Response to the Notice of Request for Public Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients
Department of Commerce
Bureau of Industry and Security, Office of Strategic Industries and Economic Security
Submitted: May 6, 2025

RE: Docket Number - 250414-0065

To Whom It May Concern:

Thank you for the opportunity to provide the Department of Commerce's Bureau of Industry and Security, Office of Strategic Industries and Economic Security, comments on the Notice of Request for Public Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients.

The API Innovation Center (APIIC) is a non-profit public benefit entity based in St. Louis, Missouri, with a mission to strengthen the domestic drug supply chain and global competitiveness while reducing manufacturing costs by deploying advanced manufacturing technology. APIIC aims to de-risk the commercialization and adoption of advanced technologies to produce drug products and active pharmaceutical ingredients (APIs). APIIC's public-private model has successfully brought together a supercluster of innovators, researchers, healthcare systems, and commercial manufacturers into project consortiums to actively participate in projects that commercialize new manufacturing technologies and drive U.S.-based biomanufacturing of APIs.

Summary Response to Request for Comment:
The U.S. generic pharmaceutical sector faces systemic disadvantages stemming from foreign government subsidies, unfair trade practices, and outdated domestic policy frameworks. While countries like India and China provide industrial incentives to dominate pharmaceutical production, the U.S. continues to see a decline in its manufacturing base, jeopardizing national health security and supply chain resilience. The following comments address key areas of concern:

- Indian and Chinese subsidies give their manufacturers a cost advantage that undercuts U.S. generic producers, weakening domestic competitiveness and discouraging long-term investments in API production.

- Foreign-subsidized production and a U.S. pricing system that commoditizes generics have led to chronic underinvestment, idle capacity, and persistent drug shortages in the domestic market.

- Increasing domestic API and drug production is feasible through utilizing existing underutilized infrastructure, investments in advanced manufacturing technology and proven models like APIIC's *Invest-Contract-Partner* (*ICP Model™*), which integrates investment, contracting, and partnership strategies.

- The Acetris ruling allows drugs made with foreign APIs to qualify as "U.S.-made," undermining federal procurement incentives for domestic production and weakening supply chain security.

- APIIC's analysis shows that more than 80% of the top 100 generic medicines by volume—including most antivirals and antibiotics—lack any U.S. API source, highlighting the urgent need to reshore essential drug manufacturing.

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

Overview:
Foreign government subsidies in India and China distort the global generic pharmaceutical market, giving their manufacturers a cost advantage that undermines U.S.-based generic drug production. Without federal support, U.S. generic manufacturers struggle to compete—threatening both U.S. pharmaceutical resilience and national security.

Background:
The U.S. generic pharmaceutical industry is under mounting pressure from foreign competitors who benefit from substantial, long-term government subsidies. In India, the Production Linked Incentive Scheme to promote the domestic production of Bulk Drugs, Key Starting Materials (KSMs), Drug Intermediates (DIs), and APIs provides financial incentives to reduce reliance on foreign pharmaceutical inputs and boost local manufacturing.[1]

For fermentation-based products, the incentive levels are structured as follows:

- 20% incentive for FY 2023–24 to FY 2026–27
- 15% incentive for FY 2027–28
- 5% incentive for FY 2028–29

For chemical synthesis-based products (i.e., APIs), the schemes offer a 10% incentive annually from FY 2022–23 to FY 2027–28**.**

These guaranteed subsidies significantly offset production costs, enabling Indian manufacturers to scale up and price their products below what U.S. manufacturers can offer.

Similarly, China has adopted an aggressive industrial policy approach to pharmaceutical and biotech development. Its Strategic Emerging Industries Initiative, launched in 2010, designated biotechnology as a top national priority.[2] Backed by considerable public investment, Chinese firms receive subsidies, R&D grants, and access to government-supported infrastructure like Zhangjiang Hi-Tech Park in Shanghai and Zhongguancun Life Science Park in Beijing.[3] These centers provide not only advanced R&D facilities that encourage innovation but also access to venture capital and regulatory streamlining that accelerate commercialization and global competitiveness.[4] While

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[1] Production Linked Incentive (PLI) Scheme for promotion of domestic manufacturing of Bulk Drugs (Key Starting Materials (KSMs)/ Drug Intermediates (DIs)/ Active Pharmaceutical Ingredients (APIs): https://pharmaceuticals.gov.in/schemes/production-linked-incentive-pli-scheme-promotion-domestic-manufacturing-critical-key.
[2] How Innovative Is China in Biotechnology?: https://itif.org/publications/2024/07/30/how-innovative-is-china-in-biotechnology/#_edn93.
[3] Ibid.
[4] Ibid.

China maintains a significant role as a global API supplier, the country is also making significant strides in biotech innovation, fueled largely by a coordinated, government-led strategy. This positions China to lead in new approaches to pharmaceutical manufacturing.

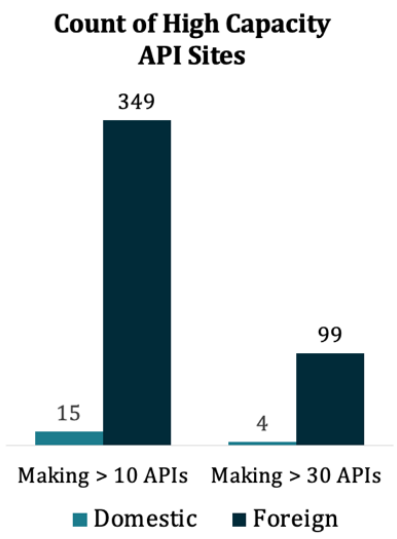

Figure 1: Nov 2020 Sourced Data: Cortellis Generics Intelligence, formerly known as Newport. Copyright Clarivate 2021

In contrast, U.S. manufacturers contend with high capital costs, stricter regulatory compliance standards, and limited direct federal incentives. Without a strategic response, domestic generic production will continue to decline, increasing reliance on foreign supply chains and exposing the U.S. to greater geopolitical and health risks. In terms of APIs, at present, the U.S. ranks lowest among the world's most prominent industrial powers, with only four companies with the capacity to make more than 30 APIs and 15 able to make more than 10 **(Figure 1)**.

To maintain national security and ensure pharmaceutical resilience, the federal government must level the playing field through targeted support and investment in the U.S. pharmaceutical manufacturing base.

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

Overview:
While foreign state-sponsored actions like subsidies contribute to artificially suppressed pharmaceutical prices, the more profound economic impact on U.S. generic medicine manufacturing stems from domestic market dynamics that have devalued essential medicines into low-margin commodities. This has created a cycle of underinvestment, underutilized capacity, and persistent drug shortages in the United States.

Background:
State-sponsored programs in countries like India and China—including production-linked incentives and strategic government investments—allow foreign manufacturers to artificially lower pharmaceutical prices to drive U.S. manufacturers out of business. This has even resulted in the use of predatory pricing highlighted during a 2024 House Ways and Means hearing.[5] However, the more jarring and crippling economic impact on the U.S. generic pharmaceutical sector comes from a domestic drug supply system that has commoditized essential generic medicines and is driven almost exclusively by price, not reliability or national need.

[5] Six Key Moments from Hearing on Chronic Drug Shortages (February 7, 2024): https://waysandmeans.house.gov/2024/02/07/six-key-moments-from-hearing-on-chronic-drug-shortages/.

This *commoditization loop*, as described by APIIC Chair Anthony Sardella, is driven by a combination of low profit margins, pricing uncertainty, and limited capital availability.[6] A 2023 analysis of the Average Manufacturer's Price (AMP) from Medicaid.gov database illustrates the industry price erosion over a six year period **(Figure 2)**. An analysis of the AMP shows a decrease of an average of $3.15 to $1.47 for high-volume generics during that timeframe.

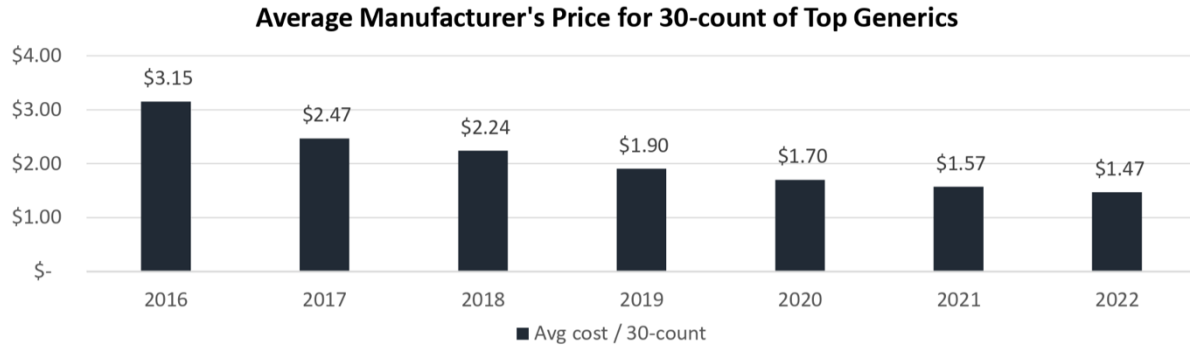

Figure 2: Data compiled by the API Innovation Center

The *loop* is compounded by foreign-driven government subsidies, lower cost of labor, and less regulatory oversight.[7] Each of these factors discourages domestic investment in modernization and expansion, leading to chronic underuse of domestic facilities. In 2022, APIIC surveyed pharmaceutical companies representing 25% of the U.S.' generic drug manufacturing infrastructure and found that over half had capacity sitting idle, not due to lack of infrastructure, but because offshore producers—sustained by lower labor costs and foreign subsidies—are prioritized in a drug pricing race to the bottom.[8] Sardella noted in both published research and congressional testimony[9] that this cycle has created fragility across the U.S. drug supply chain.[10]

Further compounding this are structural dynamics within the U.S. drug supply chain itself. Consolidation among group purchasing organizations and wholesalers has centralized purchasing power, leading to aggressive price competition that rewards the lowest-cost supplier, often at the expense of supply reliability. Meanwhile, brand-name manufacturers deploy patent protections and rebate-driven deals with public benefit managers that limit market access for generics.[11] As generic competition increases, prices plummet, and production is pushed abroad to the cheapest sites, undermining U.S. resiliency. As the FDA has acknowledged, "[t]he market does not foster a reliable supply of generic drugs," underscoring the urgent need for policy reform that prioritizes domestic capacity and public health security.[12]

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[6] US Generic Pharmaceutical Industry Economic Instability: https://apicenter.org/wp-content/uploads/2023/07/US-Generic-Pharmaceutical-Industry-Economic-Instability.pdf.
[7] Ibid.
[8] U.S. Generic Pharmaceutical Manufacturer Available Capacity Research Survey: https://apicenter.org/wp-content/uploads/2022/10/Excess-Capacity-Research_Final-2.pdf.
[9] Subcommittee on Oversight and Investigations - Examining the Root Causes of Drug Shortages: Challenges in Pharmaceutical Drug Supply Chains: https://energycommerce.house.gov/events/oversight-and-investigations-subcommittee-hearing-examining-the-root-causes-of-drug-shortages-challenges-in-pharmaceutical-drug-supply-chains.
[10] Ibid.
[11] U.S. Generic Pharmaceutical Manufacturer Available Capacity Research Survey. Ibid.
[12] U.S. Food and Drug Administration - Drug Shortages: Root Causes and Potential Solutions: https://www.fda.gov/media/131130/download?attachment.

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

Overview:
Increasing domestic capacity for generic pharmaceuticals and pharmaceutical ingredients is both practical and achievable by leveraging existing infrastructure and advancing proven models. Through targeted investment, modern technology, and collaborative frameworks like APIIC's ICP Model™, the U.S. can take meaningful steps to reduce import reliance and strengthen supply chain resilience.

Background:
There is an opportunity to expand U.S. generic pharmaceutical manufacturing capacity. For starters, it is important to appreciate that reshoring can be achieved without the need for costly and time-consuming new facility construction. While important, erecting a cGMP facility can take a decade and billions of dollars to come to fruition.[13] Just as problematic are the economic deterrents around building a new facility for generic medicines. However, existing domestic infrastructure is underutilized, with nearly an additional "30 billion doses of essential and critical medicines" that could be produced in the U.S., "without incurring the expense of building a new manufacturing plant."[14] With numerous manufacturers able to bring drug production activity to bear within a 24-36 month timeframe, repurposing this idle capacity, especially if supported by federally guaranteed contracts for essential medicines, presents an actionable, short-term solution to increase supply chain reliability.[15]

To ensure both short and long-term competitiveness, the adoption of advanced manufacturing technologies (AMTs) is essential. AMTs, such as continuous flow manufacturing, is estimated to reduce production costs by 30–50%, compress timelines, and improve quality and efficiency.[16] However, due to high upfront costs and low margins in the generic sector, many manufacturers have not adopted them. APIIC's research shows that more than half of the surveyed manufacturers could implement AMTs within a year, with the appropriate financial support in place.[17] Further upstream, the use of AMTs offers promising opportunities. For example, when AMTs are used to develop new synthesis routes for APIs, they can support the development of novel routes, uncover alternative KSMs, and identify new fine chemicals. This capability is especially critical given the lack of transparency around the compounds used to make APIs—many of which are believed to be

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[13] PhRMA Manufacturing & Supply Chain - Biopharmaceutical Manufacturing: https://phrma.org/policy-issues/research-development/manufacturing-supply-chain#:~:text=Setting%20up%20the%20manufacturing%20capacity,comply%20with%20various%20regulatory%20requirements.
[14] API Innovation Center - Building a Resilient Domestic Drug Supply Chain: The Path to National Health Security: https://apicenter.org/wp-content/uploads/2025/03/APIIC-White-Paper-2025-Building-a-Resilient-Domestic-Drug-Supply-Chain.pdf.
[15] U.S. Generic Pharmaceutical Manufacturer Available Capacity Research Survey: https://apicenter.org/wp-content/uploads/2022/10/Excess-Capacity-Research_Final-2.pdf.
[16] Ibid.
[17] API Innovation Center: Benefits and Barriers to Adopting Advanced Manufacturing Technology in the Pharmaceutical Industry: https://apicenter.org/wp-content/uploads/2025/02/APIIC-Market-Research-FINAL-1.pdf.

highly concentrated in China.[18] In response, countries such as India are examining ways to address their dependence on Chinese sources for KSMs and other raw materials.[19]

Downstream, it is widely recognized that the current model of the generic medicine supply chain, especially regarding return on investment and resiliency, must be reformed. Given its complexity and opaqueness, value is consumed by multiple entities, and little is known about the true cost to produce, distribute, and supply critical medicines to patients. A solution comes in the form of APIIC's *Invest–Contract–Partner (ICP) Model™* that connects investment, demand, and supply chain collaboration to reduce import reliance and build long-term pharmaceutical resilience.[20] At its core, the ICP Model™ aligns three pillars:

- **Invest**: Directs public and private capital into advanced chemistry, continuous manufacturing technologies, and infrastructure upgrades—particularly to modernize underused or idle facilities.
- **Contract**: Secures demand through committed volume contracts from government or strategic buyers, giving manufacturers the confidence to produce high-priority, low-margin generic medicines domestically.
- **Partner**: Brings together KSM suppliers, API manufacturers, and drug product producers in modular "mini-consortiums" tailored to specific drug classes or supply chain gaps, bridging certainty of supply for the end customer and certainty of demand for the drug manufacturer.

What sets the ICP Model™ apart is its built-in sustainability mechanism—such as royalty-based reinvestment and revenue-sharing structures—that allow early-stage investments to fund continued innovation and capacity growth. The model is also flexible, enabling different stakeholders—whether they are small innovators, academic labs, or scaled manufacturers—to plug into a coordinated ecosystem focused on reshoring production and safeguarding national pharmaceutical security. As such, the ICP Model™ offers more than just a framework—it provides a practical, tested national blueprint for rebuilding and modernizing the U.S. drug manufacturing base.[21]

(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

Overview:
Current trade policies—particularly the *Acetris* ruling—can undermine national security by allowing pharmaceuticals made with foreign APIs to qualify as "U.S.-made," weakening incentives for domestic API production. For any action to reshore U.S.' capacity to produce generic APIs and

[18] IBIS World - Pharmaceutical Raw Material Manufacturing in China – Mark Research Report: https://www.ibisworld.com/china/industry/pharmaceutical-raw-material-manufacturing/323/.
[19] Pharmaceutical sovereignty: India's path to self-reliance and global leadership: https://government.economictimes.indiatimes.com/blog/pharmaceutical-sovereignty-indias-path-to-self-reliance-and-global-leadership/120732790.
[20] API Innovation Center - Building a Resilient Domestic Drug Supply Chain: The Path to National Health Security: https://apicenter.org/wp-content/uploads/2025/03/APIIC-White-Paper-2025-Building-a-Resilient-Domestic-Drug-Supply-Chain.pdf.
[21] Ibid.

their finished drug products, targeted policy measures such as closing the *Acetris* loophole and revising federal procurement standards are necessary.

Background:
The 2020 *Acetris Health v. United States* decision redefined what qualifies as "manufacture[d]"[22] in the U.S. under the Trade Agreements Act (TAA), ruling that a drug product made in the U.S. using an API sourced overseas—in this case, from India—can still be classified as a U.S.-made good.[23] This interpretation overturned the U.S. government's longstanding position that API origin determines country of manufacture unless "substantial transformation" occurs.[24] [25] As a result, the ruling opened a critical loophole that allows foreign-sourced pharmaceutical ingredients to be used in federally procured drugs without triggering domestic sourcing requirements.

The policy shift has considerable national health security implications. By classifying drugs made with foreign APIs as U.S.-manufactured, the *Acetris* ruling undermines efforts to reshore production and disincentivizes any business case for investing in domestic API capacity. In doing so, it accelerates U.S. reliance on offshore production and weakens the resilience of our domestic pharmaceutical supply chain. Addressing this loophole—through executive action and/or phased legislative reform—is a necessary first step to align federal procurement policy with national interests and incentivize domestic pharmaceutical manufacturing.

Some attention has been given to this issue in Congress, including an amendment offered during consideration of the National Defense Authorization Act for Fiscal Year 2025, but more is necessary.[26] [27] A phased approach to reform would help avoid sudden disruptions to drug availability while giving U.S. manufacturers time to scale operations. In parallel, reducing TAA exceptions and offering financial incentives for onshoring API production would further strengthen the U.S. manufacturing base. Without these changes, current trade policies will continue to favor foreign suppliers, leaving the U.S. vulnerable, especially in times of public health and geopolitical instability.

(x) any other relevant factors

The magnitude of the U.S. reliance on foreign manufacturing cannot be understated. Utilizing data from Clarivate and Cortellis Generic Intelligence, APIIC's analysis of FDA-approved, commercial API suppliers finds the following staggering figures that illustrate the magnitude of the U.S. reliance on foreign manufacturers.[28] **(Figure 3)**

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[22] The term "manufacture" was traditional understood to coincide with "substantially transformation" standard. The Acetris case concluded that reference to "manufacture" in the U.S. is set apart from "substantially transformation."
[23] Acetris Health, LLC v. United States, No. 18-2399 (Fed. Cir. 2020).
[24] Substantial transformation is achieved when the processing of a pharmaceutical causes a change in name, character, and use of components during the manufacturing process.
[25] International Trade Administration – Determining Origin: Substantial Transformation: https://www.trade.gov/rules-origin-substantial-transformation.
[26] Congressional Research Service - U.S. Government Procurement and International Trade: https://www.congress.gov/crs-product/IF11580.
[27] Senate Amendment 2443 to S. 4638 – National Defense Authorization Act for Fiscal Year 2025 (Sens. Marco Rubio & Elizabeth Warren): https://www.congress.gov/amendment/118th-congress/senate-amendment/2443/text.
[28] The US Active Pharmaceutical Ingredient Infrastructure - The current state and considerations to increase US Healthcare Security: https://apicenter.org/wp-content/uploads/2024/07/The-US-Active-Pharmaceutical-Ingredient-Infrastructure.pdf.

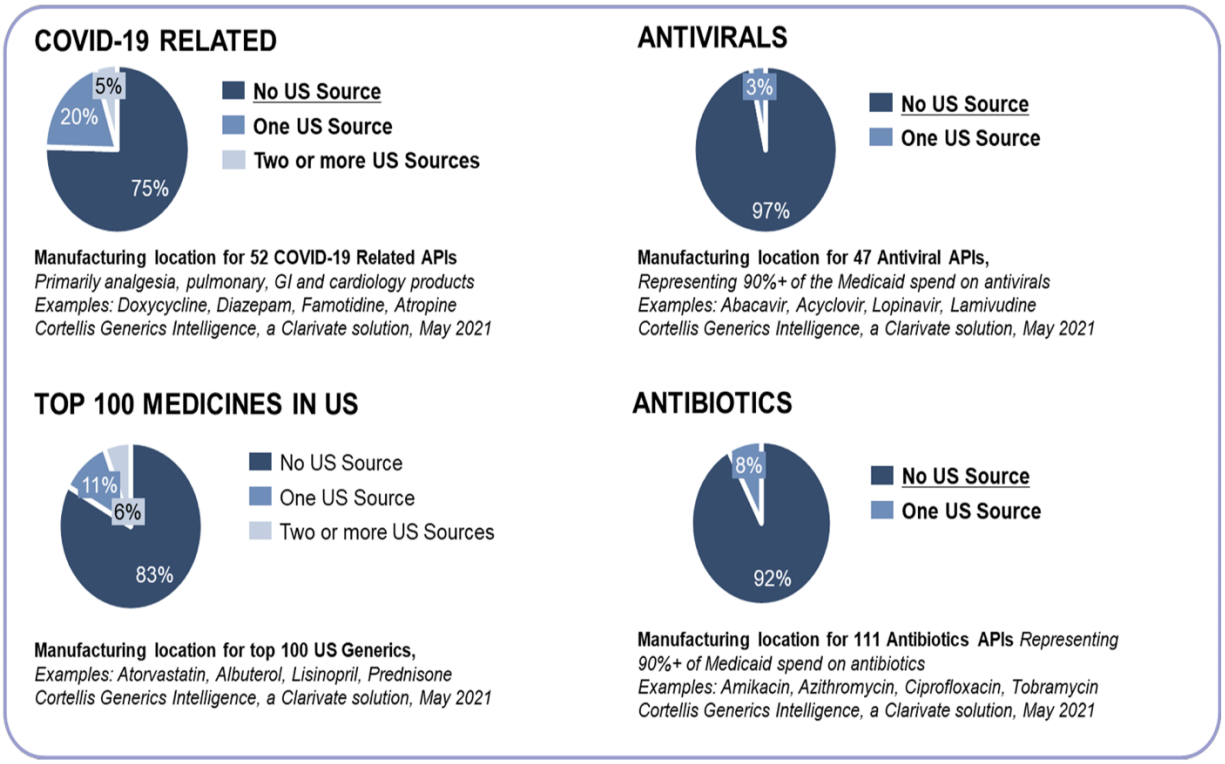

Figure 3: Sources of COVID-19, Antivirals, Antibiotics and Top 100 Medicines in the United States. Cortellis Generics Intelligence, formerly known as Newport. Copyright Clarivate 2021

An analysis of 52 COVID-related medicines found that 75% lacked a U.S.-based source for their API. Similarly, among the top 100 generic medicines consumed in the U.S., 83% had no domestic API source.[29] Notably, both datasets included controlled substances, which, by policy, must be manufactured in the U.S. and are subject to strict import/export controls. The picture is even more concerning for drug categories without such protections: 97% of the 47 most prescribed antivirals and 92% of the 111 most commonly prescribed antibiotics have no U.S. API source.[30]

The importance of intermediates in the pharmaceutical supply chain—particularly KSM and raw chemicals—should not be overlooked. APIIC assessed 60 medications across five categories, including those critical to cardiology and national security. For 47 of these drugs in which data was accessible, APIIC uncovered the supply chain from the API source back to the KSMs and raw chemical inputs.

The findings revealed that 64% of the APIs were sourced from India, 2% from China, and 27% from other countries. However, this only tells part of the story. When examining the intermediates used to produce those APIs, the dependency on foreign sources became more pronounced: 66% of KSMs originated in China, 24% in India, and 10% from other regions. The situation was even more concentrated at the raw chemical level, with 80% sourced from China, 14% from India, and only 6% from other countries.

[29] Ibid.
[30] Ibid.