

May 7, 2025

Secretary Howard Lutnick  
U.S. Department of Commerce  
1401 Constitution Avenue NW  
Washington, DC 20230

**Re: Comment on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients (Docket No. 250414-0065, XRIN 0694-XC120)**

Secretary Lutnick,

Thank you for the opportunity to comment on the Section 232 investigation into the national security implications of pharmaceutical imports. The resilience and security of pharmaceutical supply chains are vital to the health and safety of Americans. These global supply chains are vulnerable to geopolitical forces disrupting the flow of prescription drugs. Addressing such risks is essential, so I commend the Department of Commerce for gathering input on how to proceed.

The comments I submit here are based on over a decade of studying the [economics of drug supply chains](#), the lack of supply chain resilience that results from such economic forces, and drug shortages that often follow. Much of my recent work has been around geopolitical risks and [how the U.S. government should address them](#) to maximize the impact, while minimizing the cost. Most recently I published a [thorough analysis of how tariffs](#) are likely to affect different types of drugs. I enclose three relevant analyses with this letter.

The views expressed in this letter are my own and do not necessarily reflect the views of The Brookings Institution or anyone affiliated with The Brookings Institution.

I make three critical observations about the interplay between tariffs and national security:

1. **China-only tariffs incentivize Indian manufacturers to move away from Chinese active pharmaceutical ingredients (API).** Such tariffs should be further strengthened through legislation, after evaluation for drug shortage risk and appropriate mitigation strategies.
2. **Imposing tariffs on India may have the opposite effect.** Tariffs on India will not only eliminate the incentive described above but create incentives for Indian manufacturers to rely more on China for drug inputs, including API and key starting materials.
3. **Imposing tariffs on India would also exacerbate shortage risk for certain generic drugs.** In fact, the higher the tariffs, the faster manufacturers will drop out of the market because of low margins coupled with contractual and regulatory barriers to passing on tariffs. This in turn would likely result in drug shortages – a consequence that President Trump certainly did not intend.

For these reasons, the U.S. government should proceed with tariffs cautiously, supplementing China tariffs with other policy tools to reshore more of generic drug manufacturing and then supporting its growth and sustainability.

The remainder of this letter provides further support for the claims presented above. I also provide a brief discussion of policies that the U.S. Government should undertake to further enhance the national security of U.S. drug supply chains.

I focus on China and India, presuming that Europe and other OECD countries pose lesser national security risk. But the dynamics described here also apply to those countries vis-à-vis China.

***Observation 1: China-only tariffs incentivize Indian manufacturers to move away from Chinese API***

China-only tariffs, or for that matter a sizable wedge between tariffs applied to China and other countries, have a unique impact on drug supply chains—they drive API demand away from China to other locations.

This dynamic is a result of a long-standing U.S. Customs and Border Protection (CBP) [stance](#) that mixing ingredients into the final drug form (FDF) does not substantially transform the API and therefore the country of origin is the API source. There are exceptions to the API-based country of origin, either because substantial transformation takes place elsewhere in the supply chain or because of trade agreements. But for most drugs with a single chemically synthesized API, the country of origin is where the API was made.

This CBP stance means that a chemically synthesized FDF drug coming from India will pay the Chinese tariff rate if it contains API made in China. Notably, the Chinese tariff rate will apply to the declared value of the FDF drug, increasing the effective API cost for the Indian manufacturer.

The following example illustrates this dynamic. Suppose an Indian manufacturer buys API for 20 cents to make a 30-day supply of a drug that has a declared FDF value of \$1. Under the current tariff regime, there is a 20% tariff on Chinese pharmaceuticals, meaning the Indian manufacturer must pay 20 cents per 30-day supply for having sourced from China—an effective API cost increase of 100% and a strong incentive to source API from elsewhere if high volumes are involved (as there usually are).

What makes tariffs unique as a tool to incentivize Indian manufacturers is the fact that [China does not currently have a significant footprint in API](#), with about 8% of chemically synthesized generic drug volume using Chinese API. [But China's capabilities to make API is increasing](#), as can be seen through their increased number of drug master file submissions to the FDA, submissions that indicate the manufacturer is ready to make the filed API. China-only tariffs could be effective at dissuading uptake of these new API sources.

Having said that, a China [tariff raises shortage risk for select generic drugs](#) with a large share of FDF or API coming from China. For one, manufacturers will be unable to pass the tariff beyond the rate of inflation for drug sales are through Medicaid or the 340 program. Similarly, manufacturers may be under contracts that limit their ability to increase prices. This may lead them to exit the US market, triggering shortages. The U.S. government should study which specific drugs are at risk and then proactively apply mitigating measures, some of which I describe at the end of this letter.

One dynamic working against the effect identified here is uncertainty regarding whether of China-only tariffs and the potential for India tariffs will remain in place for more than a short time. The first one could be addressed through legislation that could eliminate much of the uncertainty. The latter would require a set of commitments from the administration regarding other policies to secure supply chains.

***Observation 2: Imposing tariffs on India may drive Indian manufacturers towards Chinese supplies***

In turn, imposing tariffs on India is counterproductive to efforts to reduce reliance on Chinese APIs.

The first effect of India tariffs will be the elimination of the incentive highlighted in Observation 1—now the Indian manufacturer is impacted no matter where it sources the API.

Furthermore, the Indian manufacturer affected by tariffs will seek cost-cutting measures to preserve its profit margins that will drop because the manufacturer will be [unable to fully pass on tariffs](#) to U.S. buyers. To the extent that China offers price competitive API and other inputs (key starting materials and auxiliary chemicals needed in chemical synthesis of API), Indian manufacturers will have a further incentive to purchase from cheaper Chinese sources. This, in turn, would undo the [recent efforts of the Indian government](#) to derisk their supply pharmaceutical supply chains from China—efforts from which the U.S. benefits.

***Observation 3: Imposing tariffs on India would exacerbate shortage risk for certain generic drugs***

As already mentioned, there are structural barriers in the US market preventing drug manufacturers from passing on cost increases, tariffs included. As previously mentioned, government regulation mandates Medicaid rebates for price increases beyond the level of inflation, which at the time of publication was 2.4%, so less than a tenth of contemplated tariffs. Such rebates also spill over to the 340B program in which most U.S. hospitals participate. Other barriers are contractual, as with group purchasing organization (GPO) agreements that manufacturers sign for drugs sold in hospitals and clinics.

If an affected firm is unable to maintain profitability by cutting costs, it may instead leave the U.S. market. The higher the tariff rate, the more likely exits will happen. Shortages will then result if the drop in production is substantial relative to the market's ability to absorb the supply shock.

Historically, discontinuations [have not been](#) a major driver of shortages, partly because manufacturers have tended to decrease production before exiting, leaving a more vulnerable market but not triggering a shortage. But with tariffs affecting many manufacturers, discontinuations may correlate, magnifying the impact on each.

The ability of supply chains to bounce back from production shortfalls depends on the type of drug. Extensive experience in the generic sterile injectable markets suggests that those markets are particularly [slow to adjust](#) to supply shocks. In part is the lack of capacity in the short term and lack of fungibility in the production process—cancer drugs cannot be made on antibiotic lines or a drug that comes in vials cannot be put into IV bags. With long time frames to expand production and the lack of incentives to do so for generic sterile injectables, it is clear that—should supply disruptions occur—shortages will follow.

***Policy tools for derisking drug supply chains from geopolitical threats***

De-risking drug supply chains from countries such as China should not presume that onshoring is the only solution. This is particularly true for generic drugs with low profit margins, for which the [math for building facilities in the U.S.](#) simply does not work out. But onshoring can be a part of a comprehensive strategy that also encourages so-called [friendshoring](#) or “rerouting of supply chains to countries perceived as politically and economically safe or low-risk, to avoid disruption to the flow of business.”

To improve drug supply chain resilience, the U.S. government should undertake the following actions:

- **Prioritize.** [Prioritizing should include](#) reassessing which drugs are critical, which have substantive research of footprint, and which supply chains are vulnerable. This strategic approach would update the [essential medicines list](#) to include drugs without which the healthcare system cannot function and use data analytics to monitor supply chain vulnerability.
- **Prepare and mitigate** against drug supply shocks that will inadvertently happen, whether they are geopolitical in nature or result from natural disasters. [One element of preparation](#) is having a ready assessment of a situation and a way to engage quickly with the right stakeholders—all aspects well suited for the highly underutilized role of [HHS Supply Chain Resilience and Shortage Coordinator](#). The [Strategic National Stockpile](#) only focuses on pandemics and chemical, biological, radiological and nuclear threats, so it is important to consider buffers for other critical drugs, including through an [API stockpile](#).
- **Invest** in domestic manufacturing, including through upgrades to the existing U.S. infrastructure, with it preventing further offshoring. The U.S. government has funded new [industrial construction through grants](#), but [partially forgivable, low-interest loans](#) are also a promising pathway. Putting tariffs into law would create a “pay for” for such investments. Alternately, the administration could expand the use of [Defense Production Act loans through](#) the [U.S. International Development Finance Corporation](#).
- **Support** domestic investments through subsidies if necessary. Here is where tariffs can be effective as [syringe tariffs have shown](#). But Congressional action is warranted here to leverage Medicare’s heft in the market. One mechanism is an [update to add-on Medicare payment authorities](#) that were previously used under the so called N95 mask rule. More broadly, restoring reliability of drug supplies for essential medicines requires [further refinement](#) and passage of the bipartisan [Senate Finance Committee legislative proposal on drug shortages](#).

Thank you for the opportunity to comment on this important study.

Sincerely,

Marta E. Wosińska, PhD.  
Senior Fellow  
Center on Health Policy  
The Brookings Institution  
[mwosinska@brookings.edu](mailto:mwosinska@brookings.edu)

Enclosures:

1. Wosińska (2025) [Will pharmaceutical tariffs achieve their goals?](#) *The Brookings Institution*.
2. Wosińska, Mattingly and Conti (2023) [A Framework For Prioritizing Pharmaceutical Supply Chain Interventions.](#) *Health Affairs Forefront*.
3. Wosińska (2024) [Drug shortages: A guide to policy solutions.](#) *The Brookings Institution*.

RESEARCH

## Will pharmaceutical tariffs achieve their goals?

Marta Wosińska

March 27, 2025

- Tariffs will provide a strong incentive for increasing U.S. manufacturing of brand-name drugs but not of older, off-patent generic drugs, which represent over 90% of the volume but only a small share of spending.
- Tariff pressure for both domestic and foreign manufacturers of generics will test their already low margins, potentially leading to product discontinuations or cost cutting that erodes quality. Any production disruptions in the already fragile generic injectable markets are likely to result in shortages.
- To onshore generic drug production, the administration will need to deploy tools other than tariffs.

### Introduction

Tariffs, which are taxes on imported goods, are a key part of President Trump's policy agenda. Pharmaceuticals are among the sectors targeted for tariffs. The administration has highlighted at least two objectives for tariffs on pharmaceuticals: securing U.S. drug supply chains by onshoring drug production and creating U.S. manufacturing jobs.

Understanding the impact of tariffs on pharmaceuticals is important because of the role prescription drugs play in the lives of Americans—[61% of American adults ↗](#) (157M) and [20% of children ↗](#) (15M) fill at least one prescription each year through retail or mail pharmacies. Many of the same patients also get drugs administered in [virtually all](#) (<https://www.brookings.edu/articles/federal-policies-to-address-persistent-generic-drug-shortages/>) inpatient hospital stays. And [millions of patients ↗](#) receive physician-administered drugs in the outpatient setting, for conditions like cancer or autoimmune diseases.

At the time of writing this article, there are two potential versions for sector-wide pharmaceutical tariffs. One is a [25% across-the-board tariff ↗](#) on pharmaceuticals. The other comes in the form of not yet defined [reciprocal tariffs ↗](#) that would reflect any subsidies, including tax treatments, that foreign governments use to support specific domestic industries. These proposed tariffs would supplement tariffs already

in place on all Chinese products, set at 20% for pharmaceuticals, and 25% tariffs on Canadian and Mexican products.

Although not spelled out in the announcements, the implied mechanism for accomplishing the administration's goals can be summarized as follows:

- Tariffs push up the price that foreign products cost
- As that price increases, demand shifts away from the more expensive foreign products towards domestic products
- Domestic firms not only gain market share, but also increase their prices, further increasing their profits
- Increased profitability of domestic manufacturers then encourages domestic manufacturers to expand their capacity and new manufacturers to set up production in the U.S., increasing U.S. employment.

In this article, I discuss the extent to which this basic scenario is likely to play out as a result of contemplated tariffs by answering four questions:

- How might tariffs impact drug prices?
- Will tariffs lead to onshoring of pharmaceutical production?
- Will drug shortages result from tariffs?
- Will tariffs help de-risk drug supply chains from China?

To answer these questions, I first describe key structural dynamics in drug markets that will underpin my analysis. I distinguish between newer brand-name drugs, which are currently under patent protection, and generic off-patent drugs, which are inexpensive copies of older branded products that lost market exclusivity. I also describe the structure of the manufacturing part of drug supply chains and the role that FDA plays in overseeing manufacturing.

The analysis of the four questions suggests that prices will rise across drugs if tariffs are extended to India and Europe, but the rise will not be for the full amount of the tariffs. The tariff pressure and political considerations will lead to many onshoring announcements for branded drugs. But we should not expect to see the same for generic drug makers because the return on investment for such major capital investments will be too low and uncertain. In turn, tariff pressure for both domestic and foreign manufacturers of generics will test their already low margins, potentially leading to product discontinuations or cost cutting that erodes quality. Any production disruptions in the already fragile generic injectable markets are likely to result in shortages.

I conclude with a set of considerations for the Trump administration.

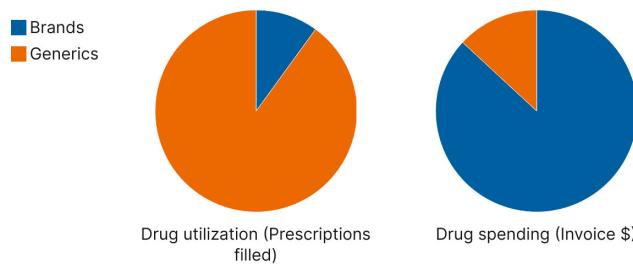
# Prescription drug market dynamics relevant to tariff analysis

To understand how tariffs might raise drug prices or lead to drug shortages, I first lay out some industry dynamics: the distinction between generic and branded drugs, how drug supply chains are organized, and the role of FDA in manufacturing quality oversight.

## We spend money on brands but use generics

When new drugs come to market, they benefit from market exclusivity that prevents others from making copies primarily because of patents. A branded drug may need to compete with other brands, but the level of competition is lower than when they face exact copycats. Once market exclusivity ends, generic and biosimilar versions can come on the market: generic for small molecule drugs, and biosimilar for biologic drugs. Of the about [257 large-molecule biologic drugs ↗](#), [about 6% ↗](#) have biosimilar competition. Of the about 2,900 approved small drug molecules, [about half ↗](#) have generic competition. Within a year or two of generic entry, [prices drop precipitously ↗](#) leading the off-patent branded version molecule to exit the market. Because older drugs are effective for many conditions and because of their price, Americans primarily take small molecule generic drugs. Generics represent 92% of U.S. retail and mail pharmacy prescriptions (Figure 1). They also represent about [three-quarters of volume](#) (<https://www.brookings.edu/articles/federal-policies-to-address-persistent-generic-drug-shortages/>) (doses) in the smaller hospital setting. In turn, spending goes towards patent-protected small molecule and biologic drugs—[over 87% ↗](#) of overall invoice spending in the retail setting is on branded drugs. Invoice prices do not account for various discounts on branded products, but even if those discounts were 25-50%, the wide gap remains—we use generics and spend on brands.

Figure 1: Role of generics in pharmacy drug spending and utilization



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Source: IQVIA (2024), [The U.S. Generic and Biosimilar Medicines Savings Report](#)

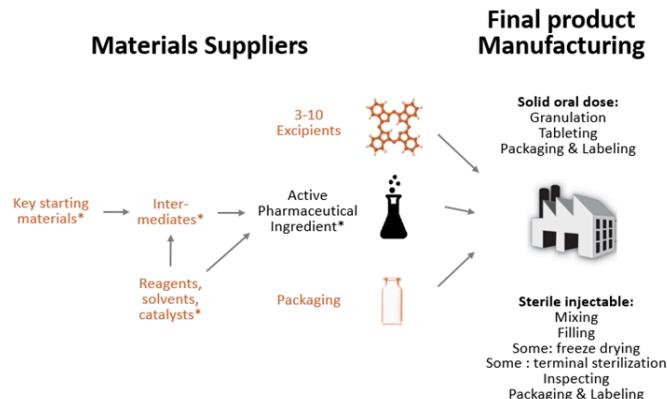
Note: Retail and mail pharmacy spending and utilization; does not include physician-administered drugs

## Drug supply chains are complex

The drugs distributed at a pharmacy counter or administered in a hospital are finished dosage form (FDF) drugs. FDF drugs contain one or more active ingredient (API) and between 3 to 10 excipients (<https://www.brookings.edu/articles/drug-shortages-a-guide-to-policy-solutions/>) that have no therapeutic effect but either serve as fillers, diluents, or otherwise affect functionality of the product, such as stability or dissolution rate (see Figure 2).

The API is product specific. It is the acetaminophen in Tylenol, semaglutide in Ozempic, or atorvastatin in Lipitor. API for small molecule drugs is chemically synthesized, often involving multiple steps, using a series of chemical reactions where key starting materials are transformed into intermediates and then API using various auxiliary agents that enable the chemical synthesis: reagents, solvents, and catalysts (see Figure 2). Biologic drugs are somewhat different in that the API step is complex but has fewer stages—it involves culturing the drug substance in living cells and then purifying that drug substance.

**Figure 2: Typical drug supply chain for small molecule drugs**



Note: Items marked in orange are not used exclusively in drug supply chains. For biologics, steps marked with \* would be replaced with cell culture and purification, all done in one facility.

Relevant to supply chain resilience and onshoring costs is the fact that FDF can have different formulations, each using a different production process. Most of what consumers use are tablets and capsules, but many drugs are either injected or infused. There are also creams, oral solutions, drops, ointments, and other specialized formulations. Also relevant is that manufacturing processes for FDF can be specialized to type of formulation and type of drug, e.g., sterile injectables are made with very different machinery than oral dose products, some drugs are freeze-dried, some can be sterilized with heat, but others are made in a sterile environment, and some require dedicated lines or even buildings to prevent cross-contamination.

What is relevant for segment-specific tariffs is that only FDF and API products are specific to pharmaceuticals, with the rest of the supply chain (marked in orange in Figure 2) shared with other industries. Excipients, such as starch, lactose, or titanium dioxide, are used in foods and cosmetics. Key starting materials and enabling chemicals are all fine chemicals with many industrial uses.

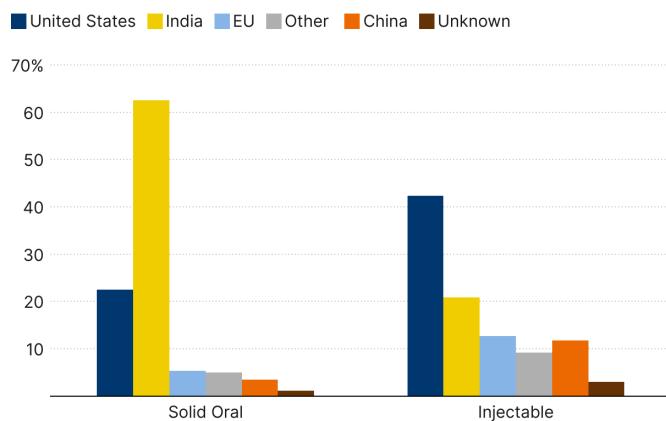
### Where drugs are made varies by type and stage

Generic solid oral dose drugs have the largest [footprint ↗](#) with American patients. These drugs include statins for high cholesterol, multiple blood pressure medications, metformin for blood sugar control, levothyroxine for thyroid disorder, and SSRI drugs for depression and anxiety. About 187 billion generic drug tablets and capsules were dispensed in retail and mail pharmacies in 2024 (source data from Figure 3), equating to about 550 pills per person or 1.5 chronic medications.

As Figure 3 indicates, generic solid oral drugs are now primarily made in India. The U.S. makes 22% unit share of generic solid oral dose drugs, a big share of it controlled substances like opioids and ADHD medications, due to Drug Enforcement Agency requirements that those products are domestically produced. China represents a 3.5% unit share, which is less than Europe's 5.4% unit share.

Sterile injectable generics, such as IV antibiotics, saline, chemotherapy agents, lidocaine, and epinephrine, are still largely made in the U.S. (Figure 3). Part of it has to do with the complexity of production relative to oral dose products and the much higher transportation costs for such drugs. But offshoring has followed, with India taking a leading role in the trend, currently at 20.9% unit share. China is almost on par with Europe when it comes to generic injectables, 11.8% and 12.7% respectively.

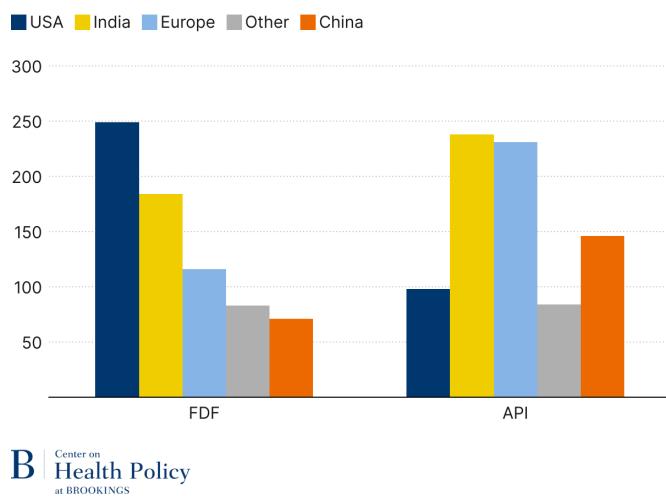
**Figure 3: Generic drug volume by location (2024)**



Note: Solid oral dose volume is measured in tablets/capsules; injectables are measured in dispensing units (vials, syringes, or IV bags)

What is more difficult to ascertain is where API for generics comes from. Using FDA Generic Drug User Fee Act [facility payment data ↗](#), we can assess the location of facilities making FDF and API for generic drugs. A comparison between FDF and API is particularly instructive. As Figure 4 indicates, the U.S. has the highest share of FDF facilities, but its share of API facilities is less than half of what Europe and India have. Even China has more generic API facilities than the U.S.

**Figure 4: Generic facilities by stage of production (2025)**



Source: FDA GDUFA facility fee payments (2025)

Note: Some facilities produce FDF and API and are counted in both

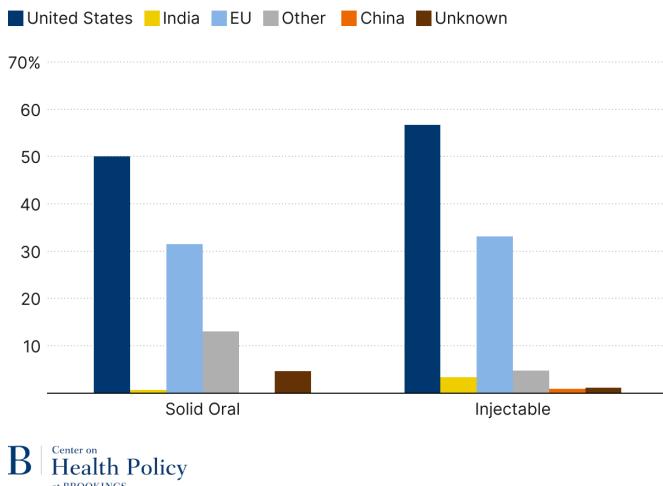
It is important to note that Figures 3 and 4 show geographic distribution across all drugs, but geographic distribution for a given drug molecule may be far from what those figures represent. For example, underlying Figure 3 is U.S.-based Baxter with a [60% market share ↗](#) of 1L saline bags, U.S.-based Hospira with a [50% market share ↗](#) of injectable morphine, and Indian-based Intas with a [50% market share ↗](#) of carboplatin. Sources of API may vary across drugs or therapeutic classes. One analysis of 32 essential medicines found that steroids had API sourced almost exclusively in Europe, API for anticonvulsants came primarily from India, and production for API dialysis agents was split between the U.S. and Europe.

There is lack of visibility into where inactive ingredients and starting materials for API come from. Discussions with industry executives suggest that excipients largely come from the U.S. and other OECD countries, but China dominates the fine chemicals market which includes key starting materials and auxiliary chemicals needed for chemical synthesis of intermediates and APIs (Figure 2).

The FDF location picture (Figure 5 below) looks dramatically different for brands—the U.S. leads in both oral dose and injectable markets, India's footprint is minimal, and China's is basically nonexistent. Canada and Mexico (listed in Other) play a greater role in oral dose markets, with 1.8% and 2.4% share overall. Europe plays a significant role, with almost a third of units sold in both market segments. Data underlying Figure 5 suggests that Ireland leads with more than a third of Europe's exports of branded oral dose drugs. Among injectables, leading European exports are Denmark, Germany, and Italy. The high declared value of branded drugs has helped make pharmaceuticals the largest European export category ↗.

When interpreting these shares, it is important to keep in mind that they are aggregated across all branded drugs. For a given brand-name drug with no generic competition, it is quite likely that production is concentrated to one or two manufacturing sites, and chances are that the share of brands produced both in the U.S. and abroad is relatively small.

**Figure 5: Branded drug volume by location**

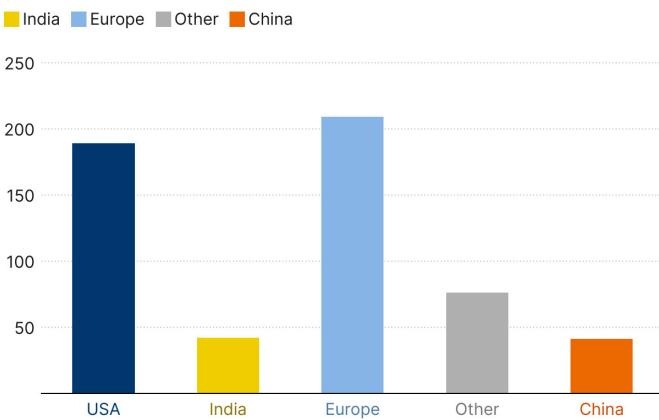


Source: USP Medicine Supply Map using IQVIA & USP data; published by permission.

Note: Solid oral dose volume is measured in tablets/capsules; injectables are measured in dispensing units (vials, syringes, or IV bags)

The picture on the brand API side (Figure 6) has a similar shift to that we see when we look at API generic—the U.S. has a smaller footprint than on the FDF side, Europe has a larger one, as does China. As with generic API data, the data are not volume weighted.

**Figure 6: Confirmed API facility count for branded products by location**



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Source: Redica Systems; published by permission.  
Note: Only includes facilities confirmed to make NDAs or BLAs  
based FDA compliance records

### Active ingredient location is center stage for tariffs on pharmaceuticals

When goods enter a U.S. port of entry, they are classified using a standardized system called the [Harmonized Tariff Schedule ↗](#) (HTS). Importers classify their goods according to the HTS and declare their value or quantity. The applicable duty or tariff they then owed to the Customs and Border Protection (CBP) is based on the HTS classification and the country of origin.

The determination of the country of origin and, therefore, the appropriate duty or tariff is not straightforward in that the country of origin is not necessarily where the product is imported from. Instead, the country of origin is determined by where [substantial transformation ↗](#) of the product happened. In some cases, the substantial transformation is relatively obvious—cars made in Germany are a product of Germany, even if parts (engine, tires, airbags) come from other countries. In other cases, substantial transformation might be before the final product. For example, if Brazilian nuts are mixed with salt and packaged in Australia, they are a product of Brazil.

The country of origin for prescription drugs follows the nuts example more closely than the cars example. CBP has long [ruled ↗](#) that mixing ingredients into the final drug form does not substantially transform the API and therefore the country of origin is the API source. This means that an FDF drug coming from India will pay the Chinese tariff rate if it contains API made in China. The determination for the country of origin is different for [government procurement rules ↗](#).

There are exceptions to the API-based country of origin, either because substantial transformation takes place elsewhere in the supply chain or because of trade agreements. Drugs that involve multiple APIs will have the mixing stage as the country of origin. The complexity of the production process can also shift substantial transformation up or down from the API stage. For example, processing of APIs not

suitable for human consumption, as with purifying and freeze-drying [↗](#) vancomycin, has been ruled to constitute the FDF be substantial transformation. The rules for products under the U.S.-Mexico-Canada Agreement (USMCA) can also differ.

Nonetheless, it is quite reasonable to use the API production country as the country of origin for single-API drugs finished in countries other than Mexico or Canada.

Of note, however, is that these rules could change.

### **Manufacturing of drugs has strict manufacturing standards for good reasons**

As we consider the response from firms to tariffs, whether it is in terms of cutting costs or onshoring their supply chains, it is important to understand the role of the Food and Drug Administration (FDA).

FDA plays a critical role in addressing a major information gap resulting from the patients' and physicians' inability to observe drug product integrity, not only before consumption, but also after. Not every drug works the same for every patient, and the patient's condition or response to the drug may change over time for physiological reasons. Because of that, when a patient stops responding to blood pressure medication, the physician will think to switch the patient to a different drug without suspecting that the drug may not be manufactured properly.

FDA requires that manufacturers of approved drugs (brands and generics) follow regulatory standards for ensuring the identity, strength, quality, and purity of drugs. This set of standards, called the [Current Good Manufacturing Practices \(CGMP\)](#) [↗](#), covers a broad range of controls over how drugs are manufactured. This includes establishing strong quality management systems, ensuring quality raw materials, having written operating procedures, identifying and investigating product quality problems, and maintaining reliable testing laboratories. This framework [evolved](#) [↗](#) as a result of many crises and many hundreds of deaths of Americans exposed to contaminated or substandard drugs.

But as with any laws, enforcement is key.

To assure that manufacturers follow CGMP standards, new-to-market drugs (brands and generics alike) must establish that their production process [can reliably replicate](#) [↗](#) the drug matching the safety and efficacy claims made on the drug label. FDA generally establishes that through pre-approval inspections of API and FDF facilities, but FDA [might forgo a pre-approval inspection](#) [↗](#) if it has reliable information about the facility and processes from other sources.

Once the product is on the market, FDA conducts [surveillance inspections](#) ↗ to assess compliance with manufacturing processes and the integrity of products on the market. FDA also makes sure that any changes to the API or FDF production process do not alter the product's safety or efficacy. FDA [requires manufacturers to report](#) ↗ manufacturing process or setting changes, the more consequential of which may require an FDA inspection.

## How might tariffs impact drug prices?

Two main factors determine whether tariffs will increase prices: tariff exposure and the ability of manufacturers to pass on price increases.

Tariff exposure reflects the extent to which production of a given drug is exposed to various tariffs. For a brand-name drug, the exposure may be quite uniform because there is only one version of the drug on the market, so it may be produced at just one site. For a generic drug, the exposure may vary because there may be many generic versions of a drug.

In the context of tariff exposure, it is worth underscoring the importance of API location. Under the current CBP rules, the country of API manufacture is generally the country of origin for a single-API drug not made in Canada or Mexico.

The ability to pass on tariffs onto buyers will depend on how competitive the markets are, how constrained production is in the short term, and the extent to which there are contracts or government regulations that limit manufacturer's ability to raise prices. These factors will differ for brand-name drugs, generic oral dose drugs, and generic injectable drugs. For that reason, my analysis addresses these groups separately.

### Brand-name drugs

As Figure 5 indicates, most FDF volume for brands is already produced in the U.S., followed by production in Europe. Although no such data exists for brand API sources, the U.S.-Europe dominance likely persists.

Under the current rules, the tariff exposure for a branded drug made in Europe would depend on where the API is manufactured. An FDF drug made in Europe will have the U.S. as the country of origin if the substantial transformation takes place in the U.S. This scenario, probably not common for drugs shipped from Europe, illustrates how consequential country of origin might be for a brand-name drug with a high price point—if the API is made in the U.S., the tariff is zero, but if the API is made in Europe, and a 25% tariff applies, a \$10K drug would owe a \$2,500 tariff.

A drug finished in the U.S. will not pay tariffs on its final product, but it may still be exposed to tariffs on its ingredients. For a branded drug, the cost of goods sold is very low relative to the price so there would not be much price pressure from input cost changes on the product's final price. What might change, however, is how firms use internal transfer prices for API. Firms use transfer pricing to minimize their tax burden and may transfer API that costs them \$100 to produce at close to final finished price. A tariff on API would change that equation, putting downward pressure on the transfer price of API.

If the \$10K drug is faced with a \$2,500 tariff, how much will its U.S. price rise? It depends.

One factor influencing the level and form of tariff passthrough is the competitive landscape faced by the affected drug product. Although a monopoly on a molecule-level, a drug may face competition from other branded drug molecules treating the same condition. For example, Novo Nordisk's Wegovy directly competes with Eli Lilly's Zepbound. If most of Wegovy's volume were subject to tariffs but the majority of Zepbound's volume were not, then Novo would find it challenging to increase the effective Wegovy price to payers.

If both molecules have high tariff exposures, we could expect the impact to be through lowered rebates, not higher list prices. That is partly driven by [Medicaid](#) and [Medicare](#) inflation rebates, which manufacturers must pay if prices of their products rise faster than the consumer price index (CPI). Those rebates limit their passthrough through list prices.

In a scenario where a brand faces little competition, rebates are low so increasing list prices is the only way to pass through the tariff. Here, again, inflation rebates would limit passthrough beyond the CPI. Manufacturers would also be limited in their passthrough in the commercial market, albeit indirectly. A large swath of purchasers (entities such as certain types of hospitals, clinics, and affiliated retail pharmacies) are eligible for the so-called [340B program](#), which allows qualifying entities to obtain drugs at a discount pegged to the Medicaid inflation rebate. This means that every unit used by a commercial patient in a 340B entity will be subject to 340B rebates.

Political considerations may also dampen tariff passthrough. [Experience from](#) the Clinton era health care reform shows that political considerations can limit manufacturers' willingness to increase prices. And currently there is a lot at stake for branded manufacturers who are interested in changes to Medicare drug negotiation and the 340B program.

## Generic injectable drugs sold to hospitals and clinics

As Figure 3 indicates, 42% of FDF production for generic sterile injectables is already done in the U.S. These products would not face tariffs on their FDF, although they would face input cost increases if sourcing from abroad—quite likely given the small generic API footprint in the U.S. (Figure 4). With low margins and a high share of API in its cost of goods sold, a tariff on API will likely put upward price pressure.

Currently, at least 15% of generic injectable volume is facing tariffs—the 13% coming from China and more than 3% coming from Canada. But China represents a much higher share of API facilities than FDF facilities (Figure 4), suggesting that more products may currently be exposed to tariffs. For instance, it is often noted that [China has a hold ↗](#) on API production of antibiotics.

Across the three market segments, GSIs face the greatest challenge in their ability to pass on price increases. One reason is immediate—group purchasing organization (GPO) contracts. All [hospitals use GPOs \(<https://www.brookings.edu/articles/federal-policies-to-address-persistent-generic-drug-shortages/>\)](#) to contract for sterile injectable generics used in inpatient settings, with those contracts locking in prices but not quantity. Hospitals not part of the 340B program also use GPO contracts to secure prices of generic injectables used in the outpatient setting.

Those contracts generally last [one to three years \(<https://www.brookings.edu/articles/federal-policies-to-address-persistent-generic-drug-shortages/>\)](#) and may limit price increases, unless courts consider tariffs as falling under [force majeure ↗](#)—a standard provision in contracts that frees parties from contractual obligations because of an extraordinary event that prevents one or both parties from fulfilling contractual obligations.

Even if GPO contracts could be sidestepped, certain generic injectables would face another obstacle—Medicaid inflation rebates and the 340B program. The Medicaid program exposure for generic injectables is unclear, but the resulting 340B exposure can be significant, especially generic chemotherapy agents and so-called supportive drugs designed to protect the body from chemotherapy or radiation therapy.

### Solid oral dose generics

As Figure 3 shows, almost 80% of all the generic drug tablets and capsules we consume in the U.S. come from abroad. Given the small API facility footprint in the U.S. (Figure 4), it is unlikely that many or any of the imported products use U.S.-based API.

The unit share of products from China, Canada, and Mexico, around 3.5%, 2.5%, and close to zero, underestimates the exposure of existing tariffs. One reason is that China has a greater representation in API than with FDF. India imports about [a third of API ↗](#) by volume, with [around 75% of it from China ↗](#).

For a given drug, the upward price pressure of current and potential tariffs will depend on the market share of the versions with tariffs and the capacity of non-exposed manufacturers to take on that volume. For this reason, even what appear limited share of Canadian products might matter. For example, if Teva's [Canadian-made amoxicillin](#) has a large market share, buyers may not have less expensive options to turn to and, therefore, tariffs will put upward pressure on prices across all producers. If we see tariffs rolled out to Indian and European generics, the tariff exposure should be high across virtually all oral dose generic markets.

Unlike branded drugs and generic injectables, the ability of oral dose generics to pass on price increases to buyers is less constrained, except for markets with high Medicaid exposure, of which amoxicillin is one. In contrast to generic injectable markets, the retail generics market largely operates as a spot market, with few long-term contracts signed. Additionally, generic drugs are [exempt from Medicare inflation rebates \(<https://www.brookings.edu/articles/drug-shortages-and-rebates/>\)](#), unless only one generic is on the market. They also have much less exposure to the 340B program than brands and injectable generics.

### Impact on buyers and payers

It is worth considering how increases in U.S. drug prices might affect buyers and payers.

Retail pharmacies buy generics on what is pretty much a spot market so any increase in prices will show up quickly in their acquisition costs. However, pharmacies are reimbursed based on contracted rates that are either a share of list price or fixed reimbursement rate. The impact will be immediate as prices rise, challenging pharmacy margins at least until contracts are renegotiated.

For hospitals and clinics, branded drug costs are passed to payers but there is a lag in reimbursement, e.g., Medicare has a six-month lag for the reimbursement rate to adjust to the average sales prices. For generics, hospitals are protected in the short run through contracts that GPOs negotiate with manufacturers. 340B hospitals are protected in the short run and the long run, but only for price increases above the CPI.

Exposure to increased prices varies by payer. As discussed above, Medicaid is protected above CPI, which means less so if the U.S. also experiences higher inflation. Medicare is protected above CPI for brands and single source generics. But any increase in prices up to the CPI will translate into higher government spending on drugs. Commercial plans will have limited protection through the end of the year when its pharmacy contracts and rebate agreements expire.

Increases in drug prices would probably be most visible to patients taking branded products because increases in list prices would directly translate into higher out-of-

pocket spending for patients in high deductible plans or with high coinsurance rates. Patients taking generics would also notice quickly if they were in high deductible plans, but the impact would be less given the low generic drug price points.

The primary impact on patient pocketbooks would be indirect—premiums would likely rise as the payer spending on drugs increases. The impact would depend in large part on whether tariffs are expanded to drugs coming from Europe and India, with it expanding the tariff exposure. It is also worth noting that commercial payers would likely face the greatest upward spending pressure, not only because they do not face the kinds of protections that Medicaid and Medicare have, but also because prescription drugs make up a much more significant share of their medical spending than what is seen in [Medicaid ↗](#) and [Medicare ↗](#).

## Will tariffs lead to onshoring of pharmaceutical production?

To understand how tariffs affect manufacturing location decisions, it is best to use the framework that firms use to make any investment decision: Is the expected net present value (ENPV) greater than ENPV in locating (or maintaining location) in other markets?

Tariffs can positively improve relative ENPV if:

- Firms expect an increase in profits from locating in the U.S.
- Firms expect the incentive will last long enough to ensure a positive return on investment
- The costs to enter the market are low enough relative to future profits to ensure a positive return on investment
- The ENPV of the current position worsens.

### Brand-name drugs

The discussion of tariffs in the previous section suggests that the economic incentive for onshoring can be significant for a brand-name drug with a high profit margin. If tariffs were to be expanded to Europe, having both API and FDF production there for a given drug would prove costly. Using the example of a \$10K drug with \$100 API, a 25% tariff on a \$10K final price drug would translate into a twenty-six-fold effective API price (from \$100 to \$2,600).

There is also a less direct incentive to onshore—the political value of onshoring. Manufacturers of branded drugs have several [key policy priorities ↗](#): revising the Medicare drug negotiation program, reforming the 340B program, and pharmacy

benefit manager reforms. Unlike tariff policy, which could change easily, any changes to Medicare drug negotiation or the 340B program would be long-lasting.

And what would it take to onshore?

For tariff purposes, perhaps the easiest path to onshoring would either be through a domestic contract manufacturer or purchasing existing infrastructure. We could also see a shift in existing U.S. production lines, to the extent that U.S. manufacturing sites make product not just for the local U.S. market but also for other countries. None of these approaches are costless or immediate—they require technology transfers, which can take a year or more and are limited by the availability of suitable production lines. But they are cheaper and faster than breaking ground on new sites.

Building a manufacturing plant can cost upward of a billion dollars. Recently infrastructure expansion includes Eli Lilly's [\\$23 billion ↗](#) investment into multiple facilities Merck's [\\$1 billion ↗](#) plant, [\\$4.1 billion ↗](#) Novo Nordisk's fill-and-finish plan expansion, Johnson & Johnson's [\\$2 billion ↗](#) biologics facility, FUJIFILM [\\$1.2 billion ↗](#) expansion of a biotechnology site, and Amgen's [\\$1 billion ↗](#) biotechnology site expansion. Site construction costs may further increase with steel tariffs because industrial construction relies heavily on steel, now subject to 25% tariffs. The same concern applies to manufacturing equipment, which is all stainless steel.

There are several factors in determining a location for a new facility. One factor is [permits ↗](#). Conversations with industry executives reveal that building a manufacturing plant from the ground up generally takes three to five years, much of it related to the local permitting process for utilities, disposal, and other community concerns. What makes local permits challenging is that they can vary dramatically across locations, increasing the risk for potential delays.

Another factor in determining location is workforce. Much of recent U.S. pharmaceutical infrastructure investment has been limited to specific localities, primarily North Carolina and Indiana, not only because of low land prices and firms' experience with local permitting, but a local, [educated workforce ↗](#), developed in partnership between industry and [local ↗ universities ↗](#). The jobs that these kinds of plants create differ from older manufacturing jobs. They require a [highly skilled ↗](#) and educated workforce—more engineers and scientists than high school graduates.

## Generic drugs

The cost to construct a manufacturing site is not any different for branded drugs than generic drugs. What matters more is the type of technology the drug is using. The complexity of API facilities will depend on the complexity of molecules involved, whether simple small molecules, complex ones, or biologics. A fill-and-finish facility is the same for brands and generics, no matter how complex the API.

There are two main reasons why generic manufacturers have been increasingly investing in India for small molecule API and FDF. One is cost. You can [build a facility in India ↗](#) for a fraction of what it costs in the U.S. because of much cheaper land, labor, and parts. You can build a facility much faster because there are far fewer local permits holding up the process. The other reason is a lower opportunity cost—generic drugs have low margins, so the cost of a shutdown due to manufacturing quality or infrastructure problems is less than for a branded drug.

But could tariffs change the onshoring calculus the way it changes incentives for branded manufacturers? The short answer is no.

To manufacturers of generic drugs, incentives for onshoring production are significantly lower than for manufacturers of branded products. The \$10K drug example with \$100 API is illustrative here. Whereas the effective increase of API cost was 26 times for a brand (from \$100 to \$2,600), a generic with the same API cost but a much smaller margin (say 20%) will face an effective API cost increase of 30% (from \$100 to \$130).

The margin upside from locating in the U.S. will be limited for other reasons. First, domestic manufacturers obtain a big share of their inputs from outside the U.S. Even if those inputs had U.S. options, those options would likely be more expensive than the foreign ones, especially on the fine chemicals side. In the meantime, generic manufacturers will keep facing price pressure from the consolidated buyer base, and unless Congress acts, some generic drugs, including those made domestically, will continue to be limited in their ability to pass on legitimate cost increases.

The strategies that branded manufacturers could use in the shorter term, like contracting with third parties or making production more local, are much less likely to work for generic manufacturers. For one, U.S. generic drug facilities likely export very little, meaning there is little to be gained from reorganizing which plants make which products. Using data supporting Figures 3 and 6, we calculate that the capacity needs for onshoring generics would be immense, with capacity needs for generic pills 27 times larger than for branded pills. Any available contract manufacturing capacity would likely go to branded products first, given their ability to pay.

Given the value of onshoring to brands, generic manufacturers would easily be outbid for any available capacity. Access to capital would also prove a challenge given the price tag involved and the financial situation of many generic firms. A branded company that has been heavily investing in U.S. infrastructure is Eli Lilly, with [\\$37B in profit ↗](#) in 2024. In comparison, Amneal had a [\\$117M loss ↗](#) in 2024, Sandoz made [\\$1M ↗](#), Hikma made [\\$612M ↗](#), and Teva lost [\\$1.6B ↗](#).

Given the uncertainty about the duration of tariffs, it is not clear that the long-time horizon necessary for capital investments is favorable for capital-intensive onshoring

of what will continue to be low margin products.

## Will drug shortages result from tariffs?

Drug shortages happen (<https://www.brookings.edu/articles/drug-shortages-a-guide-to-policy-solutions/>) when supply chains cannot absorb shocks to supply or demand.

To understand the potential for shortages, we need to understand whether tariffs could contribute to supply disruptions and whether drug markets are sufficiently resilient to absorb any such supply disruptions.

As described in the pricing section, prescription drugs face various constraints in their ability to pass on cost increases to its buyers, especially in the hospital setting. In this context, we may see the profitability of drugs, especially sterile injectable generics, to be challenged.

A firm facing margin pressure may work to source from a lower cost environment, but in the short term, the firm faces two options: further cut costs or exit the U.S. market.

The potential for further cutting costs is concerning because it can adversely affect product quality [if cost cutting happens ↗](#) through equipment maintenance, quality of materials, process control, or quality assurance. If problems arise, for example, the product is contaminated with other API, bacteria, or metal shavings (all actual examples), manufacturers may temporarily shut down or slow down production, leading to a potentially dramatic drop in output. But if FDA oversight is concurrently weakened, economic theory and experience suggests we should expect product quality to decrease.

Another bad option is to discontinue production of the unprofitable drug. Historically, discontinuations have not been a major driver of shortages, partly because manufacturers have tended to decrease production before exiting, leaving a more vulnerable market but not triggering a shortage. But companies may be less shy about exiting if they can blame tariffs they cannot control. Discontinuations of production by manufacturers with smaller shares can occur in close succession, magnifying the impact on each.

Can markets adjust to temporary shutdowns and permanent discontinuations so that shortages do not result?

Extensive experience in the generic sterile injectable market suggests that the generic injectable market is particularly [slow to adjust ↗](#) to supply shocks. Part is lack of capacity in the short term and lack of fungibility in the production process—cytotoxic drugs cannot be made on antibiotic lines or a drug that comes in vials cannot be put into IV bags. With long time frames to expand production and the lack of incentives to

do so for generic sterile injectables, it is clear that—should supply disruptions occur in sterile injectable markets—shortages will follow.

## Will tariffs help de-risk drug supply chains from China?

De-risking drug supply chains from China is very different than onshoring pharmaceutical production in the U.S. As described above, the exposure of drug supply chains to China is primarily in small molecule drugs through key starting materials and auxiliary materials. Conversations with industry executives suggest that China dominates the fine chemicals industry of which those inputs are part. Exposure of drug supply chains to China diminishes as production shifts from chemicals to drug manufacturing, but both API [↗](#) and FDF footprint have been growing.

Much of the exposure to China is indirect because much of the API and FDF production for generics takes place abroad. This means that it is the Indian and European companies that source chemicals from China. The governments of those countries have recognized that exposure and have put forward plans to reduce their dependence on China. Since 2020, [India has actively been ↗](#) decreasing its reliance on China, largely through subsidies for infrastructure. The [EU's proposal ↗](#) has not yet been implemented but it intends to use subsidies to strengthen supply chains of select critical medicines, including antibiotics, which are known to have high China exposure.

The impact of tariffs on exposure to China depends on how they are structured.

China-only tariffs, or for that matter, a substantial wedge between China tariffs and other locations, have a unique impact on drug supply chains—they drive API production away from China to other locations. We might see a lot more friendshoring than reshoring if China-only tariffs are in place because low-cost options would exist.

In turn, sector-wide pharmaceutical tariffs could end up being counterproductive to de-risking efforts. One reason is that China exposure is primarily indirect, through other countries, and, therefore, tariffs on U.S. imports have no impact other than on API sourcing. Decreasing reliance on countries actively subsidizing de-risking initiatives means that the de-risking burden would need to shift to the U.S. Decreasing U.S. exposure to inexpensive Chinese fine chemicals would require a much broader strategy, well beyond the reach of pharmaceutical tariffs.

## Considering next steps

Many observers will raise higher prices as an argument against tariffs. I take a more nuanced approach—we may have to accept higher prices for generic drugs if we want to have resilient supply chains.

However, I am worried that without further policy interventions, tariffs will not make supply chains more resilient. In fact, I am worried that the resilience of many supply chains, already weak for drugs like sterile injectable generics, will be significantly challenged.

Of course, the scope and level of tariffs will matter for how they affect specific markets in the short and long run. It will also depend on the structure of specific markets, with generic sterile injectable drugs at the most risk of disruption that might lead to shortages. Most importantly, the impact will depend on what other policy actions the administration and Congress might take to buffer the supply chain.

This paper is not intended to provide a comprehensive policy proposal for how to supplement the tariffs, but four main themes arise if the administration intends to move forward with across-the-board pharmaceutical tariffs affecting branded and generic drugs alike.

First, the administration should add pressure valves to prevent shortages. This is important because generic margins will be threatened, leading manufacturers to pull unprofitable products from the market. A big factor here is the limited ability of manufacturers to pass on tariffs onto buyers. Some of it has to do with private contracts, but it also relates to the congressionally mandated Medicaid inflation rebates on multisource drugs and the spillover they have on sales to 340B entities. Another policy to consider is substantially delaying tariffs on API used by domestic manufacturers, with it improving their profitability.

Second, the administration should increase, not decrease, FDA's capacity to oversee drug manufacturing. One reason is that generic drug margin squeeze may lead manufacturers to cut costs by cutting corners, which, especially if coupled with weakened FDA oversight, could lead to a higher rate of substandard drugs being shipped to American patients. Another reason is that any onshoring of facilities will increase the existing demand for FDA services—services that are critical for assuring that facilities are set up to consistently manufacture products to specification, with that assuring the safety of drugs that American patients take.

Third, the administration should directly finance generic drug onshoring, in recognition that tariffs alone will not create a sufficiently strong business case to attract private investment in pharmaceutical infrastructure. Identifying sources of funding for such initiatives can be challenging. However, here, branded drug tariffs will likely generate significant revenue, which could then be used to stimulate onshoring of generics.

The fourth point is perhaps the most challenging—de-risking drug supply chains from China will be significantly more challenging, if not counterproductive, without collaboration with India and Europe.

## AUTHOR



**Marta Wosińska** Senior Fellow - Economic Studies, Center on Health Policy  @MWosinska

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## A Framework for Prioritizing Pharmaceutical Supply Chain Interventions

[Marta E. Wosińska](#), [T. Joseph Mattingly II](#), [Rena M. Conti](#)

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The assured, consistent availability of pharmaceuticals is a cornerstone for patient wellbeing, effective treatment, and equal access to needed medical care. Pharmaceutical supply disruptions compromise medical care and may place patients' health and even their lives at risk through treatment delays, [rationing](#), increased likelihood of [medication errors](#), and the substitution of possibly [inferior alternatives](#).

Yet, pharmaceutical supply chains in the United States (US) are [vulnerable to disruptions](#). Shortages in some pharmaceuticals have disrupted medical care delivery for decades, with no sign of abatement. In 2023 alone, a [tornado ripped through a North Carolina facility](#) that produces a sizable share of several dozen sterile injectable drugs used in US hospitals; quality assurance issues led to the [suspension of production in an Indian plant](#) representing about half of the cisplatin (generic chemotherapy) supply; and one of only two suppliers of liquid albuterol (generic asthma drug) [went out of business](#). Geopolitical instability and trade challenges also affect pharmaceutical supply chains.

Economic considerations drive these challenges. Manufacturers' incentives to maintain or increase profits lead them to pursue economies of scale and produce in low-cost environments, including offshore, or exit altogether. [Generic manufacturers](#) facing [low profit margins](#) do not stand to reap strong financial rewards from [investing in quality systems](#), creating backup ingredient sourcing, or carrying buffer inventory of ingredients.

When industry-specific economics are not adequate to achieve a societal need, governments often step in. Because of the role that the government can play, experts have called on the federal government to reduce supply chain vulnerabilities through promoting [better coordination](#) and mitigation strategies, creating [buffer inventories](#), [incentivizing hospitals](#) to purchase from more

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reliable manufacturers, and providing financial assistance to subsidize production and [improve infrastructure](#).

Yet, for the US government to engage, policymakers need to assess which tools to employ, and which supply chains to support. [Prioritization](#) is important given the complexity and size of the pharmaceutical industry. The US Food and Drug Administration (FDA) is responsible for the [oversight of more than 20,000 prescription drug products, with more than 13,000 facilities](#) registered to make either active pharmaceutical ingredients (APIs) or finished-dose drug products. Beyond that, there are countless facilities making inactive ingredients, precursor materials, and packaging.

To help determine how the US government should proceed with prioritizing pharmaceutical supply chains for intervention, we provide a framework that builds on the [work of the National Academies](#) of Science, Engineering, and Medicine (NASEM) and helps generalize some existing prioritization efforts. After describing the main essential drug lists (the World Health Organization (WHO), the FDA, the Agency for Strategic Preparedness & Response (ASPR), and the US Department of Commerce), we discuss how those lists fit within a framework that distinguishes among drugs based on their criticality, reach, and supply chain vulnerability. We refer to this as the Criticality-Reach-Vulnerability (CRV) framework.

## Government Efforts to Define Essential Drug Lists

An early attempt at defining essential drugs was the 1977 [WHO list](#) of essential medicines. As described by the WHO, the list, now with 502 drugs, presents the “minimum medicine needs for a basic health-care system, listing the most efficacious, safe and cost-effective medicines for priority conditions,” selected using “current and estimated future public health relevance, and potential for safe and cost-effective treatment.”

The first US government effort to define essential drugs came more recently, prompted by President Trump’s [August 2020 executive order](#). The president directed the FDA to identify the drugs needed in the face of “outbreaks of emerging infectious diseases and chemical, biological, radiological, and nuclear (CBRN) threats.” The [FDA list](#) identified 227 drugs that, as [the agency describes](#), “are most needed for patients in US acute care medical facilities, which specialize in short-term treatment for severe injuries or illnesses, and urgent medical conditions.”

The FDA list was further refined by what is now the [Agency for Strategic Preparedness & Response \(ASPR\)](#) in response to President Biden’s [February 2021 executive order](#) directing vulnerability assessments of critical supply chains across the economy. [ASPR engaged](#) clinicians and pharmacists in culling down the FDA list and making some substitutions, arriving at 86 drugs “considered as either critical for minimum patient care in acute settings or important for acute care, with no comparable alternative available.” ASPR and its partners then conducted thorough vulnerability assessments for a subset of these drugs.

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A less well known effort, also in response to the [February 2021 executive order](#), is the US Department of Commerce's draft list of critical goods and materials in sectors that include public health and biological preparedness. The Commerce department [is still developing](#) this list of critical goods and materials, which "will serve as a tool to facilitate ongoing targeted analysis of trade data and the evaluation of policies to strengthen these supply chains."

## A Pharmaceutical Supply Chain Prioritization Framework

Our framework builds on one presented in the 2022 consensus NASEM [study report](#). That report recognizes that resources are limited and recommends that policymakers prioritize pharmaceuticals for which the product of three independent elements is greatest: the expected patient harm from a shortage, the number of affected patients, and the probability of expected supply shortage in any given year.

We broaden two of the NASEM framework elements: the patient number and probability of shortage. When prioritizing pharmaceutical supply chains most in need of reinforcement, we propose that policymakers consider three elements: criticality, reach and vulnerability.

### Criticality

To assess criticality is to address the following question: Without which pharmaceuticals will individual patients suffer great harm?

The answer to this question will necessarily consider the severity of the condition the medicine treats and the [comparative effectiveness](#) of the drug relative to alternatives. In the criticality assessment, it is important to consider heterogeneity of treatment effect and the drug's importance to specific vulnerable subgroups that face challenges in accessing needed medical care. Examples include selected antibiotics and attention-deficit/hyperactivity disorder (ADHD) drugs used in children, hydroxyurea commonly used by patients with [sickle cell anemia](#), and hormonal contraception for women of childbearing age.

The FDA and ASPR lists focus on criticality, but only in the acute-care setting (and with regard to medical countermeasures in the case of the FDA list), even though life-saving drug are used in outpatient settings—anti-cancer drugs are one such example. This is a significant omission that conflicts with the [medical necessity determinations](#) performed by the FDA in its drug shortage assessments. Also, neither the FDA nor the ASPR list explicitly consider vulnerable populations. The WHO list does recognize select vulnerable populations as it maintains a [list of essential medicines for children](#).

### Reach

The concept of reach embodies the idea that some drugs may not be critical to individual patients, but their lack may have significant adverse effects on the population and the health system. This set of essential medicines will necessarily be broader than a list of critical drugs.

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The reach of selected drugs is a dimension missing in the FDA and ASPR lists, but it is a core element in the WHO list and in the draft Commerce list.

One aspect of reach is the number of affected patients. Take cholesterol drugs, for example. These drugs will lower the risk of cardiovascular events. They might not be considered critical for a given patient, though: a patient with uncontrolled cholesterol has an elevated probability of experiencing an adverse cardiovascular event, but this elevated probability may not be significantly high. Thus, if the drug lowers this probability, it may not meaningfully improve the individual's health. However, when statins are taken by many people, the use of statins reduces the probability of adverse events among the population as a whole. In this sense, the use of statins for an individual may not be meaningful, but when statins are used by a population, their use may save thousands of lives.

Reach [also includes components](#) that cross many products, supporting the care of millions. For example, Magnesium Stearate, an inactive ingredient, is common to over [30,000 oral solid dosage drug products](#). Disruption in the production of Magnesium Stearate could affect care for many millions of patients because the compound does not have good substitutes. The draft Commerce list is the only one that includes inactive ingredients, [albeit not all](#) common ones.

Another aspect of reach is the externality that a specific shortage might have on other people and the health care system as whole. For example, a disruption of access to antidepressants might lead to both patient self-harm and potentially spillover to employer productivity. Lack of access to medications used to treat pediatric ADHD can lead to [poorer education outcomes and increased burden on the family](#). Shortages in certain antivirals and selected antibiotics may foster spread of communicable diseases.

## Vulnerability

Evaluating vulnerability creates a roadmap for how the government, with limited resources, should correct for the existing, insufficient private incentives for creating reliable drug supply chains. For example, resource constraints will necessarily limit what can be onshored. Without proper vulnerability assessments, onshoring can easily become a feel-good strategy in response to geopolitical concerns, misallocating funds to supply chains that are otherwise not as vulnerable due to existing diversification of sources.

There are two ways in which vulnerability assessments can guide government action:

- Vulnerability assessments help further refine ***which supply chains*** would benefit most from direct government support, be it financial incentives for sourcing in specific countries, subsidies for adopting technology, or carrying buffer inventories.
- Vulnerability assessments help identify ***which policy interventions*** the government should pursue.

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When conducting vulnerability assessments, it is useful to differentiate between triggers, potentiators and buffers. Triggers are precipitating events, whether demand-side or supply-side. Potentiators are factors that scale up the impact of triggers. Buffers are then factors that can moderate the supply chain shock that triggers and potentiators create. We illustrate these factors in exhibit 1.

Exhibit 1. Vulnerability assessment categories



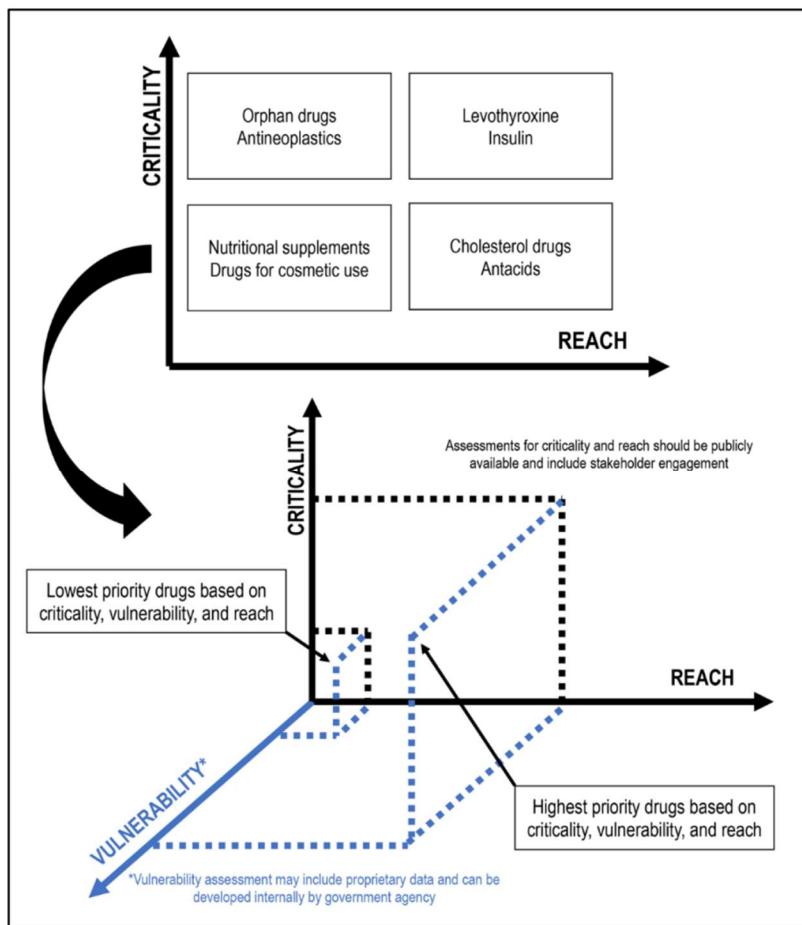
*Source: Authors' analysis*

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## Implementing The Criticality-Reach-Vulnerability (CRV) Framework

Exhibit 2 provides a visual representation of how the criticality, reach, and vulnerability concepts relate to each other and how they may be practically combined to inform government prioritization.

Exhibit 2. The Criticality-Reach-Vulnerability (CRV) framework for supply chain prioritization



Source: Authors' analysis

As exhibit 2 and our discussion of reach indicates, the CRV framework differentiates between *critical* and *essential* pharmaceuticals. The difference lies in scope: Critical drugs are those required to address a specific patient's health need while essential drugs are those that are needed to ensure a population's health and that have a large impact on the health care system—in other words, “essential” refers to the drug’s reach, and essential drugs are therefore a combination of the first two elements of our framework: criticality and reach.

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Critical drugs and their reach may be assessed using data that already exists, combined with clinical and population health expertise. As a first step in improving current lists, HHS can update their list of essential medicines to more closely align with WHO's list. The WHO includes cancer drugs as well as the frequently used drugs without which the broader health care system does not function well. The Commerce list also moves in the right direction, going beyond the WHO list in considering at least some of the common ingredients that cross many drugs.

We recommend the use of both qualitative and quantitative assessments combined with a robust engagement strategy to support diverse stakeholder buy-in to the concepts of criticality, reach, and vulnerability and their natural potential for intersectionality and tradeoffs. Criticality and reach assessments should also be updated with emerging evidence and treatment evolution.

Once criticality and reach assessments are completed, the government can then overlay vulnerability assessments to establish the highest-priority drugs for government intervention. The result of vulnerability assessments of critical drugs does not need to be a rank-ordered list of drugs, but rather a starting place for consideration of the tools the government has at its disposal to improve pharmaceutical supply chain resiliency. Consideration of patient vulnerability would enable higher prioritization for drugs that disproportionately benefit disadvantaged patient groups and marginalized communities to acknowledge where shortages could exacerbate health disparities.

As exhibit 1 indicates, assessing the vulnerability of a pharmaceutical product requires a broad range of data elements. A concerted effort is needed to support the building out of such infrastructure. Some of the needed data are already available to the FDA (e.g., location of API manufacturers); other data are not available in a structured format (e.g., geopolitical factors such as trade disputes and military conflicts) or have yet to be put together in ways that are productive for this exercise (e.g., API and excipient volume made in specific facilities or locations, and the location of pharmaceutical manufacturing overlaid with natural disaster risk prediction).

The stakeholder input and visibility into the different elements of the CRV framework will and should differ. As we argue above, public input and transparency is important in creating essential drug lists. However, vulnerability assessments may by necessity require some opacity because some measures of vulnerability may entail the evaluation of proprietary data, trade secrets, and/or national security concerns.

## Conclusion

The availability of pharmaceuticals is vital for safe, effective, and accessible medical care, but US drug supply chains have faced disruptions, including those related to natural disasters, quality assurance lapses, and non-redundant, foreign supply. These vulnerabilities arise from economics-driven decisions like concentrating production in large facilities, offshoring for reduced costs, and avoiding buffer inventories due to tight profit margins. We offer a practical framework that

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independently assesses the criticality, reach, and vulnerability of drugs to help guide the prioritization of government interventions supporting supply chain resiliency.

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# DRUG SHORTAGES

## A GUIDE TO POLICY SOLUTIONS

MARTA E. WOSIŃSKA, PH.D.

High-profile shortages of amoxicillin, cancer drugs, and medications to treat attention deficit hyperactive disorder (ADHD) have put drug shortages in the headlines over the past year. Less visible but equally alarming have been shortages of lifesaving emergency drugs such as atropine and epinephrine. Many of these shortages are persistent.

These shortages throw into question the reliability of the U.S. drug supply chain. They also highlight how shortages can undermine patient care, endangering patient health and lives through delays in treatment, rationing, potential substitution with less effective alternatives, and increased risk of medication errors. Such shortages cost patients time and cause untold anxiety and flare-ups of underlying conditions.

The severity of drug supply disruptions has prompted the Biden administration and Congress to energetically search for solutions. Many policy solutions have been offered, including stockpiles, onshoring, advanced manufacturing, changes in Medicare reimbursement,

greater transparency, and more. But how should we think about which policy ideas are the best? Given the number and variety of options, it is critical to determine which strategies are both effective and cost-effective. Without a strategic approach that recognizes different causes of shortages, we risk implementing expensive fixes that do little to make the U.S. drug supply chains more reliable.

In this paper, I describe a four-part test for assessing whether policy solutions are likely to accomplish improvements in supply chain reliability and whether they would do so cost-effectively. I also provide some background information to help understand different types of shocks that trigger shortages and the factors that prevent supply chains from withstanding those shocks. I do so for a range of types of supply disruptions. I then apply the four-part test to different types of policies that are being proposed to address the shortages, including transparency, buffer inventories, domestic manufacturing, advanced manufacturing, and reforms to hospital payments.

# A four-part test for potential drug shortage solutions

Designing effective policy solutions calls for a full [understanding of the problem](#) to be addressed, as well as a consideration of [unintended consequences](#) and [cost-effectiveness](#). Building on these general concepts of policy evaluation, I propose a four-part test for drug shortage solutions:

- 1. Does the policy address the actual cause(s) of shortages?** This is perhaps the most important question to ask when assessing a potential policy solution. Without properly mapping the solution to the problem, the solution may fall short on effectiveness, cost-effectiveness, or both.
- 2. Can the policy work by itself or does its effectiveness depend on presence of other policies?** Policymakers should consider whether additional policy changes are necessary for the proposed policy to have the desired effect.

**3. Does the policy anticipate and limit potential unintended consequences?** Policy changes can change incentives for market participants or can enable those participants to act on existing incentives. To assess potential unintended consequences, it is important to consider how incentives of different market participants may be affected through the policy change.

**4. Is the policy cost-effective relative to alternatives?** Building reliability into supply chains is costly – the more reliable we want supply chains to be, the more we will have to pay for it. Policymakers should assess the policy's relative cost-effectiveness, especially considering the enormity of the U.S. drug supply chains.

## The drug shortage problem(s)

In this section, I describe a general framework for how shortages can arise and then present how existing persistent shortages differ from potential shortages.

### GENERAL FRAMEWORK FOR HOW DRUG SHORTAGES ARISE

Shortages occur when supply chains cannot quickly adjust to demand shocks or cannot respond to disruptions to production or distribution of their products.

In this section, I describe the [vulnerability framework](#) referenced in Figure 1, which categorizes shock types that may trigger drug shortages, as well as the factors that may enhance (or potentiate) the size of the shock and the buffers that may absorb or minimize it.

Demand shocks can occur for several reasons. One reason is a rapid increase in disease prevalence. For example, COVID-19 rapidly increased demand for ventilator drugs and the post-pandemic rise in respi-

tory diseases drove demand for amoxicillin. A demand shock can also be a drastic change in how a drug is used, as has been the case with the increase in the use of GLP-1 inhibitors for weight-loss. Demand can also spill over from a drug in shortage to another drug that might serve as substitute. Chemical, biological, radiological, and nuclear (CBRN) threats for which the government [prepares](#) could also cause major demand increases for [medical countermeasures](#).

Disruptions to the supply chain can also occur [for many other reasons](#), from manufacturing quality problems, natural disasters, and manufacturers discontinuing select products in their portfolio to disruptions in international trade [due to geopolitical conflicts](#). These disruptions can occur at any stage of the production process, from raw materials to production of active pharmaceutical ingredients (API), inactive but critical ingredients, finished dosage form of a drug, and delivery mechanisms such as syringes.

**Figure 1: Schematic for how shortages arise**



Source: Wosińska, Mattingly, Conti (2023)

But not every one of these shocks triggers a shortage. The extent to which a meaningful shortage results depends on the size of the resulting shock and the buffers that may exist.

Shocks often vary in size for reasons that cannot be controlled (e.g., size of a hurricane), but shock magnitude can also be determined by how the market is structured or operates. For example, a single facility may represent a large share of product sales, or manufacturing facilities may concentrate in one geographic area, making them vulnerable to a single shock like natural disaster or geopolitical instability. Structural dynamics can also affect the shock size through panic buying – uncertainty, low prices, ease of returns, and lack of allocation mechanisms can lead buyers to stockpile a drug at risk of shortage, with that precipitating or deepening the shortage.

A shortage ultimately results if a shock cannot be properly buffered. Buffering strategies can include dual sourcing, excess capacity, and reliance on manufacturing lines fungible enough to accommodate different types of products. Buffering strategies also include various inventory management practices: stockpiles set aside for times of emergency or buffer inventories where inventory levels in the supply chain are high enough so they can absorb greater shocks. Allocation mechanisms and coordination systems can also minimize the harm that results from shortages.

## CHARACTERISTICS OF EXISTING PER-SISTENT DRUG SHORTAGES

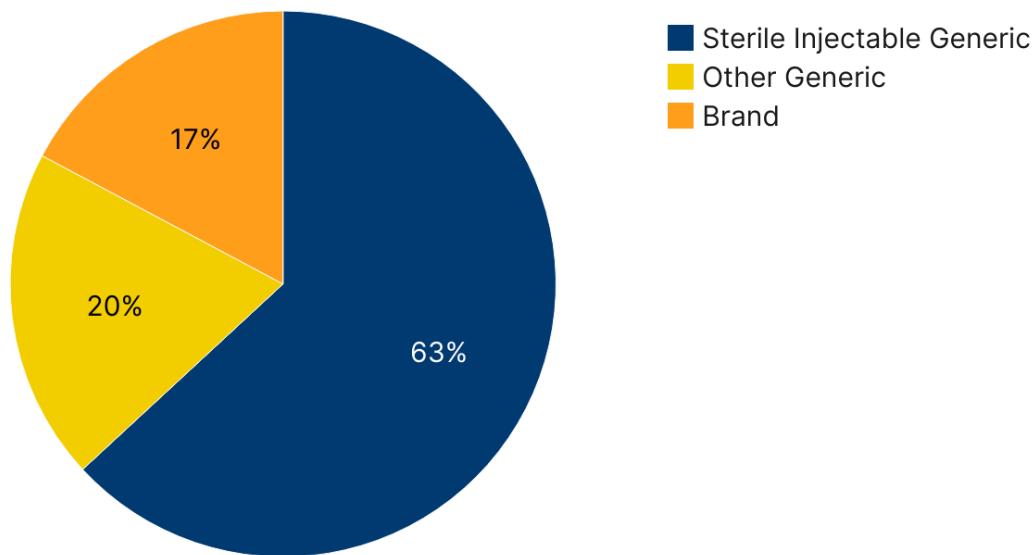
Historically, shortages in the U.S. have been concentrated with generic sterile injectable drugs administered in hospitals and clinics. These drugs include baseline cancer therapies, intravenous (IV) nutrition, IV antibiotics, crash cart drugs to revive trauma patients, morphine, and saline. Figure 2 shows a recent snapshot in time, with 63% of all drugs in shortage attributed to generic sterile injectables. This high percentage continues to follow historical patterns for with [73% in 2011](#) and [63% between 2013-2017](#) (both numbers including an unknown but likely small number of branded drugs).

Manufacturing quality problems have persistently topped the list of reasons for drug shortages, representing [56% in 2011](#), [62% between 2013-2017](#), and [46% in 2022](#). Anecdotally, manufacturing problems disproportionately affect finished dosage form (FDF) facilities making generic sterile injectable drugs, and many large facilities are in the United States and Europe. [The U.S. leads GSI production](#) with over 40% of overall production volume.

Other causes of shortages – natural disasters, discontinuations, upstream supply disruptions, and demand increases – have followed manufacturing quality in varied order, depending on the year. To the extent there is a pattern to these causes, it is the increased

## Figure 2: Drug Types in Shortage

As of January 2023



Source: FDA Drug Shortage Database

Note: Author's analysis. Shortages (N=122) only include drugs listed on Drugs@FDA.

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frequency of demand-driven shortages that began with the pandemic, with shortages in that category reaching an all-time high in [2022 of 29%](#).

Notably, no shortages in the last 20 years appear to have been caused by export restrictions related to geopolitics, even during the pandemic.<sup>1</sup>

Sterile injectable drugs are [particularly vulnerable](#) to shortages because of the high rate of manufacturing quality disruptions they experience, coupled with inability of supply chains to absorb many such shocks.

The manufacturing quality disruptions are a result of [market dynamics](#) that start with hospital reimbursement mechanisms that incentivize hospitals to use the lowest priced drug available. These price pressures, coupled with inconsistent FDA surveillance, create a dynamic for manufacturers where there is little room for and return on investing in facilities, staffing, and oversight.

Generic drugs that are formulated as tablets or capsules also face similar price pressures from pharmacies, but they are [less vulnerable](#) to shortages because they face a different manufacturing environment and market structure. Manufacturing of those products is less complex, not requiring specialized facilities with employees following complex manufacturing processes and controls. Generic oral dose product markets are also [less concentrated](#) than sterile injectable ones, and there is more fungibility in oral dose production lines that can also be ramped up faster.

The shortage vulnerability of branded products, including injectable ones, also [differs](#) from that of generic injectables. Although branded sterile injectables face an equally, if not more, complex manufacturing environment, stable demand limits the need for switching between products on a line. Additionally, high margins earned by their products [provide manufacturers](#) with strong incentives to invest in trying to prevent disruptions to those products. Branded manufacturers have a greater incentive to invest in quality systems and to

<sup>1</sup> Interview with Erin Fox, University of Utah Drug Information Service.

maintain spare capacity in case production unexpectedly must shut down. When production disruptions of this kind occur, they tend to [resolve faster](#).

It is also worthwhile to highlight that two drug classes are responsible for much of the recent uptick in demand-driven shortages. On the one hand is the increase in demand for GLP-1 inhibitors, in shortage because of a significant increase in demand for off-label weight loss use. Given their production complexity, expansion of manufacturing capacity is lagging demand. Another prominent set of demand-driven shortages is the largely generic oral-dose group of drugs to treat ADHD. ADHD medications are controlled substances and although simpler to produce, the supply response is [constrained by](#) the aggregate and manufacturer-specific quota established by the Drug Enforcement Administration (DEA).

## CHARACTERISTICS OF POTENTIAL DRUG SHORTAGES

Without structural changes to how generic sterile injectable markets function, we are unlikely to see a change in the persistence of generic sterile injectable drugs. It is therefore encouraging to see Congress exploring policy [ideas directly aimed](#) at those shortages.

But pandemics, natural disasters, and export restrictions can also challenge supply chains. The question is: which supply chains would such shocks affect and to what extent?

A major geopolitical conflict could compromise many supply chains, potentially ones quite different from those currently at high risk of shortage. Such a conflict could also compromise production sites along many different stages of production, beyond the more limited set of FDF sterile injectable facilities that are at the heart of most current shortages. For these reasons, the location of API production has caught the attention of policymakers. But the U.S. government's visibility falters beyond that, even though the exposure to countries with higher geopolitical risk is [greater in the upstream](#) supply chains.

One area that is particularly nontransparent to the U.S. government is the supply chain for precursors of API. A typical API will combine 2-5 [starting materials](#) with the help of so-called support materials. These support materials may include 1-3 catalysts, 3-10 solvents, and in some cases enzymes. An API may require several dozen inputs, with more complex APIs typically requiring more steps and therefore more starting materials to assemble the different intermediates that feed directly into the final API.

Government's visibility is also lacking in the supply chain for excipients, the inactive ingredients that often make up 90% of a drug's volume. "Inactive" is somewhat a misnomer because excipients help guarantee stability and bioavailability of the API, determine the texture and taste of the drug, and the rate at which it dissolves or binds. A given drug may typically have between 3 and 10 excipients, many of them [not readily substitutable](#). Oral solid dose products typically have more excipients than injectables because they need excipients to help with the bioavailability of the API, while injectable products have almost complete bioavailability. Magnesium Stearate is perhaps the most common excipient, [appearing in over 36,000 drug products](#).

In some ways, vulnerability of supply chains to natural disasters mirrors that of geopolitical risks: they can affect any part of the supply chain and there is similarly limited visibility upstream, limiting opportunities for a comprehensive vulnerability assessment beyond FDF and API. The difference is that supply disruptions due to natural disasters are likely more localized than geopolitical risks.

In turn, pandemics and CBRN threats primarily result in demand shocks for a relatively narrow set of products. For some pathogens, drugs and vaccines are known, but for others, drugs, tests, or vaccines may not exist. These threats also have the possibility of creating supply chain disruptions for which previous discussion offers a guide.

Table 1 summarizes the trigger characteristics across the most common trigger types.

# Identifying appropriate policy solutions

The above discussion about various causes of drug shortages suggests that different strategies are needed to address existing and potential shortages. It also suggests that an effective strategy should consider prevention mechanisms that lower the chance of and the likely size of a specific shock type. Figure 3 characterizes the three major levers policymakers have in addressing shortages.

An effective strategy is multipronged, addressing the three levers to varying degree. The most effective and most cost-effective combination of Figure 3 levers will

depend on the nature of the shortage and the relative effectiveness and cost-effectiveness of the three types of levers. Policymakers can arrive at the right combination by identifying the actual problem, avoiding incomplete solutions, addressing unintended consequences, and considering return-on-investment – the four-part test I lay out earlier in this article.

Table 1 presents a simplified output of such an analysis for key shortage triggers.

**Figure 3: Policy levers for addressing shortages**



# Refining drug policy solutions

To help illustrate how I arrived at the policy solutions listed in Table 1, I apply the four-part test to the baseline version of several policy proposal categories: transparency, stockpiling, domestic manufacturing, advanced manufacturing, and hospital payment reforms. I show here how the tests might play out in different cases and under different circumstances.

For exposition purposes, the discussion below may not follow the order of the four-part text. In addition, the analysis here represents key aspects but is by no means a complete assessment of these policies. I also note that the criticisms included here do not imply that the policies have no standing, but rather that there are important aspects that policymakers need to consider and address.

## TRANSPARENCY

Transparency initiatives are often [invoked](#) among reforms to address shortages. They cover a gamut, from government's visibility and buyers' visibility into supply chains, to whether government shares information in enough detail or in a readily available manner.

In the right context, transparency can [help](#) "assess, mitigate, prepare for, and respond to risks of medical product shortages." For example, [reforms](#) in 2011 and 2012 gave FDA greater visibility into supply disruptions, enabling the agency to coordinate a response. With greater visibility into supply chains, the federal

government can assess which supply chains are most vulnerable, [prioritizing](#) those for intervention. With more detail about what triggered a particular shortage, buyers can get [feedback](#) on which manufacturers are more reliable. With more information about reliability of manufacturers, buyers can shift purchasing accordingly.

However, transparency by itself will not accomplish anything if recipients of the information have no incentive to act on it. Releasing more information about reliability of manufacturers is not likely to succeed without a change in incentives to hospitals that currently focus on the lowest cost generic option. In fact, much relevant information about reliability of manufacturing already exists, but it is [underutilized because](#) hospitals are reluctant to buy anything but for the lowest price available.

In the wrong context, transparency can have unintended consequences. Take early warning systems for shortages. To a hospital, an early warning signal of shortage is a signal to start stockpiling, precipitating the shortage. Similarly, placing country of origin on a retail prescription label could backfire with higher rates of nonadherence if the only choice that a patient has at a pharmacy is whether to pick up a prescription or not, unlike in a retail store where a consumer has options to choose from multiple versions of the same product.

A proper assessment of transparency initiatives would involve applying the four-part test to each transparency proposal separately, paying particular attention to the intended audience and their ability and incentives to act on the information.

## STOCKPILING AND BUFFER INVENTORY

Holding higher levels of inventory can buffer against the adverse impact of a shock, no matter the shock's etiology. This common application makes stockpiling and buffer inventories a potentially attractive policy solution.

Stockpiles and buffer inventory can be important because not every shock can be prevented. But one cannot buffer every drug product, and with most shortages lasting over a year, it would be prohibitively expensive to buffer a shortage with reserve stock that will last until the supply shortage is resolved. For this reason, it is important to [prioritize](#) which products are stockpiled, considering not only whether these products are medically necessary but also whether their supply chains are vulnerable. For other products, such as highly used large volume products like saline, stockpiling the FDF product may not be practical, requiring an alternative set of buffering strategies.

Stockpiling or buffer inventory proposals are also incomplete if they do not address panic buying that [ensues](#) at the first sign of a potential shortage. If the government creates a buffer inventory and then releases it, a "bank run" on the product is likely to result. Currently such "bank runs" are uneven, usually with the large hospital systems [able get to the product first](#). For this reason, any government funded stockpile [should have](#) allocation mechanisms in place, even if they are simply historical allocations. Otherwise, providers most likely to currently suffer from shortages will continue to suffer.

Lastly, it is important to acknowledge that stockpiles or buffer inventories are a form of insurance in case shocks cannot be prevented or minimized. It may be near impossible to prevent a natural disaster, but on the other hand, quality lapses, which are the primary reason behind shortages, are not only possible but important to address. Without addressing the root cause of manufacturing quality problems, products not made to specification may and can [reach patients](#) during non-shortage times, potentially causing harm.

## DOMESTIC MANUFACTURING

Domestic manufacturing is offered as a solution to drug shortages perhaps more often than any other policy proposal. This policy appears steeped in concerns over the loss of U.S. [manufacturing base](#), coupled with concerns over supply chain [exposure](#) to geopolitical risks that were starkly [underscored](#) during the pandemic.

But for all the attention it attracts, the standard “we need to bring manufacturing back to the U.S.” proposal is challenged on three of the four parts of the test: addressing the right problem, completeness of the solution, and assuring cost-effectiveness.

On the right-problem front, domestic manufacturing can be a solution for addressing geopolitical risks. But proposals tend to focus on either the finished dosage form through “buy-American” policies or onshoring of API production. It is true that much FDF and API manufacturing has moved offshore, but does subsidizing U.S. production of drugs substantially improve supply chain reliability when those companies still rely on inputs from China? Without addressing that reliance, such proposals are incomplete, presenting poor return on investment for taxpayers.

Domestic manufacturing also does not address the drivers of persistent shortages of generic sterile injectable drugs. These shortages are not a result of geopolitics or domestic versus foreign quality differences. Rather, these shortages result because hospitals, the buyers of these drugs, do not reward manufacturing quality and reliability, leading to manufacturing quality shortfalls in [domestic](#) and [foreign](#) facilities alike.

The pricing market pressures driving existing shortages also highlight the need to [attach strings on quality](#) to domestic manufacturing investments or else such investments will falter. Any government subsidies to bolster domestic manufacturing in response to geopolitical risks should [consider other types of shocks](#), such as natural disasters. For example, we might have a lot of idle capacity in Puerto Rico, but that is also an area vulnerable to hurricanes.

Domestic manufacturing as a solution is also challenged on the cost-effectiveness front. As described in the section on potential shortages, the pharmaceutical industry and the chemical industry that feeds the key starting materials for drugs may have extensive exposure to countries with high geopolitical risk. To lower this risk, a proper risk mitigation would make [diversification](#) through friend-shoring and near-shoring an integral part of U.S. government strategy.

## ADVANCED MANUFACTURING

Because outdated production technologies contribute to the high rate of manufacturing quality problems, the use of advanced manufacturing technologies – [continuous manufacturing](#) in particular – is often proposed as a solution that [could lower](#) the likelihood of manufacturing disruptions.

These proposals fail to recognize just how strongly economic forces driving shortages of generic sterile injectable drugs [work against](#) adoption of such tools. The low margins on drugs at greatest risk of shortage mean that the federal government would have to heavily if not fully subsidize these technologies. And even with full subsidies of installation costs, these technologies may not translate well into reliability in an environment where the unstable nature of the demand can lead to 20-30 products being run on a single line over a course of a year, leading to frequent switchovers that are at the heart of many of the existing disruptions.

To the extent the federal government were to subsidize technology improvements, it should consider whether other, potentially much simpler technology solutions may be more cost-effective. There may be appropriate cases for using advanced manufacturing but tying a significant share of subsidies to advanced technologies would limit the reach of widely-needed infrastructure investments.

## HOSPITAL PAYMENTS FOR BUYING RELIABLY

Changing hospital payments to encourage hospital pharmacy procurement from more reliable manufacturers directly addresses the root cause of persistent shortages of generic sterile injectable drugs. By modifying how CMS pays for such generic sterile injectable drugs, [CMS can steer hospitals](#) away from their heavy emphasis on price and towards reliability of supply.

But even though this policy area addresses the root cause of the problem, how it is designed would influence its cost-effectiveness. To the extent that CMS were to adopt add-on payments, the effectiveness of such an add-on payment in preventing shortages

would depend on CMS's (or FDA's) ability to identify which manufacturers are reliable. The better the predictive power of such measures, the greater the impact of an add-on payment program tied to such list of reliable manufacturers. If those measures are not reliable, CMS would be increasing government spending without making a difference on the shortage front. This in turn would translate into poor taxpayer return-on-investment.

Changing hospitals reimbursement for generic sterile injectable markets would also [likely falter](#) without changes to Medicaid inflation rebates for outpatient

generic drug markets with a large 340B presence (e.g. generic cancer drugs recently in shortage). Medicaid inflation rebates neutralize price increases in the Medicaid and the 340B market segment. But without the ability to pass on cost increases, however reasonable, manufacturers will have little incentive to make the investments necessary to differentiate themselves on manufacturing reliability, which is the entire premise behind payment reforms to address shortages.

## Conclusion

Our drug supply chains are not as reliable as we expect them to be, resulting in disruptions in medical care and causing patient harm. But little progress will take place unless there is a systemic change in the economic dynamics and the misaligned incentives that exist in the marketplace. Because economic dynamics are at play, there is an important role for the U.S. government to drive change.

But building reliability into supply chain does not come for free. Between the enormity of the drug supply chains and the limited resources that Congress is likely to appropriate toward solving drug shortage problems, government intervention can easily become a feel-good strategy that does little to improve supply chain reliability where it matters most. Policymakers can avoid such fate by properly mapping solutions to the underlying problem, avoiding incomplete solutions, considering return-on-investment, and addressing unintended consequences. This article presents a guide to the nature of shortages and ways to accomplish the best outcome we can obtain with limited resources.

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# Mapping shortage preparation strategy to nature of the shock

Trigger type	Shock characterization	Appropriate strategy
Pandemics and CBRN* threats	<ul style="list-style-type: none"> <li>Primarily a demand shock</li> <li>For some triggers, drugs at risk of shortage are known</li> <li>For some triggers, drugs, tests, or vaccines may not exist</li> </ul>	<ul style="list-style-type: none"> <li>Early detection and containment mechanisms are important</li> <li>For buffering against medical countermeasures, key decision is how much to stockpile versus use other buffering strategies like holding excess capacity</li> <li>For buffering against new pathogens, need infrastructure to develop vaccines, drugs, and tests, scale up production quickly, and get it to patients quickly</li> </ul>
Natural disasters	<ul style="list-style-type: none"> <li>Supply disruption of varying strength</li> <li>Can affect any part of the supply chain</li> <li>Vulnerability can be assessed</li> </ul>	<ul style="list-style-type: none"> <li>In the short term, buffering is the primary option (stockpiling, diversification, excess capacity)</li> <li>In the short term, vulnerability to natural disasters can be assessed</li> <li>In the long term, can prepare by strategically selecting where facilities are located, how they are constructed, where inventory is stored</li> </ul>
Manufacturing quality	<ul style="list-style-type: none"> <li>Most common in final stage of generic sterile injectable production</li> <li>Most production is in the U.S. and Europe</li> <li>These shortages have economic underpinnings</li> </ul>	<ul style="list-style-type: none"> <li>Buffering strategies can help but key to address the root cause of quality lapses because otherwise product not made to specification may reach patients, causing harm</li> <li>Markets currently do not allow generic manufacturers to differentiate themselves on reliability of supply</li> <li>Policy solutions must shift hospital buying behavior away from heavy emphasis on price towards reliability</li> <li>For outpatient multiple source generic injectables, need to eliminate Medicaid inflation rebates, which currently do not allow manufacturers to pass on legitimate cost increases</li> </ul>
Geopolitical risk	<ul style="list-style-type: none"> <li>Not a current trigger but a possible one</li> <li>Greater exposure for upstream supply chains</li> <li>Would be a supply disruption, potentially long-term and widespread</li> </ul>	<ul style="list-style-type: none"> <li>A strategic approach is necessary because of the sheer size of potential disruption: <ul style="list-style-type: none"> <li>Need to revise the essential medicines list</li> <li>Need better analytics to identify vulnerabilities</li> <li>Must consider full supply chains</li> <li>Need to consider common links between drugs</li> </ul> </li> <li>For priority supply chains, lower risk though diversification, selective onshoring, otherwise friend-shoring</li> <li>For priority supply chains with much geopolitical risk exposure, apply buffering strategies</li> <li>When onshoring, address the possibility of other shock types</li> </ul>

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1775 Massachusetts Ave NW,  
Washington, DC 20036  
(202) 797-6000  
[www.brookings.edu](http://www.brookings.edu)