JOHNS HOPKINS
BLOOMBERG SCHOOL
of PUBLIC HEALTH

Baltimore, May 07, 2025

To: United States Secretary of Commerce
Re: Notice of request for public comments
Department of Commerce - Bureau of Industry and Security
Docket No. 250414-0065 - XRIN 0694-XC120

Response to the Request for Public Comments- Effects on national security of imports of pharmaceuticals and pharmaceutical ingredients, and their derivative products

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We have been conducting research on the U.S. pharmaceutical supply chain and the resiliency of the broader public health supply chain for the past five years. Our work spans global supply chain de-risking, manufacturing dependencies, and policy levers that influence supply stability.

We would like to provide commentary on the potential effects of importation of pharmaceuticals on US national security, focusing on 1) active pharmaceutical ingredients and 2) finished drugs.

1) Imports of active pharmaceutical ingredients (APIs)

Our research has shown that the US relies on other countries for the supply of active pharmaceutical ingredients (APIs) for generic products. APIs are the substances that provide a drug's therapeutic effect. APIs cannot be consumed by a person; they must be transformed into a finished drug such as a capsule or a solution to be adequate for human consumption. Only about 16% of the different APIs for generic drugs destined to the US market are produced in the US. Imported APIs supply US domestic manufacturers with the essential components that they need to produce finished drugs. Except for the cases where the imported API is just passing through US borders and is exported in the original form that was imported, **imported APIs can generally be understood as key inputs for the US domestic pharmaceutical industry**.

Among the sources of generic APIs for the US market, we have found that India concentrates the highest number of manufacturing facilities and produces over 62% of the different APIs for the

US market.[1] China is the second place with respect to the number of facilities (13.8%) and it produces about 22% of all APIs. Italy is the close third place, with 10.6% of facilities that produce about 1/3 of all APIs (see Exhibit 1 below).

EXHIBIT 1

Top 10 global manufacturers of generic active pharmaceutical ingredients (APIs) for the US market, 2020–21

	Facilities		APIs	
Country	**Number**	**Percent**	**Number**	**Percent**
India	171	30.3	856	62.1
Italy	60	10.6	455	32.3
China	78	13.8	303	22.0
United States	44	7.8	193	14.0
Spain	27	4.8	189	13.7
Taiwan	9	1.6	120	8.7
Israel	8	1.4	114	8.3
Germany	23	4.1	97	7.0
France	21	3.7	60	4.4
Netherlands	7	1.2	41	3.0
Top 10 total	448	79.3	1,317	95.5
Global total	565	100.0	1,379	100.0

SOURCE Authors' analysis of facilities producing generic APIs for the US market during 2020–21 from Cortellis Generics Intelligence data extracted December 31, 2021. **NOTES** Values reflect the number of unique APIs produced in each country. API percentages were calculated over the 1,379 unique generic APIs identified in this study. API percentages may add to more than 100% because the same API may be manufactured in multiple countries.

Exhibit extracted from: Socal MP, Ahn K, Greene JA, Anderson GF (2023) Competition and vulnerabilities in the global supply chain for US generic active pharmaceutical ingredients. *Health Affairs* 42(3):407–415.

We found that the global facilities producing generics APIs for the US market sell to, on average, about two other global markets in addition to the US (see the average number of international inspectors that have surveyed the facility in Exhibit 2 below). Global markets may represent a single country like Japan or multiple countries such as the European Union. This suggests that the US competes with on average 2 other markets for the same API sources, i.e., that the same global manufacturers are supplying multiple global markets simultaneously. Today, the

[1] Socal MP, Ahn K, Greene JA, Anderson GF (2023) Competition and vulnerabilities in the global supply chain for US generic active pharmaceutical ingredients. *Health Affairs* 42(3):407–415.

consequences of having multiple global markets competing for the same sources of pharmaceuticals are largely unknown.

Our study also found that about one third of generic APIs were single-sourced, i.e., were produced by a single facility, and 30.4 percent were produced by 2-3 facilities. Only 35.9 percent of APIs were produced by four or more facilities, suggesting that there is limited redundancy in generic API manufacturing (see Exhibit 3 below).

EXHIBIT 2

Characteristics of facilities manufacturing generic active pharmaceutical ingredients (APIs) for the US market, 2020–21

Characteristics	Overall[a]	India	China	Italy	US	*p* value
No. of facilities	565	171	78	60	44	—[b]
Average no. of APIs produced per facility	8.9	15.3	5.0	10.7	5.8	0.642
Average year of last FDA inspection[c]	2017.5	2018.0	2016.9	2018.3	2017.1	0.023
No. of facilities with FDA warning letter	68	17	11	5	10	0.409
Average no. of international inspectors who surveyed the facility	1.8	2.8	2.6	1.8	0.3	<0.001

SOURCE Authors' analysis of facilities producing generic APIs for the US market during 2020–21 from Cortellis Generics Intelligence data extracted December 31, 2021. **NOTES** India, China, and Italy were the top producers of generic APIs for the US market. International inspectors represent international regulators carrying out inspections on behalf of other non-US countries (for example, Japan's Pharmaceuticals and Medical Devices Agency) or regions (for example, the European Medicines Agency). *p* values shown are for the comparison between India, China, Italy, and the US; obtained by unpaired *t*-tests and chi-square tests. FDA is Food and Drug Administration. [a]There were 42 countries overall. [b]Not applicable. [c]The decimal places in each year represent a fraction of the year.

Exhibit extracted from: Socal MP, Ahn K, Greene JA, Anderson GF (2023) Competition and vulnerabilities in the global supply chain for US generic active pharmaceutical ingredients. *Health Affairs* 42(3):407–415.

Finally, our findings revealed about one in four generics markets had upstream vulnerabilities to the supply chain because a robust level of competition among finished drug manufacturers obscured a fundamentally uncompetitive market of three or fewer API producers (exhibit 4 below). These markets should be a concern because one or two manufacturers of APIs shutting down could create drug shortages even if there were four or more manufacturers of finished generic drugs licensed by the Food and Drug Administration (FDA). Currently, the FDA gives priority to the review of abbreviated new drug applications (ANDAs) for generic drugs that have three or fewer manufacturers of the finished drug product, but this approach overlooks the possibility that the API production lacks diversification. At the very least, initiatives aimed at identifying vulnerable markets should examine the number and location of API sources, in addition to the number and location of finished drug form manufacturers.

EXHIBIT 3

Key characteristics of active pharmaceutical ingredients (APIs), by number of manufacturing facilities producing the APIs, 2020–21

Characteristics	Overall	No. of facilities producing the APIs		
		1 facility only	2–3 facilities	4 or more facilities
No. of APIs (percent)	1,379 (100.0)	465 (33.7)	419 (30.4)	495 (35.9)
Average no. of facilities manufacturing each API	3.7	1.0	2.5	7.2
Average year of first ANDA approval[a]	2001.6	1999.1	1998.3	2004.8
Average no. of companies with ANDA approved[b]	4.5	0.94	3.5	8.6
No. of APIs not linked to any company holding ANDA approval	546	318	150	78
No. of APIs by route of administration				
Oral only	623	175	175	273
Injectable only	216	90	71	55
External only	106	46	37	23
Multiple routes	282	50	97	135
Unspecified	152	104	39	9
No. of APIs by therapeutic class				
Neuromuscular	337	99	109	129
Anti-infectives	245	99	77	69
Respiratory and cardiovascular	208	60	58	90
Genitourinary and hormones	182	59	57	66
Alimentary tract and metabolism	172	71	54	47
Hematology and oncology	159	37	44	78
Other	76	40	20	16

SOURCE Authors' analysis of facilities producing generic APIs for the US market during 2020–21 from Cortellis Generics Intelligence data extracted December 31, 2021. **NOTES** p values were calculated for comparisons between APIs produced at 1 facility, 2–3 facilities, and 4 or more facilities; obtained by unpaired t-tests and chi-square tests. ANDA is abbreviated new drug application. $p < 0.001$ for all characteristics except year of first ANDA approval ($p < 0.01$) and number of facilities manufacturing each API (p value not applicable). [a]$n = 943$ APIs with information. The decimal places in each year represent a fraction of the year. [b]Conditional on having at least one company with an ANDA approval linked to the API; $n = 833$ APIs.

Exhibit extracted from: Socal MP, Ahn K, Greene JA, Anderson GF (2023) Competition and vulnerabilities in the global supply chain for US generic active pharmaceutical ingredients. *Health Affairs* 42(3):407–415.

EXHIBIT 4

Competition levels in US generic drug markets, by number of active pharmaceutical ingredient (API) manufacturers and abbreviated new drug application (ANDA) holders, 2020–21

	Number of API manufacturers			
	3 or fewer		4 or more	
Number of ANDA holders	Number	Percent	Number	Percent
3 or fewer	224	26.9[a]	56	6.7[b]
4 or more	192	23.0[c]	361	43.3[d]

SOURCE Authors' analysis of facilities producing generic APIs for the US market during 2020–21 from Cortellis Generics Intelligence data extracted December 31, 2021. **NOTES** $n = 833$ generic APIs with at least one company with an approved ANDA. Each ANDA may represent one or more products. [a]Noncompetitive market. [b]Downstream vulnerability. [c]Upstream vulnerability. [d]Competitive market.

Exhibit extracted from: Socal MP, Ahn K, Greene JA, Anderson GF (2023) Competition and vulnerabilities in the global supply chain for US generic active pharmaceutical ingredients. *Health Affairs* 42(3):407–415.

Beyond empirical indicators of risk concentration, there are deeper structural challenges in how the U.S. currently approaches pharmaceutical supply chain resilience. Tariffs are often framed as a way to reduce U.S. dependence on foreign pharmaceutical inputs. But this logic focuses on the international trade aspect of global supply chains—flow of goods across borders; in reality, supply chains operate through four interconnected flows: materials, information, capital, and people. Disruptions in any of these can jeopardize access to critical medicines.

In pharmaceuticals, this complexity is amplified. The U.S. depends on China for APIs, on India for finished dosage forms (FDFs), and on global freight and data systems to coordinate delivery and compliance. Imposing tariffs on one node does little to enhance supply chain resiliency. In fact, as our modeling and simulation[2] show, a 25% tariff on a core API results in less than a 1% increase in final drug price — not enough to change incentives, but enough to complicate procurement and cloud price signals. Meanwhile, the risk of unintended shortages or supplier exits increases, and the eroding margins of generic drug manufacturers reduce their incentive to maintain quality and safety.

[2] Dada, Maqbool, Tinglong Dai, Yunxiang Sun, and Mariana Socal. 2025. "Tariffs as a Hidden Tax: Price Pass-Through in Multi-Stage Supply Chains." Johns Hopkins University Working paper. http://doi.org/10.2139/ssrn.5237643.

2) Imports of finished drug forms (FDFs)

Historically, prescription drugs have been exempted from tariffs—a move justified to prevent raising health care costs.7 Together with countries such as Canada, the United Kingdom, Japan, the European Union, and others, the United States is a signatory of the 1994 Agreement on Trade in Pharmaceutical Products, which eliminated tariffs on pharmaceutical products and APIs.8 The United States pays on average 3 to 4 times higher prices than other industrialized countries for the same prescription drugs,5 with detrimental consequences. About one in 4 Americans have difficulty affording the drugs they need due to cost.6

Drug shortages, a frequent problem in the US health care system in the last decade, further compromise access to treatments, with significant clinical, public health, and spending implications. According to the FDA, 90 drugs were in short supply in January 2025, some for more than 2 years. Drug shortages most frequently affect generic products and are primarily driven by quality problems, which could be linked to the quality of the APIs or finished drugs.

Our research[3] has found that drug shortages involved about 11% of all generic APIs produced for the US market (Table 1 below). Shortages lasted on average 844 days and primarily affected APIs linked to older drugs and facilities producing many different drugs.

Table 1. Characteristics of Generic APIs With and Without Drug Shortages Recorded in the US Market, 2020-2021[a]

Characteristics	APIs			
	Overall (n = 1379)	Linked to shortage (n = 147 [10.7%])	Not linked to shortage (n = 1232 [89.3%])	*P* value
Facilities manufacturing each API, mean (SD) [range], No.	3.7 (3.5) [1-27]	3.6 (3.1) [1-17]	3.7 (3.5) [1-27]	.81
Year of first ANDA approval, mean (SD)	2001.6 (13.4)	1992.5 (11.3)	2002.9 (13.1)	<.001
Companies with approved ANDAs, mean (SD), No.	4.5 (6.1)	7.2 (8.2)	4.1 (5.7)	<.001
Shortage duration as of December 31, 2021, mean (SD), d	844.6 (633.8)	844.6 (633.8)	NA	NA

Exhibit extracted from Socal MP, Crane MA, Anderson GF. Global Production of Active Pharmaceutical Ingredients for US Generic Drugs Experiencing Shortages. JAMA. 2024 May 28;331(20):1763-1765.

[3] Socal MP, Crane MA, Anderson GF. Global Production of Active Pharmaceutical Ingredients for US Generic Drugs Experiencing Shortages. JAMA. 2024 May 28;331(20):1763-1765.

We also found that facilities producing APIs linked to shortages were larger – they produced up to 103 different APIs in the same facility, whether those facilities producing APIs not linked to shortages produced a maximum of 37 APIs (see Table 2 below). Most facilities were in India. On average, facilities producing APIs linked to shortages produced for more global markets in addition to the US than those producing APIs not linked to shortages (average (sd): 2.1 (1.7) vs. 1.5 (1.4) global markets, $p<0.001$). Interestingly, the timing of the last inspection and the facility having received a warning letter from the FDA were not associated with shortages.

Table 2. Characteristics of Facilities Producing Generic APIs for the US Market, 2020-2021

Characteristic	Facilities[a] Overall (n = 565)	With ≥1 shortage APIs (n = 272 [48.1%])	Without shortage API (n = 293 [51.9%])	*P* value
APIs produced per facility, mean (SD) [range], No.	8.9 (12.4) [1-103]	13.7 (15.5) [1-103]	4.5 (5.5) [1-37]	<.001
Shortage APIs per facility, mean (SD) [range], No.	0.9 (1.4) [0-10]	1.9 (1.5) [1-10]	NA	NA
Country, No. (%)				
India	171 (30.3)	96 (35.3)	75 (25.6)	
China	78 (13.8)	29 (10.7)	49 (16.7)	
Italy	60 (10.6)	33 (12.1)	27 (9.2)	
US	44 (7.8)	26 (9.6)	18 (6.1)	
Spain	27 (4.8)	15 (5.5)	12 (4.1)	
Germany	23 (4.1)	9 (3.3)	14 (4.8)	.02
Japan	21 (3.7)	7 (2.6)	14 (4.8)	
France	21 (3.7)	8 (2.9)	13 (4.4)	
Switzerland	13 (2.3)	5 (1.8)	8 (2.7)	
UK	10 (1.8)	3 (1.1)	7 (2.4)	
Other[b]	97 (17.2)	41 (15.1)	56 (19.1)	
Inspections				
Last FDA inspection year, mean (SD)	2017.5 (3.6)	2017.3 (4.0)	2017.8 (3.1)	.06
FDA warning letter, No. (%)	68 (12.0)	33 (12.1)	35 (11.9)	.95
Non-US inspectors, mean (SD), No.	1.8 (1.6)	2.1 (1.7)	1.5 (1.4)	<.001

Exhibit extracted from Socal MP, Crane MA, Anderson GF. Global Production of Active Pharmaceutical Ingredients for US Generic Drugs Experiencing Shortages. JAMA. 2024 May 28;331(20):1763-1765.

3) Recommendations

We contend that adding tariffs on imported active pharmaceutical ingredients can have strong detrimental effects on US domestic drug manufacturers. APIs are a key determinant of the quality of the finished drug and generally contribute between 20% and 30% of the final drug cost. Tariffs on imported APIs could increase the costs of domestically manufactured drugs, potentially limiting their competitiveness both in the U.S. and globally. This policy approach may inadvertently undermine the very goal of strengthening domestic pharmaceutical manufacturing.

Reshoring manufacturing of generic drugs has been proposed as a solution to strengthen the US prescription drug supply and help prevent or mitigate drug shortages. However, maintaining a reliance on global sources of APIs may jeopardize the success of this solution due to the potential for supply disruptions including those from quality problems. Made-in-America products are likely to be more expensive than those globally sourced due to higher production costs. **Tariffs on globally sourced APIs could increase the costs of made-in-America products even further, possibly limiting the competitiveness of domestically manufactured drugs in the global as well as the domestic market.**

Tariffs on finished dosage forms might contribute to increased drug prices, especially for branded products. The monopolistic nature of branded drug production allows drug manufacturers to have greater control over the supply chain and could possibly allow the manufacturers to pass more of the added cost of tariffs down the supply chain up to the consumer. For generic products, tariffs may increase shortages due to export quotas or due to quality concerns – with further-reduced profit margins, generic manufacturers may opt to send substandard products to the US, with possible supply disruptions.

In addition to further increasing drug prices, **tariffs on pharmaceutical finished drug forms and APIs may trigger unintended consequences through retaliatory behavior by our trade partners**. For example, countries targeted by tariffs could implement export quotas. China is the sole producer for APIs for the antibiotic tetracycline. If China were to restrict the exports of this API, then a shortage of tetracycline is quite plausible. An export ban would not only threaten the health of Americans battling infectious diseases; it could also harm US drug manufacturers who might have to pause production, losing their global market share and lowering their revenue.

Other unintended consequences may include retaliatory tariffs harming US exporters; supply chain disruptions due to manufacturers relocating to other countries in response to tariffs; and cost cuts implemented by drug manufacturers raising quality and safety concerns about the drugs that get supplied.

It is possible to reallocate supply, but it takes time, investment, requires FDA approval, and may increase prices. Importantly, reallocation may not be to the US but to other countries with more favorable tax or regulatory profiles.

More broadly, the U.S. can learn from other countries for lessons in de-risking supply chains. Our research[4] shows that for decades, just as it became the center of today's global supply chains, China has been actively de-risking its own supply chains — but not through tariffs and other trade barriers alone. It has been doing so by investing in domestic alternatives to Western manufacturers, directly subsidizing capacity building and maintenance of essential supply chains, building parallel payment systems to SWIFT, and tightening control over essential material exports. These moves are not about isolation — they are about strategic optionality. The U.S. should learn from that: real resilience means building flexibility into the system, not cutting off trade in ways that boomerang back onto critical services.

De-risking should not be conflated with decoupling. The goal is not to eliminate dependence — it is to shift exposure away from adversarial chokepoints and toward trusted partners. That means expanding sourcing options (not narrowing them), improving supply chain transparency beyond the first tier, and investing in infrastructure that supports resilient, not just domestic, production.

Rather than rely on blunt instruments like tariffs, the U.S. should focus on targeted industrial policy — using tools like long-term procurement contracts, reserve manufacturing capacity, and formal friend-shoring agreements.

We appreciate the opportunity to provide comments, and we welcome any questions that you may have.

Sincerely,

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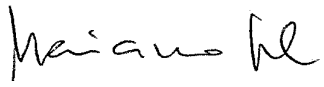
[4] Dai, Tinglong, and Christopher S. Tang. 2024. "De-risking Global Supply Chains: Looking Beyond Material Flows." *Asia Policy* 19 (4): 153–176. https://doi.org/10.1353/asp.2024.a942841



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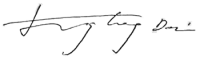

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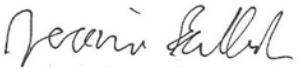

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Conflict Of Interest Disclosure

We currently lead two projects that aim to strengthen the resilience of the U.S. prescription drug supply: 1) development of the Johns Hopkins Prescription Drug Supply Chain Data Dashboard – a publicly available data source on global manufacturers producing prescription drugs for the US market (funded by Johns Hopkins); and 2) development of Make-Buy-Invest strategic actions to identify target markets and design actionable policies to strengthen the US prescription drug supply, including for the Military (funded by the Defense Logistics Agency, Department of Defense).

Appendix - Questions Presented in the Notice of Request for Public Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients

https://www.federalregister.gov/documents/2025/04/16/2025-06587/notice-of-request-for-public-comments-on-section-232-national-security-investigation-of-imports-of

(i) the current and projected demand for pharmaceuticals and pharmaceutical ingredients in the United States;

(ii) the extent to which domestic production of pharmaceuticals and pharmaceutical ingredients can meet domestic demand;

(iii) the role of foreign supply chains, particularly of major exporters, in meeting United States demand for pharmaceuticals and pharmaceutical ingredients;

(iv) the concentration of United States imports of pharmaceuticals and pharmaceutical ingredients from a small number of suppliers and the associated risks;

(v) the impact of foreign government subsidies and predatory trade practices on United States pharmaceuticals industry competitiveness;

(vi) the economic impact of artificially suppressed prices of pharmaceuticals and pharmaceutical ingredients due to foreign unfair trade practices and state-sponsored overproduction;

(vii) the potential for export restrictions by foreign nations, including the ability of foreign nations to weaponize their control over pharmaceuticals supplies;

(viii) the feasibility of increasing domestic capacity for pharmaceuticals and pharmaceutical ingredients to reduce import reliance;

(ix) the impact of current trade policies on domestic production of pharmaceuticals and pharmaceutical ingredients, and whether additional measures, including tariffs or quotas, are necessary to protect national security; and

(x) any other relevant factors.