



Medicines supply chain

USP Global Public Policy Position

Key Elements to Building a More Resilient Supply Chain



Issue

Today, patients in the United States and around the world depend on medicines—and the ingredients used to make those medicines—sourced from and manufactured around the globe. This global supply chain for medicines, while providing some inherent risk mitigation, has numerous vulnerabilities that can be challenged by acute disruptions. When such a disruption occurs, concerns arise regarding the quality and safety—as well as shortages—of medicines, particularly those used for critical treatments. Unfortunately, the COVID-19 pandemic brought these impacts into sharp focus.



11 Key Elements for a More Resilient Supply Chain

USP supports a comprehensive public policy framework to build a more resilient supply chain, including advancing the use of pharmacopeial standards across the supply chain, to help ensure the supply of quality medicines. We propose the following key elements be integrated into policy frameworks to build more resilience into the medicines supply chain.

Foster more, not less, supply chain diversity

- 1 Increase geographic diversity for ingredients and manufacturing – Policymakers should incentivize geographic diversity among the sources of medicine ingredients and drug manufacturing to reduce the risk of shortages from acute disruptions that occur in one geographical location (e.g., earthquake, hurricane, political disruption) or that move from one part of the world to others (e.g., pandemic).
- 2 Establish baseline of local production capacity – Governments and manufacturers should facilitate the development of local production capabilities to secure a supply of essential quality-assured medicines and vaccines for their population when acute disruptions arise.

Invest in more manufacturing capacity for critical medicines

- 3 Facilitate an adequate supply of therapeutics and vaccines – Governments should help ensure an appropriate supply of the medicines and vaccines needed to address the most urgent public health concerns by leveraging capital investments to facilitate additional manufacturing capacity, implementing policy reforms to encourage greater competition, and ensuring access to quality and affordable medicines.
- 4 Invest in advanced technologies – Governments should incentivize advanced technologies (e.g., continuous pharmaceutical manufacturing) through direct investments and other measures to enable more efficient and nimble production of essential medicines and vaccines and to buffer against disruptions in supply during a global crisis.

Enable more transparency and data sharing

- 5 Increase transparency across the supply chain – To enable appropriate actions—in and across countries—to address and avoid potential supply chain concerns, governments should expand public reporting requirements to healthcare providers and industry for indicators on existing or potential drug shortages. Drug manufacturers and ingredient suppliers should be required to monitor and report to governments on their capacity and the quality of ingredients they source.
- 6 Enhance global cooperation – Pharmacopeias and regulators around the world should increase information-sharing and consider recognition and reliance agreements. This will help to efficiently mobilize resources during public health emergencies such as pandemics, coordinate access to essential medicines and vaccines, and disincentivize a market for substandard and falsified medicines.

Conduct crisis contingency planning and action

- 7 Require contingency planning – Policymakers should encourage and incentivize medicine manufacturers to develop backup plans, including for production lines and quality control. Manufacturers of critical medicines also should have other redundancies in place in the event of an acute disruption, to ensure continued access to quality medicines.
- 8 Build and maintain critical medical product stockpiles – Governments should build and maintain stockpiles of critical medicines and medical products to be prepared to meet the needs of patients and healthcare providers if product shortages result from a crisis. The composition of products in national stockpiles should be continually reviewed and modified to address the most likely shortages of the most critical products. Medical supplies to protect the safety of frontline healthcare workers should be a priority.

- 9 Plan for distribution resilience – Governments should issue enforceable guidance to ensure the free flow of ingredients and materials (including quality standards and physical reference standards) to enable medicine manufacturing to continue during a crisis. In addition, governments should develop contingency plans to ensure that distribution logistics are in place to transport critical medical products to providers.

Strengthen regulatory systems and quality assurance

- 10 Strengthen regulatory oversight – Governments should invest in stronger regulatory systems that can efficiently review applications for therapeutics and vaccines, and enforce existing regulations that protect patient safety, including adherence to quality standards. Reliance mechanisms or regional regulatory systems can operate as networks to share information on quality, efficacy, and safety, thereby reinforcing regulatory oversight.
- 11 Bolster quality assurance systems and adherence to public quality standards – Regulators should strengthen quality assurance systems through investments in workforce training and national drug quality control laboratories and should stress adherence to science-based public quality standards, which are essential to maintaining the trust of healthcare professionals and patients in medicine quality. Moreover, countries around the world should ensure compliance to international standards, including good manufacturing practices and science-based public quality standards, so that medicines and ingredients from more locations can be trusted in the global supply chain.

Discussion

Over the last decade or so, global medicines supply chains have moved from being vertically integrated, where a drug manufacturer owns or controls most aspects of production (including suppliers), to horizontal, where many functions in the supply chain (such as the production of both active pharmaceutical ingredients (APIs) and inactive ingredients) are increasingly outsourced to many companies around the world. In many cases, these companies are concentrated in certain geographical areas.

The COVID-19 pandemic has exposed vulnerabilities in the current way the medicines supply chain works, including geographically concentrated sourcing and manufacturing, uneven regulatory environments, and regulatory enforcement or inspection capacity constraints. Many countries may soon, if they have not already, face disruptions such as medicine shortages, concerns over substandard or falsified medicines, and price volatility. Having policies in place to build a more resilient supply chain can help ensure the continued availability of safe, quality medicines for patients around the globe—even in times of a pandemic crisis. While the current COVID-19 crisis points to the supply chain impact of a pandemic, other acute supply chain disruptors include weather events such as hurricanes and earthquakes, as well as product recalls.

The globalization of supply chains has led to geographic concentration of manufacturers of both ingredients and finished medicines in certain locations where labor and

raw material costs may be lower, environmental regulations more permissive, and infrastructure subsidized by the public sector. While this concentration has likely led to lower costs for many medicines and their ingredients, it poses a risk to the reliability of supply in crisis situations and raises quality and safety concerns.

During a pandemic, sourcing from only a few countries can have unintended consequences. For example, countries that make medicines and APIs may withhold essential public health resources—including therapeutics intended for COVID-19—as well as other therapies needed to address national health priorities. For instance, India briefly withheld exports on selected medicines, including some antibiotics and painkillers, and has restricted the export of antimalarials now being considered as potential (though still unproven) treatment options for COVID-19.¹² Countries may also compete with each other to procure medications. Diversifying sources of both pharmaceutical ingredients and finished medicines can help reduce the risk of concentration in only one place, and appropriate incentives to facilitate this diversification should be considered.

Increased line-of-sight across all parts of the supply chain can also help make the supply chain stronger. Regulators, along with pharmacies, hospitals, and providers, need to know more about where medicines and ingredients are manufactured and how they have passed through the supply chain. This information can inform risk mitigation decisions and help governments and providers plan for the supply of quality medicines needed to treat patients. This is essential to building and maintaining the public's trust.

Today, regulators have limited and inconsistent information on the sources of the ingredients in medicines or the volume of medicines produced from manufacturing facilities around the world. Information-sharing between regulators and industry is also needed to see clearly across the supply chain. New reporting requirements for finished drug products and ingredient makers can increase transparency and should be balanced with appropriate protections for trade secrets and confidential commercial information. Further, if manufacturers can use new technologies (e.g., AI) to strengthen their ability to monitor their suppliers, and thereby understand the global presence of both their suppliers and their subcontractors, they may be able to mitigate problems more immediately as they arise.



A requirement for drug and API manufacturers to develop contingency plans in the event of a disruption in production would help to ensure a continued supply of quality medicines. Such measures should include establishing alternative sources of API and other ingredients, shifting production lines, and implementing quality control. These contingencies should also apply to ensuring the availability of medical products such as personal protective equipment, bags for intravenous fluids, syringes, and other supplies needed to provide care that would be impacted by supply chain disruptors.

Strong regulatory oversight is needed to withstand disruptions in the supply chain. Strengthened oversight by regulatory authorities includes deployment of tools such as supplier verification and audits to ensure the quality of ingredients, along with track-and-trace mechanisms to determine drug and ingredient current and past locations. Risk-based analysis can help countries understand the most critical—or vulnerable—points in the supply chain. In the absence of tracking and tracing of products, especially as the supply chain diversifies, quality testing can serve as a last line of defense. During times of crisis, aggressive enforcement action by regulatory bodies against substandard and falsified products, unverified or false claims of treatments or cures, and price gouging, is needed to prevent further harm.

Advanced manufacturing technologies, such as continuous manufacturing, provide more streamlined, consistent, and efficient production of medicines than traditional approaches. Efforts to operationalize this technology, including incentives to allow for its rapid deployment, should be pursued. Given the current global pandemic, countries should incentivize and accelerate longer-term efforts to help expand the continuous manufacturing infrastructure in both the United States and in other countries for generic and branded medicine production.

Enhanced global cooperation can help countries secure critical medicines, especially in light of challenges caused by border closures as a result of COVID-19. Regulatory authorities that share information have expedited the approval of essential vaccines and medicines, prevented the distribution of substandard and falsified medicines, and quickly mobilized resources during drug shortages and public health emergencies. A recognition or reliance



arrangement, whereby one agency recognizes or relies on another's work as equivalent to its own, allows medicine regulators to make use of shared information while being able to make their own decisions. Examples of information that regulators can share with each other include clinical assessments, manufacturing site inspections, and post-market safety data.

Maintaining the quality of medicines during a global crisis is paramount to ensuring they work in the way they are intended. In responding to disruptions, countries may purchase medicines from untested suppliers, which in turn could create a market for substandard or falsified medicines.³ Low- and middle- income countries are especially vulnerable, as their already under-resourced regulatory systems would come under additional stress. Consumers may also buy medicines from the internet, where oversight is weaker and bad actors proliferate. In addition, the urgency to develop new therapeutics and vaccines cannot be separated from the need to assure quality. Ensuring pharmacopeial standards are met across the supply chain can help regulators and industry ensure continued access to quality medicines.

Encouraging greater competition, especially for products with either a single source or few manufacturers, would help lead to increased access to critical medicines. Once a vaccine for COVID-19 is discovered and approved for use, local capacity to manufacture may become a priority to ensure widespread, equitable, and rapid distribution.

It also is important that governments plan for resilience in distribution. Regulators should issue standing guidance that clarifies the ingredients, materials, and standards that must remain available in global commerce for the manufacture of critical medicines. Moreover, contingencies for the transport of medicines and medical supplies is essential to account for the potential malfunction of traditional transportation modalities in a crisis situation. In addition to contingency planning for medicines, it is equally essential for personal protective equipment to protect the safety of frontline healthcare workers. Distributors, including wholesalers, must follow good distribution practices to assure medicine and ingredient quality through procurement, purchasing, transport, distribution, repackaging, relabeling, storage, and documentation. Logistics and transport considerations are critical to ensuring essential medicines can make it to patients.

Finally, to be prepared to meet the needs of patients and healthcare providers if product shortages result from a crisis, governments should build and maintain stockpiles of critical medicines and medical products with unexpired inventory. The composition of products in national stockpiles should be continually reviewed and modified to address potential shortages of the most critical medical products.

Call to Action

USP encourages investment and policy reform toward building a more resilient global supply chain. The current vulnerabilities in the supply chain are the result of a number of factors, so solutions to address these vulnerabilities must account for these variations. The key elements outlined above require action by all those in the supply chain, including manufacturers, distributors, policymakers and regulators, and public health experts.

About USP

Founded in 1820, USP is an independent, nonprofit, science-based organization that safeguards the public's health globally by developing quality standards for medicines, dietary supplements, food ingredients, and healthcare quality. USP standards describe specifications and tests for identity, strength, quality, and purity. USP standards are enforceable by the U.S. Food and Drug Administration (FDA) for medicines and their ingredients imported into or marketed in the United States and have been used in more than 140 countries. Such standards also assist industry in the development, manufacturing, and testing of medicines. USP standards are developed by independent experts through a transparent scientific process, with input from stakeholders and federal agencies such as FDA and the Centers for Disease Control and Prevention.

USP's Promoting the Quality of Medicines Plus (PQM+) program improves access to quality-assured priority medicines and addresses the proliferation of poor-quality medical products in low- and middle-income countries. PQM+ strengthens medical product quality assurance systems in low- and middle-income countries through cross-sectoral and systems strengthening approaches and the application of international quality assurance standards across the pharmaceutical system.

USP is implementing a comprehensive program to support the public health response to the COVID-19 pandemic. Our immediate work is focused on facilitating the supply of quality medicines across the global supply chain—especially for those medicines that treat symptoms associated with the virus—by working closely with regulators, manufacturers, and other stakeholders around the world. We are also engaging in middle- and long-term activities to assess vulnerabilities in the global supply chain for medicines, advocate for greater transparency and more diversity in the sources of medicines and their ingredients, and ultimately help build a more resilient supply chain.

¹ Government of India Ministry of Commerce & Industry. Department of Commerce. Directorate General of Foreign Trade. Amendment in Export Policy of APIs and formulations made from these APIs. New Delhi. March 3, 2020. https://dgft.gov.in/sites/default/files/Noti%2050_0.pdf

² Government of India Ministry of Commerce & Industry. Department of Commerce. Directorate General of Foreign Trade. New Delhi. Amendment in Export Policy of Hydroxychloroquine. https://dgft.gov.in/sites/default/files/notification%2054_0.pdf

³ Pisani, Elizabeth. The COVID pandemic increases the chance that your other medicines won't work. Medium. March 29, 2020. <https://medium.com/@elizabethpisani/the-covid-pandemic-increases-the-chance-that-your-other-medicines-wont-work-66b7e272bb20>