, 238–240 and 246.

[99]See European Commission, supra n. 79, question 11; European Commission, 'Structured Dialogue on Security of Medicines Supply', https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/structured-dialogue-security-medicines-supply_en.

[100]European Commission (2022), supra n. 2, 12; European Commission (2023), supra n. 2, 6, 9, and 12–14; European Commission (2020), supra n. 2, 18.

[101]European Commission (2023), supra n. 2, 12 and 14; S. Fischer, V. Knoll, F. Alleweldt and S. Vogler, Potential Measures to Facilitate the Productions of Active Pharmaceutical Ingredients (APIs), European Parliament, March 2023 (www.europarl.europa.eu/RegData/etudes/STUD/2023/740070/IPOL_STU(2023)740070_EN.pdf) 6–7.

[102]Fischer et al., supra n. 101, 26.

[103]CSIS, supra n. 5, 33–34.

[104]WTO Committee on Trade-Related Investment Measures, 'Minutes of the Meeting Held on 23 February 2023' (3 April 2023) WTO Doc G/TRIMS/M/53.

[105]CSIS, supra n. 5, 33–34.

[106]WTO Committee on Trade-Related Investment Measures, 'Minutes of the Meeting Held on 17 October 2018' (8 March 2019) WTO Doc. G/TRIMS/M/45.

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are mainly directed at 'maintaining the sustainability of public health system' and 'reach[ing] sustainable development goals'.[107]

According to the US Congressional Research Service, China's 'Made in China 2025' industrial policy includes a 70% local content target for manufacturing biopharmaceuticals and high-performance medical devices.[108]

Finally, the Turkish local content programme, which the EU challenged in the *Turkey – Pharmaceutical Products (EU)* litigation, required foreign pharmaceutical suppliers to establish manufacturing operations in Turkey for their medicines to be reimbursable under Turkey's social security scheme.[109] This scheme covered almost 90% of pharmaceuticals sold in Turkey, and thus, being eligible for reimbursement was a *de facto* pre-condition for a foreign supplier's access to the Turkish market. Before the WTO dispute, Turkey had framed its local content programme as a form of government procurement and part of its approach to financing its social security system.[110]

7. Implications for International Economic Law & Policy

Recent shifts towards reshoring pharmaceutical production, ostensibly for enhancing national security and public health resilience, pose critical questions for international economic law and policy. The re-emergence of performance requirements, such as local content rules, marks a significant departure from the longstanding scepticism these measures have faced within the trade community. This section explores the implications of these changes for trade and investment law, offering a foundational perspective for ongoing scholarly and policy debates.

Local content initiatives often breach Article 2.1 of the TRIMs Agreement and Article III of the GATT, and if they involve subsidies, they also potentially contravene Article 3.1(b) of the SCM Agreement. The efforts by various nations to domesticate pharmaceutical production, as detailed above, are no exception. Measures that clearly incorporate local content requirements are particularly at risk unless they utilize flexibilities and exceptions within the WTO Agreements. The legal position for measures aimed at replacing imports that do not explicitly mandate the use of local content is less clear.[111]

The justifications for specific onshoring measures in pharmaceutical manufacturing hinge on the WTO obligations they engage.[112] Most onshoring actions are subject to the national treatment requirement of Article III of the GATT and Article 2.1 of the TRIMs Agreement due to their comprehensive scope. However, measures such as subsidies not related to tax exemptions or those involving government procurement are generally exempt from these obligations if any discriminatory impacts are limited solely to the procured products or subsidized producers. Discrimination affecting upstream materials and inputs or downstream sales, however, would not be covered by these exemptions concerning procurement and subsidies.

Furthermore, the public health exemption in Article XX(b) can excuse measures under scrutiny per Article III of the GATT and Article 2.1 of the TRIMs Agreement, provided they are a

[107]WTO Committee on Trade-Related Investment Measures, 'Minutes of the Meeting Held on 17 October 2018' (8 March 2019) WTO Doc. G/TRIMS/M/45; WTO Committee on Trade-Related Investment Measures, 'Minutes of the Meeting Held on 6 June 2019' (20 September 2019) WTO Doc G/TRIMS/M/46.

[108]Congressional Research Service, supra n. 4, 1–2; Geneva Network, supra n. 4, 2–3; Mercator Institute for China Studies, supra n. 4, 17.

[109]Panel Report, *Turkey–Pharmaceutical Products (EU)*, para. 7.210.

[110]WTO Committee on Trade-Related Investment Measures, 'Minutes of the Meeting Held on 17 October 2018' (8 March 2019) WTO Doc. G/TRIMS/M/45.

[111]Using pharmaceuticals as a case study, A. Mitchell (2024) 'Hometown Heroes: Onshoring, Promoting Local Content & WTO Law', *Journal of World Investment & Trade* 25(4), 481–496 (https://doi.org/10.1163/22119000-12340333), explores the rationale, scope, and implications of WTO rules on local content policies.

[112]On how flexibilities can support onshoring initiatives while adhering to international trade obligations, see generally A. Mitchell (2024) 'Home Remedies: Flexibilities to Onshore Pharmaceutical Manufacturing Under WTO Rules', *Journal of International Economic Law* (forthcoming).

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response to 'actual' or 'probable' import-related shortage risks and are precisely tailored to the identified risks. Yet, the panel's stance in the *Turkey–Pharmaceutical Products* case suggests that measures based on 'hypothetical' risks or broadly aiming to domesticate pharmaceutical production without targeting shortage-prone products may not meet the criteria of Article XX(b).

The national security exemption under Article XXI(b) may justify onshoring initiatives that contravene Article III of the GATT and Article 2.1 of the TRIMs Agreement if enacted during an 'emergency in international relations'. However, in the absence of a pandemic-scale event or a significant geopolitical crisis, justifying such measures under this exemption could be challenging, especially since pharmaceutical onshoring typically aims to prevent future crises rather than address current shortages.

Subsidy measures governed by the SCM Agreement that necessitate choosing domestic over imported goods – including those related to government procurement, reimbursement schemes, and tax exemptions – generally will not benefit from these flexibilities. Nonetheless, initiatives that delineate domestic content requirements as a 'rule of origin' – defining which products are 'domestic' versus 'foreign' – might bypass the prohibitions of Article 3.1(b) of the SCM Agreement, as indicated in *Brazil–Taxation*. Additionally, measures aimed at correcting market failures that cause fragile supply chains in the pharmaceutical industry might be exempt from the SCM Agreement through the 'benefit' analysis, provided they do not excessively compensate manufacturers for addressing these weaknesses.

The range of WTO rule flexibilities that might support onshoring measures for pharmaceutical manufacturing, especially those involving local content requirements, indicates only limited and strict options for maintaining WTO compliance. Does this limitation reflect a deficiency in the flexibility of these rules, or in the goals of states aiming to onshore pharmaceutical manufacturing? The WTO panel's decision in the *Turkey–Pharmaceutical Products* appeared to reject the idea that a measure could simultaneously serve economic and public health goals. Yet, this perspective seems to overlook the complexities of policy-making in a global context where geopolitical tensions encourage states to onshore or nearshore critical sectors for public policy reasons. The clear-cut distinction between protectionism and legitimate regulation appears overly simplistic in such scenarios.

This shift in the policy landscape opens several avenues for research, particularly in exploring how nations can implement reshoring and local content strategies within the bounds of WTO obligations and what reforms might be necessary to reconcile these strategies with global trade norms and the needs of nations in health emergencies. Additionally, the role of bilateral and regional trade agreements in facilitating or constraining these measures deserves closer scrutiny.

8. Conclusion

The measures being pursued by some States to onshore pharmaceutical manufacturing can be understood as a location-based solution to a location-based problem. The highly globalized pharmaceutical supply chain is prone to shortages, especially for generic medicines. Quality-related issues cause most shortages. However, this does not mean such shortages are unrelated to the location of manufacture. Some jurisdictions seem to generate disproportionate levels of warning notices by regulators, and it is easier for regulators to conduct oversight in their jurisdiction.[113] Moreover, the pharmaceutical supply chain is characterized by high levels of geographic concentration and low supplier diversity, particularly for generic medicines, which adds to the likelihood and impact of shortages. This is compounded by disincentives on suppliers to invest in supply-chain resilience and barriers to new entrants that inhibit self-corrections to supply-side problems in the market.

[113]A.S. Rathore et al. (2023) 'FDA Warning Letters: A Retrospective Analysis of Letters Issued to Pharmaceutical Companies from 2010–2020', *Journal of Pharmaceutical Innovation* 18, 665.

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The COVID-19 pandemic sharply exposed these existing structural fragilities in the pharmaceutical supply chain. It also saw the emergence of a supply-side risk that was previously hypothetical: widespread State interventions to restrict exports of domestically produced pharmaceuticals and APIs. These interventions seemed to add dramatically to the sense of insecurity around reliance on foreign suppliers for pharmaceuticals, particularly where those suppliers were based in jurisdictions with geopolitical frictions. This, in turn, added a new location-based supply-side risk, namely the possibility that an unfriendly State could disrupt pharmaceutical supply chains for geopolitical reasons.

Against that background, the pursuit of measures to onshore pharmaceutical manufacturing has blossomed, with a particular focus on local content measures. Of course, some States' local content measures pre-date the COVID-19 pandemic and were motivated more by economic or industrial reasons. That said, it would be surprising if those same States did not now equally invoke geopolitical and public health-related rationales for maintaining those measures in the post-pandemic environment.

The article highlights the challenges and opportunities presented by local content measures and reshoring initiatives, suggesting pathways for future research and policy development. Researchers should examine how current international trade and investment agreements accommodate or restrict onshoring efforts. Future research should also assess the economic outcomes of onshoring pharmaceutical manufacturing, including analyzing the cost implications for national health systems, impacts on drug pricing, and effects on healthcare access and equity. Comparative analyses between countries that have adopted varying levels of onshoring policies could provide valuable insights into the most effective strategies and potential pitfalls. The geopolitical consequences of pharmaceutical onshoring are also profound and deserve more investigation. Future studies should analyze how shifts in manufacturing capacities affect global power dynamics, especially concerning countries traditionally dominant in pharmaceutical production, such as India and China. This research could also explore how onshoring may alter global supply chain vulnerabilities and dependencies, potentially reshaping alliances and international trade relations.

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