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Howard Lutnick
Secretary

Jeffrey I. Kessler
Under Secretary of Commerce for Industry and Security

Stephen Astle
Director, Defense Industrial Base Division

US Department of Commerce
1401 Constitution Ave. NW
Washington, D.C. 20230

May 7th, 2025

Comments of Doctors Without Borders USA regarding Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients

Dear Mr. Lutnick, Mr. Kessler, and Mr. Astle:

Médecins Sans Frontières/Doctors Without Borders (MSF) is an international medical humanitarian organization working in some of the most difficult contexts imaginable in over 70 countries around the world. We are committed to independence, neutrality, and impartiality, and provide humanitarian assistance to people based solely on need, irrespective of race, religion, gender, or political affiliation. MSF is not a recipient of any US funding or aid.

MSF is a major global purchaser of pharmaceuticals and health products. Nearly 40 years ago, due to the growing demands of the organization and the increasing complexity of our operations, we opened the first of our major procurement, supply and logistical centers, which in 2023 exceeded $200 million in turnover and shipped nearly 10,000 tons of product across the globe. Given our footprint in global supply chains, MSF has developed a deep well of expertise in pharmaceutical markets and supply chains. Our patients often need medicines that are not well-served by markets, and our supply chains are among the most complex

in the world, as we seek to deliver health products to some of the hardest to reach and remote places on the planet. Twenty-five years ago, we invested in deepening and expanding our technical capacity in these areas by establishing the MSF Access Campaign, a team of world-leading experts in supply, economic, legal, medical, and pharmaceutical issues who work to improve access to medical tools, both for MSF and around the world. Our decades of on-the-ground experience delivering pharmaceutical products globally and deep medical, pharmaceutical, and supply expertise give us a comprehensive and nuanced perspective on global supply chains and how they react to different stressors.

As an institution, MSF relies on stable, well-functioning supply chains to purchase and deliver medicines to our patients. It is from this position and experience, as we will articulate within our submission, that we raise questions and serious concerns about the likely spillover effects and unintended consequences of pharmaceutical tariffs, both on the populations with whom we work and in the United States. Medicines have historically held a privileged, protected place in national and international policy because actors—including the United States—recognize their life-saving importance. For many years, we have advocated that medicines should never be treated as luxury goods. Today, we emphasize that they must also never be used as a tool for economic leverage. We strongly urge policymakers to weigh the health implications of trade decisions and to pursue policies that expand, rather than restrict, access to medicines.

We address the questions from the call for public comments in the following sections.

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

The persistent lack of reliable data on the volume of global pharmaceutical flows severely undermines the US government and other actors' ability to forecast demand, anticipate shortages, and prepare for emergencies. Later in this submission, we will address questions about the effectiveness of pharmaceutical tariffs in promoting supply security and their likely unintended consequences, but we urge policymakers to first confront the glaring data deficit: without accurate, transparent, and readily available metrics on production capacity, redundancy, and distribution, policymakers and global stakeholders lack the baseline visibility needed to design targeted health and industrial policies, anticipate risks to mitigate against the worst consequences, and ultimately, to assess whether or not implemented policies succeed in achieving their intended objectives.

Baseline data must be a necessary antecedent to enacting significant policy shifts—particularly those with the potential to destabilize global pharmaceutical supply chains and jeopardize access to medicines for humanitarian organizations like MSF as well as health systems around the world, including the US's own. We stress that these data do not exist (yet). Selected indicators should undergo thorough evaluation by relevant stakeholders and independent experts, including public review and comment, prior to inclusion. We strongly urge policymakers to implement essential transparency and reporting measures, and to adequately resource and empower regulators to build the data infrastructure necessary to facilitate and support systematic, transparent reporting of core indicators.

Demand for pharmaceuticals in the United States should be assessed in terms of both market value and production volume. Estimates from the HHS Office of the Assistant Secretary for Planning and Evaluation (ASPE) suggest that the US spent approximately $600 billion on pharmaceuticals in 2021 [1]; net of rebates, estimated spending is likely around $435 billion [2]. Data sources on pharmaceutical demand vary in quality and collection methodologies, but are generally underpinned by direct and indirect reporting from pharmacies, insurance companies, manufacturers, and routine administrative data from import/export duties. There are also specialist public agencies that collect and analyze these data, for example the United Nations' COMTRADE [3].

In contrast to the market value data above, reliable data on production volume are entirely lacking. A recent FDA Drug Shortages Task Force report notes that "FDA's data do not capture how much of a drug is produced at each manufacturing facility" [4]. In 2019 testimony to the House Committee on Energy and Commerce, Subcommittee on Health, Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research (CDER) at the FDA stated "data available to FDA do not enable us to calculate the volume of active pharmaceutical ingredients (APIs) being used for US-marketed drugs from China or India, and what percentage of US drug consumption this represents" [5]. When asked about the resilience of the US manufacturing base, Dr. Woodcock noted that this question is also not possible to robustly answer due to severe data limitations [5].

While some statistics are available, from trade data alone it is generally not possible to assess what volume of API is in a shipment of finished product (there are too many unknown variables, for example varying dosage, varying weights of package sizes, etc). Volume is sometimes back-calculated from purchasing data, but this tends to be too incomplete to be useful (for example, data sourced only from some cooperating retail pharmacies). In its place, market value is typically the default metric used in academic and trade publications describing global and US pharmaceutical market trends. Market value is sometimes presented ambiguously, leading non-specialists outside the field to sometimes misapprehend or underestimate the fundamental data limitations and to misinterpret what the data actually represent. Unfortunately, market value is a less informative indicator than volume if the goal is to understand the factors that matter most for supply resilience: production capacity, redundancy, and supplier diversity.

If volume data are elusive, data on production distribution across unique firms (ie, the number and distribution of upstream manufacturers by API and finished dosage forms (FDFs)) are practically non-existent.[1] In recent years—largely in response to the uptick in shortages associated with the COVID-19 pandemic market shocks—the US government has made important reforms to improve supply chain transparency which should be continued and built upon. For example, Section 3112(e) of the CARES Act amended section 510(j)(3) of the FD&C Act to include requirements that manufacturers report the volume of drugs manufactured, prepared, propagated, compounded, or processed for commercial distribution [6]. In February 2024, FDA released related implementation guidance *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* [7].[2] Previously,

[1] Finished dosage form (FDF) is often used interchangeably with finished pharmaceutical product (FPP).

[2] The amendment reads: "(3)(A) Each person who registers with the Secretary under this section with

while the FDA was notified of manufacturers expectation of a shortage, they did not have the visibility needed to understand the wider market, and the scale of the gap to be filled. While gaps remain, these reforms represent meaningful steps toward improving oversight and building a healthier information ecosystem.

Supply chain data gaps are extensively documented and emphasized in government reports, yet they persist due to systemic failures and inadequate investments in basic data infrastructure. Not only are data not collected, but even basic category definitions needed to plan data collection are absent [8]. While some private firms, such as IQVIA, claim to fill these gaps, their methodologies are inconsistent— often relying on press releases, surveys, or incomplete regulatory filings. Because commercial datasets are costly and confidential, they are available to few researchers for scrutiny, and there is no practical means to audit them. As one example, IQVIA, the most prominent commercial data vendor, whose data underlie most academic and trade publications, was subject to a formal complaint by the FDA in 2019 over errors in their volume reporting [9]. While IQVIA can be criticized for their data practices, the primary responsibility for accurate and timely data collection lies with national regulators, who have failed to invest in robust systems for collecting, verifying, and publicly disseminating critical supply chain indicators, as well as Congress, which has failed to provide sufficient statutory authority and the resources needed to do so.

(ii) the extent to which domestic production of pharmaceuticals and pharmaceutical ingredients can meet domestic demand & (iii) the role of foreign supply chains, particularly of major exporters, in meeting United States demand for pharmaceuticals and pharmaceutical ingredients;

We address questions (ii) and (iii) together, as they fundamentally concern the same issue: the balance between domestic pharmaceutical production and foreign supply chains.

Does the US currently have production capacity to completely isolate itself from global markets and go it alone? No.

Is this situation unique, ie, does every nation, across nearly all sectors, participate in globally integrated supply chains? Yes.

This line of questions obscures the more consequential policy questions to medicine availability and affordability. We encourage policymakers to instead ask:

1. Can domestic demand sustain pharmaceutical and pharmaceutical ingredient production at the scale required for economically viable, let alone competitive, production?
2. Would relying on domestic manufacturers make the supply chain more or less resilient and better equipped to prevent shortages?

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regard to a drug shall report annually to the Secretary on the amount of each drug listed under paragraph (1) that was manufactured, prepared, propagated, compounded, or processed by such person for commercial distribution. Such information may be required to be submitted in an electronic format as determined by the Secretary. The Secretary may require that information required to be reported under this paragraph be submitted at the time a public health emergency is declared by the Secretary under section 319 of the Public Health Service Act.

3. What are the consequences of abrupt shocks to highly interdependent markets?

Again, as emphasized in our response to question (i), measures available to measure global supply flows are not fit for purpose. Nevertheless, in this section we briefly outline the literature.

Perhaps the best estimate of US imports of medical products comes from a 2020 Congressional Research service report, which joins data from the US Census Bureau, US Bureau of Economic Analysis, and the US International Trade Commission (USITC) [8]. See Table 1 reproduced from that report below [8].

Table 1: Estimate of the Imported Share of US Domestic Supply: Selected Medical Products (Share of Domestic Supply (%) in 2018)

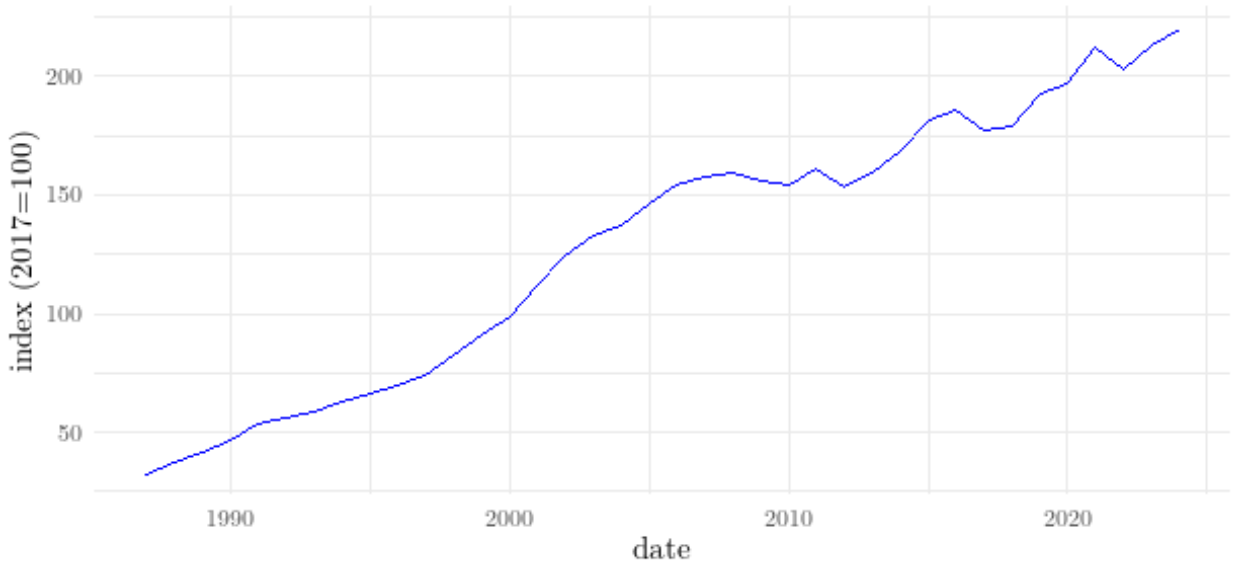
NAICS Code and Description	**Total Imports (%)**	**US Imports from EU28 (%)**	**US Imports from China (%)**
325414: Biological Products [vaccines, toxoids, blood fractions]	79	59	<0.05
325411: Medicinal and Botanical Drugs and Vitamins [uncompounded medicinal chemicals and derivatives, botanicals]	48	34	8
325413: In-Vitro Diagnostic Substances [chemical, biological, or radioactive diagnostic substances]	48	27	3
325199: All Other Basic Organic Chemicals [isopropyl alcohol, glycerin]	42	14	9
334517: Irradiation Apparatus [X-rays and other ionizing radiation apparatus]	41	25	4
339113: Surgical Appliances and Supplies [orthopedic devices, prosthetic appliances, surgical dressings, crutches]	39	15	6
325412: Pharmaceutical Preparations [in-vivo diagnostic substances]	39	23	<0.05
339112: Surgical and Medical Instruments [syringes, needles, catheters, anesthesia apparatus, blood transfusion equipment, medical thermometers]	36	10	2

NAICS: North American Industry Classification System.

Table 1 demonstrates the heterogeneity of US supply dependence across different categories. For surgical and medical instruments, the majority of domestic supply (64%) is not imported. For other categories, there is a range of import reliance. Strikingly, despite deep consternation expressed by some US policymakers about dependence on China, imports from China account for a relatively small share of US domestic supply.

While some policymakers have described US drug production as in a state of stagnation, estimates from Federal Reserve data show steady growth in the sector [10].

Figure 1. Industrial Production: Pharmaceutical and Medicine (NAICS = 3254)



Several academic studies and industry reports use data from Drug Master Files (DMFs) as a proxy to understand the distribution of API and FDF production.

Shivdasani et al (2021) offer one of the most comprehensive assessments of the geographic spread of generic firms [11]. The analysis relies on data from the FDA's Generic Drug User Fee Program (GDUFA), which contain information about the geographic location of manufacturing facilities. The authors find that API sites for API intended for US markets are located 26% in India, 18% in China, 8% in Italy, and 4% in Germany [11]. For FDFs, the US accounts for the largest share (41% of global sites), followed by India (21%) and China (8%) [11]. Again—these data report the number of facilities, rather than output *volumes*, let alone production *capacity*, and therefore do not necessarily provide us with a complete enough picture to make sufficiently informed policy decisions.

US API and FDF domestic production is increasing for some key market segments. The *Quadrennial Supply Chain Review* reported an increase in the percentage of US generic drug manufacturing facilities, with FDF facilities rising from 37% to 46% and API facilities increasing from 13% to 18% between 2021 and 2024 [12].

To our knowledge, only two studies have matched pharmaceutical manufacturing geographic location data to individual drugs and APIs [13, 5]. Socal et al (2023) use commercial data with product-firm information to identify 565 facilities producing 1,379 unique generic APIs, of which they were able to link 833 APIs to at least one company and Abbreviated New Drug Application (ANDA) approval. They find that for API intended for US markets, 62% of generic APIs were manufactured in India, 32% in Italy, and 22% in China [13]. However, these data do not provide information about the volume at different facilities (or indeed, if facilities are producing at all), and the underlying data source (Cortellis, a commercial database) relies on information like company press releases, which may not be current or reflect what is actually being produced [13].

Beyond this, not all drugs are of equal public health importance. Reflecting the varying importance of different medicines, the FDA focused its analysis on 370 priority essential medicines. By linking confidential data to specific production sites, the FDA identified 1,079 API facilities. Of these, 166 (15%) were located in China, 221 (21%) in the United States, and 687 (64%) in other countries [5]. The study also identified the number of drugs which had manufacturers solely based in China: only three were identified (capreomycin and streptomycin, both indicated to treat *Mycobacterium tuberculosis*, and sulfadiazine, used to treat chancroid and trachoma [5]. These three drugs are not currently preferred treatment options, nor are the conditions they treat prevalent in the US.[3]

The questions that should be at the front of policymakers' minds in considering supply security is not "how many API or FDF facilities are located in the US versus abroad," but rather "how many priority drugs have vulnerable supply chains because they are manufactured with materials supplied by a single facility?" A drug produced by four independent facilities overseas offers a more secure supply chain than one manufactured at a single domestic site. Data needed to answer these questions are urgently needed.

[3] MSF is the world's largest non-profit TB treatment organization, and we have historically advocated for consistent, resilient and affordable supply of TB medicines. But it bears noting that not only does the US has a very low burden of drug-resistant TB, capreomycin has been replaced in TB treatment guidelines with new, safer medicines, and was removed in 2019 from the WHO Model List of Essential Medicines [14, 15, 16, 17]. Similarly, streptomycin is only recommended in cases where no preferred, alternatives are available [14]. Sulfadiazine is also no longer the preferred treatment for trachoma and chancroid [18]. While multi-source procurement is important, these drugs are likely not priorities for US patients.

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

Some pharmaceutical products are manufactured by a limited number of producers, rendering them particularly vulnerable to supply chain disruptions and fluctuations in demand. A 2023 study published in *Health Affairs* found that 34% of generic APIs intended for the US market between 2020 and 2021 originated from a single facility, while 30% were produced by two or three facilities [13].[4]. On average, each API was manufactured at 3.7 facilities [13]. The FDA prioritizes ANDAs corresponding to drugs for which there are not more than three approved drug products [19]. In line with this benchmark, the authors defined "competitive markets" as those with four or more actors. The study found that 43% of drugs met this threshold for both API manufacturers and ANDA holders and were categorized as 'competitive' [13]. 23% had three or fewer API manufacturers but four or more ANDA holders, while 7% had four or more API manufacturers but three or fewer ANDA holders, and were categorized as having mixed levels of competition [13]. The remaining 43% had three or fewer manufacturers and ANDA holders, and were classified as uncompetitive [13]. These findings should be viewed as broadly indicative of market structures but nevertheless interpreted with caution.

While national-level aggregates highlight general trends, substantial variation and idiosyncrasies exist across different drug classes. As noted previously, the analysis is constrained by previously discussed limitations of the commercial database. Further, it does not account for shared sources of key starting materials (KSMs), nor does it fully capture the influence of technology licensing, corporate subsidiaries, or cooperative production agreements in assessing concentration and competition [13]. But the evidence for the underlying conclusion is compelling and important: concentration tends to increase further upstream, and many drugs fall short of the four-producer threshold that the FDA targets to promote competition and supply chain resilience.

Single-source suppliers introduce major vulnerabilities into global supply chains, as any disruption— whether from natural disasters, contamination, or other quality-related issues—can halt global production entirely. In addition to these operational risks, buyers face strategic disadvantages, since the supplier's exclusivity provides significant leverage to increase prices or impose unfavorable terms.

ASPE analyzed the risks posed by natural disasters to US manufacturing sites, as measured by linking the FEMA National Risk Index (NRI) data to manufacturer location data. They found that more than a quarter of drug and device manufacturers (and more than a third of site manufacturing essential drugs) were located in locations categorized by FEMA as very or relatively high risk [20]. In the high-risk subset, 58% percent of drug manufacturers and 47% of device manufacturers were located in areas vulnerable to tornadoes, hurricanes, earthquakes, and extreme weather events [20]. This analysis was conducted in 2024; we are deeply concerned about the ability of health systems and policymakers to continue to monitor the risk of pharmaceutical manufacturing facilities for priority products in the wake of severe recent cuts at FEMA and ASPE [21, 22]

Termination of vital systems that support monitoring and predicting risk to supply chains

[4] This study used commercial data with known limitations; see discussion in sections (ii/iii)

has already affected MSF's operations. The Famine Early Warning Systems Network (FEWS NET), established in the wake of the devastating 1984 famine in East Africa, has long provided humanitarian actors like MSF with detailed food security forecasts, developed by integrating data on climate patterns and agricultural productivity and modelling likely scenarios [23, 24]. FEWS NET plays a crucial role in strengthening the resilience and responsiveness of humanitarian supply chains by enabling more accurate forecasting of food supply needs and facilitating the timely delivery of aid. Robust data monitoring systems like FEWS NET and the NRI are essential not only for food security but also for predicting and managing risks to pharmaceutical supply chains. We urge policymakers to consider these vital functions in planning risk monitoring and mitigation for policies likely to shock markets, including pharmaceutical tariffs.

This analysis has focused on generic/biosimilar drugs, as markets for originator drugs under patent are non-competitive by design. However, single-source production is high-risk, whether for generic/biosimilar drugs or for those under patent. These risks are illustrated in the case of ritonavir, an HIV drug. The emergence of a late polymorph form which spread to other facilities forced Abbott to recall the drug and remove it from market in 1998 [25]. Biotherapeutic manufacturing is particularly exposed to these risks due to its reliance on specialized input materials and longer, more complex regulatory processes. For example, the production of N,N'-methylenebisacrylamide, an ingredient in Sephacryl chromatography media, was disrupted by the 2011 tsunami in Japan [26]. Manufacturing had to be relocated, and a validated supply was not restored for two years [26]. These examples highlight that supply chains for high-price, patented drugs are not immune to supply chain issues.

Nevertheless, policymakers have greater leverage to address supply vulnerabilities in generic drug manufacturing because they need only solve supply-side challenges, rather than both supply and intellectual property (IP) constraints. In many jurisdictions, including the US, patent holders can block alternative suppliers from entering the market even if they are themselves unable to meet demand [27].[5] There are, however, some tools available to strengthen the supply security for drugs under legally enforceable monopolies. Some are already practiced, for example the FDA expands exceptions permitting drug compounding for drugs in shortage [28]. Additional strategies include requiring or incentivizing larger buffer stocks and formal risk mitigation plans, or invoking legal flexibilities such as 28 U.S.C. § 1498 to authorize third-party manufacturing [29]. Gotham (2018) proposes that originators be required to submit cell line stocks to regulators and disclose detailed information about manufacturing processes [30]. While this intervention was intended to address biosimilar regulatory delays and facilitate competition, it serves dual purpose in providing critical backup resources that can more easily be deployed to establish new supply lines in cases of emergency.

Markets with multiple, geographically diverse producers—whether they exist in the United States, China, India, or Lichtenstein —are best positioned to respond to surges in demand and mitigate the impact of supply disruptions. Rather than viewing cross-border or globalized production as a threat, policymakers should recognize the benefit: supply chain diversity supports supply resilience, flexibility, keeps prices in check, and ensures that shortages in one region do not lead to global disruptions.

[5] By contrast, some countries provide safeguards against enforcement of non-practiced patents.

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

Many countries provide subsidies and policy incentives to support the pharmaceutical sector. Experts agree that most such instruments are generally not in violation of international trade law and other instruments governing anti-competitive commercial practices.

The United States provides the pharmaceutical industry with significant subsidies and incentives. Puerto Rico's growth as a major domestic supplier can be traced to the 1976 Possession Tax Credit, Section 936, which granted US-based corporations tax exemptions on income generated in Puerto Rico. Other US subsidies or incentives include the Research and Experimentation (R&E) Tax Credit (1981), Orphan Drug Act (1983), tropical disease priority review voucher (PRV) (FDA Amendments Act of 2007), Rare Pediatric Disease PRV (FDA Safety and Innovation Act 2012), and Medical Countermeasure PRV (21st Century Cures Act 2016). Substantial US investments in R&D, which through the Bayh-Dole Act allow transferrable intellectual property to the private sector, could also be understood as a form of subsidy. Programs like Operation Warp Speed transferred billions of dollars in subsidies as well as technical know-how to the private sector, enabling the unprecedentedly rapid development of COVID-19 vaccines.

MSF strongly supports public investments that enhance the availability and quality of medical tools and strengthen global supply chains both during epidemics and in order to support and improve routine medical care. Investments that improve the availability, quality, and affordability of global drug supply are undertaken by most governments, including the United States, and should not be mischaracterized as inappropriate, unfair, or predatory subsidies or trade practices.

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

There is no credible evidence to support the claim that pharmaceutical prices are being artificially suppressed by foreign unfair trade practices or state-sponsored overproduction. Such assertions fundamentally misunderstand the economic and structural factors that drive global drug pricing disparities. In reality, lower prices in many countries are better understood as resulting from market efficiencies, including economies of scale, investments in process engineering, and competitive generic markets rather than "cheating."

While the US plays a major role in global pharmaceutical research and manufacturing, it is far from the only engine of innovation or production. Countries such as Brazil, China, France, Germany, India, Italy, Switzerland, the United Kingdom, and others have made and are increasingly making significant contributions to drug development and process engineering. In recent decades, advances in manufacturing efficiency, population growth, and the expansion of global markets have enabled significant reductions in production costs through both technological innovation and economies of scale.

Although the US market is highly lucrative in terms of size and the ability to charge higher

prices, many pharmaceutical companies choose to widen their engagement to include regions frequently underserved by US firms. While FDA approval opens access to the US market, for some firms—especially those targeting certain disease or low-margin market segments—the cost and complexity of US regulatory compliance may outweigh the benefits to entering the market [31, 32]. Conversely, many US companies do not market their drugs in much of the world, even where there is significant public health need, because they do not yield the desired profit margins. The 2024 Access to Medicines Index reported that more than half (87 of 179) of reviewed drugs had not been registered in any of the ten countries with the highest respective disease burden [33]. Among innovative products approved between 2019 and 2024, 43% were not registered in a single African country [33].

For some generic drug manufacturers targeting markets often overlooked by US firms (such as those in low-income countries across Africa and Asia), high-volume, low-margin commercial strategies have been one approach to scale production, achieve efficiencies, and offer lower prices. A virtuous cycle is possible: affordable pricing expands market access, which in turn drives further cost reductions through economies of scale and broader distribution networks. This logic is the fundamental principle underlying pooled procurement and advanced volume guarantees, which have been successfully employed—including by MSF as well as the Presidents Emergency Plan for AIDS Relief (PEPFAR)—to improve access to treatments for HIV, tuberculosis, malaria, and other diseases [34].

Concerns about "artificially suppressed prices" reflect a fundamental misunderstanding of why the United States does not similarly lead in global price competitiveness. This misconception stems from a flawed conflation of innovation with cost efficiency that overlooks the structural and regulatory factors that determine price dynamics. In short, the US has the highest drug prices in the world not because of distortions or malfeasance by foreign actors, but because its own system lacks meaningful price controls or other measures that can keep prices at reasonable levels, a reality acknowledged by politicians across all parties. Until recently and unlike nearly all high-income countries, federal programs were barred from negotiating drug prices, while at the same time, long exclusivities and low thresholds for patentability entrench monopolies well beyond international average monopoly periods [35, 36, 37, 38, 39].

Companies do not always have strong incentives to invest in manufacturing process optimization research that could drive prices down where markets are not competitive and there are not otherwise deflationary price pressures. Take the hepatitis C drug sofosbuvir (Sovaldi) as an illustrative example: in the US, average prices are $29,000 per treatment course (down from $84,000 in 2016) [40]. In India, prices are around $40 per treatment course [41].[6] Relative to the opportunity cost of other activities, the returns of reducing sofosbuvir manufacturing costs by 10% are negligible to the originator, in this case the American company Gilead, in the context of their overall absolute margins. By contrast, generic manufacturers such as those based in India operate in a high-volume, low-margin context where process optimization and innovation are imperative for commercial survival, let alone global competitiveness. Price differences are thus not compelling evidence of unfair trade practices, but

[6] Research has shown that even with a 10% margin and generous, conservative assumptions about production costs, prices could fall to $28/course [41].

instead better explained by divergent market incentives resulting from US policy choices, as well as competitive advantages within the broader structure of global markets.

Concerns about "state-sponsored overproduction" of medicines are similarly misplaced. This framing presumes that managing scarcity is necessary to uphold market prices, a logic borrowed from commodity markets such as oil or diamonds, where supply restrictions serve to keep prices at a desired level far above the marginal cost of production, but wholly inappropriate in the context of pharmaceutical markets. Far more often, business practices and intellectual property abuse—not a chimera of foreign overproduction—create deadly gaps between medical need and market supply. For example, in a context of insufficient global supply for COVID-19 treatment, Pfizer refused to allow manufacturers in the Dominican Republic to serve the domestic market with its drug Paxlovid (nirmatrelvir/ritonavir), despite Pfizer having neither the manufacturing capacity nor available stock to be able to supply the country at any price [42, 43]. In South Africa and India, Novo Nordisk has pulled out of human insulin pen markets, a move widely interpreted by industry observers as driven by the opportunity cost of dedicating production lines to moderately profitable insulin rather than to extremely profitable GLP-1 drugs (eg, Ozempic and Wegovy) [44, 45]. The United States is not immune to these dynamics: after years of defending its monopoly against potential competitors, Novo Nordisk abruptly discontinued insulin detemir in the US market before any alternative supply had been secured [46].

Millions of people around the world are unable to access or afford the drugs they need, not because of market dysfunctions caused by oversupply, but because of market incentives and constraints that deliberately and knowingly allow undersupply regardless of public health need. In our work as an international humanitarian medical organization, we witness on a daily basis the illness, suffering, and deaths of people who have been unable to afford or otherwise access their medicines, and we have worked for decades to address these issues.

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

International trade law narrowly circumscribes the very limited circumstances under which countries may restrict pharmaceutical exports. Rather than chasing unlikely, hypothetical supply chain threats, we urge policymakers to focus on solving well-documented vulnerabilities that already have evidence-based solutions waiting to be implemented.

International trade law strictly limits pharmaceutical export restrictions. Article XI of the General Agreement on Tariffs and Trade (GATT) prohibits "duties, taxes or other charges, whether made effective through quotas, import or export licences or other measures [from being] instituted or maintained by any contracting party on the importation of any product of the territory of any other contracting party or on the exportation or sale for export of any product destined for the territory of any other contracting party" [47]. While there are exceptions—for example "prohibitions or restrictions temporarily applied to prevent or relieve critical shortages of foodstuffs or other products essential to the exporting contracting party"—these are temporary in nature and can only be used to relieve an immediate shortage and categorically cannot be weaponized as economic leverage [47].

In the wake of some emergency COVID-19 export controls, the G20 reaffirmed that the Treaty should be understood such that even in emergency pandemic contexts, "emergency measures designed to tackle COVID-19, if deemed necessary, must be targeted, proportionate, transparent, and temporary, and that they do not create unnecessary barriers to trade or disruption to global supply chains, and are consistent with World Trade Organization (WTO) rules "[48].

Medicines and health care have historically been given protected status and deemed too important to be permitted to be weaponized in conflicts. Humanitarian exemptions for medicines are a longstanding norm in nearly all sanctions regimes, and both US national legislation and international law carve out protections for medical supplies during sanctions and conflict. In 2000, Congress passed the Trade Sanctions Reform and Export Enhancement Act (TSRA), which includes carveouts and protections for medicines in sanctions [49]. The Office of Foreign Assets Control (OFAC) issues general licenses authorizing the export of medicines and medical devices to sanctioned countries [50]. While humanitarian carveouts within trade sanctions have been criticized by some[7] as inadequate, the principle still stands that availability of medicines is too important to allow blockages, even in times of extreme geopolitical friction. International law, including Articles 18 and 19 of the Geneva Convention, affirms the special protected status of healthcare providers and the free flow of medicines even in times of war [52]. MSF has been outspoken in condemning breaches of these obligations when they have occurred, including attacks on healthcare facilities in Afghanistan, the Central Africa Republic, Ethiopia, Gaza, Mali, South Sudan, Sudan, Syria, Ukraine, and Yemen in recent years [53]

We strongly urge policymakers around the world to continue to preserve medical exceptionalism, and to ensure that life-saving goods are never weaponized or used as a bargaining chip or leverage in trade disputes.

Rather than viewing access to medicines as a zero-sum game or an inevitable source of conflict, the history of drug development underscores the importance of collaboration, even, and perhaps most critically, among geopolitical rivals.

During the Cold War, scientists were among the few granted passage across the Iron Curtain, and this cross-border cooperation led to breakthroughs that defined modern medicine in the twentieth century: the polio vaccine, malaria control innovations, and the eradication of smallpox [54, 55]. More recently, many if not most medicines were the result of some degree of international cooperation. Some more recent examples of medicines which require cross-border supply chains include:

- Artemisinin, used to treat malaria, is derived from *Artemisia annua*, a plant native to China [56].
- Captopril and cilazapril, used for hypertension, were derived from the venom of *Bothrops jararaca*, a Brazilian snake [57].
- Cyclosporine, an immunosuppressant used by organ transplant recipients and people

[7] Some argue that exemptions for medicines in sanctions are too narrowly defined, such that countries are unable to obtain necessary components like API or equipment to manufacture medicines [51].

with rheumatoid arthritis, psoriasis, and amyotrophic lateral sclerosis (Lou Gehrig disease), was developed from fungus identified in Norwegian soil [58].

- Cytarabine, used for acute lymphocytic and non-lymphocytic leukemia, was derived from *Cryptotheca crypta*, a Caribbean sponge [59].
- Exenatide, the first GLP-1, whose discovery paved the way for semaglutide (Ozempic/Wegovy) and tirzepatide (Mounjaro), was developed as a synthetic version of saliva from *Heloderma suspectum*, also known as Gila monsters, which are native to some parts of the United States, Mexico, and Guatemala [60].
- Ivermectin, used to treat parasitic infections, was derived from compounds found in Japanese soil [61].
- QS-21, a purified extract from bark from *Quillaja Saponaria*, a Chilean soapbark tree, is one of the most important and promising vaccine adjuvants, used in herpes zoster, malaria, avian influenza, and respiratory syncytial virus (RSV) vaccines [62].
- Vincristine and vinblastine, both used to various cancers, are manufactured from Madagascar periwinkle *Catharanthus roseus* [63].

These achievements stand as a testament to what humanity can accomplish when health transcends politics and international cooperation is understood as an opportunity and not liability.

The flexibility for US actors to pivot to global suppliers has proven lifesaving in the face of unexpected supply chain disruptions. In 2017, the US had a domestic manufacturer of heparin, a widely used blood thinner [64, 65, 66, 67]. However, Hurricane Maria devastated several manufacturing facilities in Puerto Rico, including those of Baxter, a major producer. To mitigate the resulting shortages, the US turned to imports from the United Kingdom. Yet soon after, global supply came under renewed pressure due to an outbreak of African Swine Fever, which threatened the pig populations, whose intestinal mucosa is the primary source of pharmaceutical-grade heparin [64, 65, 66, 67].

This case illustrates that domestic production is not protective against the events most likely to cause catastrophic shortages—unplanned, unanticipated long-term shutdowns of key facilities. It is also a testament to the importance of geographically diverse production: in this case, two major manufacturing sites globally were simultaneously affected. For most products, policymakers should aim for at least three suppliers. International flexibility is a fundamental protection for domestic supply availability. Notably, heparin may not have appeared on policymakers' radar as a priority vulnerable drug, given manufacturing capacity in several countries. While expanding production capacity across multiple US sites may reduce the risk posed by localized natural disasters, it does little to address regional vulnerabilities, such as pandemics or issues like illnesses among animals used in product manufacturing, that affect upstream supply inputs.

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

Technical feasibility: While expanding domestic pharmaceutical production is technically feasible, doing so at meaningful scale is economically questionable. The core challenge is not whether the United States can manufacture more FDFs and APIs domestically, but whether doing so would actually improve affordability, resilience, or supply security domestically or otherwise. In most cases, the answer is no. In the limited set of cases in which the answer is yes, policymakers should adopt clear criteria to guide investment, such as targeting single-source drugs with high-risk supply chains, addressing drugs chronically in shortage, or promoting affordability initiatives (for example, California's CalRx insulin manufacturing effort). Any intervention—especially interventions that risk severely impacting global supply chains and markets—should be weighed against viable alternatives, with a careful assessment of both costs and benefits.

As an illustrative example of the challenges in meeting economies of scale for some drugs, consider trastuzumab, a widely used breast cancer drug for HER2 positive breast cancer. How many companies could manufacture this drug and achieve adequate economies of scale to be competitive in global markets? Consider that an estimated 50,000 new cases of HER2-positive breast cancer are newly diagnosed in the United States annually, of which 85% are indicated to receive trastuzumab [68]. Assuming standard weight and dosing, we can assume demand in the United States of 351 kg/year (68). At this volume, we would expect the per kilogram cost of API to range between $100,000/kg and $280,000/kg, depending on volume and manufacturing modality [69]. At volumes of 3,000kg/year, costs fall to $45,000 - $60,000/kg [69]. This corresponds in per-patient API costs of $1,400-1,900 at commercially competitive economies of scale, in contrast to costs as high as $9000/patient/year for smaller batches.

This example illustrates the serious risk that high tariffs on pharmaceuticals could lead to a tripling of some generic/biosimilar drug prices solely from the loss of economies of scale, even before accounting for additional costs introduced by supply chain disruptions. This is likely an underestimate for many drugs. Policymakers should also take into account the likely competition-reducing effects of high tariffs: there is robust evidence that meaningful price competition in generic/biosimilar drug markets only emerges when there are at least four independent manufacturers. For the US to replicate that level of competitive pressure domestically, it would need to scale up demand for trastuzumab to roughly 12,000 kg per year, or 34 times its current level. This is unrealistic. Although policymakers might consider addressing the limitations of domestic markets too small to be viable, such as the case outlined above, by expanding into export markets, they must also account for likely retaliatory tariffs. US manufacturers are unlikely to be cost-competitive with large-scale manufacturers in China and India, who achieve dramatic economies of scale due to their domestic market, regardless of US tariff policy.

The growth in pharmaceutical manufacturing capacity in China, India, and other countries should not be viewed as a threat to the United States. Instead, it benefits the resilience of US and global supply chains by enabling greater economies of scale and associated cost

decreases, building redundancy and buffer to ensure supply stability in the face of natural disasters or quality disruptions, and fostering competitive conditions needed to keep prices in check. Expanding global manufacturing capacity is also critical to meet the rising burden of disease, particularly in low- and middle-income countries. Novo Nordisk's recent withdrawal from several insulin markets in middle-income countries underscores the urgency of ensuring supply continuity in middle-income countries, which have the highest burden of diabetes [70]. Moreover, even when setting aside altruistic motivations, ensuring global access to essential medicines is critical from a public health perspective, as inadequate treatment access can accelerate the spread of infectious diseases and antimicrobial resistance (AMR), both of which pose significant threats to all countries and are otherwise counterproductive to infectious disease response and control.

Finally, some proponents of onshoring argue that US manufacturers can overcome scale disadvantages through superior technology [71]. But this argument overlooks how innovation actually develops in generic/biosimilar process optimization and manufacturing. Unlike originator firms that enjoy monopoly pricing power, generic/biosimilar manufacturers must compete on cost and are therefore constantly pressured to invest in and optimize production efficiency. The value of this technical capacity in process optimization is widely recognized: some licenses issued by the Medicines Patent Pool (MPP) include grant-back clauses, allowing originator companies to benefit from improvements made by licensee manufacturers [72]. The clauses exist because originator firms value the innovations made by generic/biosimilar firms enough to write them into licensing contracts.

Import reliance should not be conflated with supply security: The government has a strong and compelling interest to promote supply resilience, thereby ensuring patients have reliable access to essential medicines. However, onshoring manufacturing does not guarantee supply security. Supply security hinges on diversification, redundancy, and flexibility, not just geographic location. There is no evidence to suggest that onshoring will lead to better outcomes than the status quo, and all evidence points to the conclusion that widespread onshoring would underperform tried and tested solutions like using regulatory and purchasing power to incentivize multisource, diverse procurement, investing in data infrastructure to have greater visibility over supply chains, empowering and resourcing regulators to identify and mitigate shortages before they happen, and investing in manufacturing science to improve efficiency and quality.

Onshoring is far from a certain remedy for shortages. As one example, generic sterile injectables are disproportionately domestically produced compared to other classes of drugs (40% US, vs. 21% India, 13% EU, 11% China), yet remain the most shortage-prone [73]. Nor is onshoring a guarantee for improved quality: a recent study found that manufacturing facilities located within the US had quality problems comparable to those located abroad [13].

A geographically diversified supply chain with multiple API manufacturers is more resilient than a single domestic facility. There is consensus among supply chain experts that, for example, having three independent, geographically diverse penicillin G benzathine API manufacturers would address chronic shortages far more effectively than putting all proverbial eggs into just one US-based manufacture. The case for fully onshored production is exceptionally

narrow: it would require assuming a disaster enveloping the entire world but sparing the US, a simultaneous war with every other pharmaceutical-producing nation (of which there are many), the abandonment of existing medical stockpiles, and the collapse of the US's proven ability to rapidly scale production in urgent, emergency contexts, as demonstrated during Operation Warp Speed.

While supply diversification is necessary—no drug should be manufactured just one facility globally—onshoring does not necessarily mean an increase in the number of firms. Higher trade barriers may disincentivize some manufacturers from entering or remaining in the US market altogether. This stands in tension with longstanding US pharmaceutical policy, which has actively promoted the adoption of generics and biosimilars to enhance market competition and reduce costs. Supporting a strategy that may ultimately lead to greater supplier concentration and thereby undercut price competition, raising serious questions about policy coherence and long-term public health outcomes.

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

We are surprised by the US's newfound interest in imposing pharmaceutical tariffs, given its long-standing bipartisan trade policy of criticizing other countries for similar measures. The Office of the United States Trade Representative (USTR) underscores this stance in its annual Special 301 Report, a Congressionally-mandated annual review evaluating, among other trade concerns "market access barriers, including nontransparent, discriminatory or otherwise trade-restrictive, measures that appear to impede access to healthcare" [74]. In recent years, the USTR has explicitly objected to pharmaceutical tariffs in Brazil, India, Indonesia, and Pakistan" [74]. In addition to expressing trade concerns, critiques of pharmaceutical tariffs in some Special 301 reports reference research demonstrating that pharmaceutical tariffs negatively impact access to medicines and harm public health [75]

The economics literature does not support the assertion that import tariffs will have positive trade effects. Handley, Kamal, and Monarch (2020) review the implementation of tariffs in 2018-19, during which time 12% of total US imports ($290 billion) were subject to an average tariff increase of 24 points [76]. Using confidential firm-trade linked data, they find that these tariffs resulted in not only foreign-imposed retaliatory export tariffs, but additionally resulted in (negative) supply chain spillover effects that further dampened export growth [76].

The rationale for tariffs as a policy tool to incentivize onshoring warrants careful scrutiny. The strongest version of this argument goes something like this: if Country X increases tariffs enough, manufacturers will be incentivized to onshore production. However, the underlying mechanism is often glossed over: firms are not drawn to domestic production through subsidies or efficiency gains or patriotism, but because tariffs raise import prices, sometimes dramatically. Dramatically increased prices mean many patients will not be able to afford needed medicines.

Consider the following thought experiment: Country X imposes substantial tariffs in an effort to encourage domestic manufacturing, prompting a number of other countries to retaliate with tariffs of their own. For a pharmaceutical manufacturer, the domestic market in Country X may not be large or profitable enough to justify the significant capital investment required to establish production facilities solely for that market.[8] Moreover, retaliatory tariffs and broader spillover supply chain disruptions reduce the likelihood that facilities based in Country X could viably serve export markets. As a result, the intended reshoring effects of the tariff regime may fail to materialize, leaving firms disincentivized to shift production domestically, and critically, leaving consumers with higher medicine bills.

In a recent response to a question from a journalist about the effects of tariffs, President Trump acknowledge the likely increased costs, stating that "Well, maybe the children will have two dolls instead of 30 dolls. And maybe the two dolls will cost a couple bucks more than they would normally."

But medicines are not dolls. Patients cannot make do with 2 pills when they need a 30-day supply. Pharmaceutical access is already a critical issue—nearly one in four Americans reports rationing insulin—and tariffs risk compounding these access challenges by further driving up costs [77, 78].

Furthermore, the economics literature suggests that tariffs may intensify troubling trends observed over the past five years: mounting supply chain fragility, inefficient allocation of critical inputs, and pricing behavior that suggests tacit coordination among suppliers. Tariffs—or even market turbulence resulting from anticipation and stockpiling—risks amplifying these effects, potentially accelerating market distortions that harm consumers and strain public health systems. Similar dynamics have contributed to what some economists describe as "seller's inflation," wherein supply chain shocks (like COVID-19) provide an opportunity for firms to raise prices [79, 80]. In both the COVID-era disruptions and a potential future shaped by pharmaceutical tariffs, consumers generally accept higher prices, particularly for inelastic goods like medicines, regardless of whether those increases reflect legitimate cost pressures or opportunistic pricing.

Beyond the impact on affordability and access, a key structural challenge to implementing tariffs in a targeted manner that could mitigate against likely harms to health is the opacity of drug prices in the US: price increases will occur in the already notorious 'black box' of US drug pricing, making it difficult for regulators and consumers alike to distinguish between justified cost pass-throughs and abusive markups. There is a compelling body of evidence that these dynamics occurred during COVID-19 when 1) consumers anticipated price increases and 2) the social and political context permitted and even encouraged manufacturers to freely signal through public communications their intentions to raise prices. Health products are intrinsically inelastic goods, and increased prices have consequences on access.

But we should speak plainly when talking about elasticity of pharmaceuticals: economists describe medicines as inelastic because people are observed to highly value their lives, and to reallocate whatever resources they have to purchase medicines. For life-saving medicines,

[8] See discussion of the issue of economies of scale in the above response to section viii.

behind what economists euphemize as 'observed elasticity' is a person who became sick and perhaps died because they could not afford to purchase their medicine when prices increased.

As described in detail throughout this submission, the US lacks both the necessary data collection infrastructure and accompanying transparency policies to be able monitor and mitigate likely harms to the affordability and availability of health products.

(x) any other relevant factors.

Ensuring a robust, reliable drug supply and promoting access to medicines are worthy and important priorities for policymakers. The US has many tried and tested tools available, including:

- Improving visibility across the supply chain to identify vulnerabilities, particularly:
  - Mapping the number and distribution of KSM and API manufacturers of priority drugs;
  - Requiring reporting of production capacity;
  - Making volume and shortage data available to researchers at the firm, API, and FDF level, to deepen the evidence base on market dynamics;
  - Cooperating with other national regulators and global actors to enhance and link data to improve visibility of global supply chains; and
  - Developing definitions and standardize reporting standards for tracking KSM, API, and FDF volume, value, and spread.
- Supporting generic/biosimilar markets through
  - Enabling generic biosimilar manufacture, through intellectual property reform and competition enforcement that target abusive patent 'evergreening' and related business practices;
  - Incentivizing generic and biosimilar purchase and multisource procurement; and
  - Increasing demand for generic/biosimilar drugs through patient education and PBM reform.
- Investing in R&D for priority health areas;
  - Investing in supply chain-oriented research, for example assessments of shelf-life and thermostability of health products. In a context of no private sector incentives to undertake this research, organizations like MSF have had to step in to conduct such research on priority products ([81]. This research is vital to reduce waste, manage stockpiles, and optimize supply in shortages.
- Negotiating fair and affordable prices and using competition enforcement to monitor and address infractions that drive up prices;

- Requiring risk planning by firms and modelling "stress tests" to identify dynamic and system-wide failure and chokepoints.
- Investing in alternative manufacturing modalities for drugs with no private sector interest (for example, medical countermeasures and many vaccines).

As we have outlined in our submission above, our experience in global markets, particularly in humanitarian contexts, and general expertise in supply chains and pharmaceutical market dynamics have led us to conclude that pharmaceutical tariffs are at best ineffective instruments in achieving desired policy ends, and at worst, risk destabilizing global drug markets and harming access to patients both in the United States and in the contexts in which MSF has operations.

The HHS report *Draft research plan for addressing shortages of medical products and critical foods and strengthening the resilience of medical product and critical food supply chains* highlights in bold text the following conclusion: "Further research is needed to identify and develop effective strategies to increase domestic capacity and supply chain diversification, including an examination of the socioeconomic, demographic, environmental, and trade impacts, and how to ensure that demand-side support can sustain industrial base investments in domestic manufacturing over-time." We echo their call for caution, evidence, and a comprehensive understanding of the risks involved.

As a neutral, independent international humanitarian medical organization, MSF does not have a position on US industrial strategy or trade competitiveness. We do, however, a position on ensuring access to medicines. We urge policymakers to take seriously the overwhelming evidence that pharmaceutical tariffs, particularly those implemented abruptly and at high rates, will likely destabilize global supply chains and negatively impact access to medicines in the US and abroad. We further urge policymakers to at minimum, prioritize the development of critical data infrastructure, risk mitigation plans, and research—repeatedly recommended in government reviews—before high-risk policies are undertaken which might otherwise lead to serious harms within the US and elsewhere in the world.

We also express concern that many of the agencies that would have played a critical role in conducting risk assessments, identifying emergent problems, and conducting mitigation activities have been among those severely reduced in recent HHS staffing cuts. In particular, we are concerned about the reported termination of key staff, including at the FDA's Center for Biologics Evaluation and Research (CBER) and Center for Drug Evaluation and Research (CDER). This technical capacity saves lives, preventing 236 shortages in 2023 alone [12]. Also critical is the FDA Office of International Programs (OIP), which did important work in improving global capacity and visibility to improve supply chain stability and drug quality, as well as the Office of Inspections and Investigations.

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