

Supporting Resilient Drug Supply Chains in the United States

Challenges and Potential Solutions

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DISCLOSURES

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EXECUTIVE SUMMARY

The brief builds on and complements the White House's recently released "[100-Day Review](#)" on Building Resilient Supply Chains," proposes solutions to increase transparency and prepare for emergency situations not contemplated in the "100-Day Review," and also highlights how recently proposed legislation can contribute to a system-wide resiliency solution.

Reliable and robust medical product supply chains are critical to prevent shortages of life-saving medications and assure the US is prepared for pandemics and other systemic threats. Over the past decade, tens to hundreds of drugs have gone into shortage each year, and as of June 2021, more than 100 drugs are listed as in shortage by the U.S. Food and Drug Administration (FDA). Moreover, during the COVID-19 pandemic, manufacturing capacity for vaccines took months to ramp up and caused the production of other critical drugs to be deprioritized. These crises show that the U.S. must do more to ensure that it has a resilient drug supply chain.




A *resilient* supply chain ensures that patients have safe and effective drugs, in adequate quantities, when they're needed. The supply chains that produce drugs and medical consumables for the U.S. are complex, but comprise four key components that may be the source of resilience failures: the specialized personnel ("*staff*") that work within supply chains; the ingredients, associated supplies, and equipment used to make drugs and medical products as well as a finished goods inventory ("*stuff*"); the manufacturing, storage, and distribution facilities themselves ("*space*"); and the data infrastructure, processes, and other "*systems*" that support supply chains. Resiliency is in large part reliant on the supply chain's ability to prevent and respond well to disruptions in demand or supply that may affect each of these components. Supply chain breakdowns have most often occurred in two subsets of pharmaceutical products: 1) low-margin, generic products in chronic shortage, and 2) public health emergency products, especially advanced biologics such as vaccines or monoclonal antibodies, that experience large spikes in demand due to pandemic or other factors. In many cases, policy responses to these two distinct issues will be complementary; addressing resiliency issues in one subset of products will likely bolster resiliency in the other as well.

Four drivers contribute to a lack of supply chain resilience: adverse market forces, geographic concentration, quality and oversight challenges, and limited transparency. Market forces lead manufacturers to operate on small margins and offer drugs at the lowest possible price, often at the expense of investments in resilient manufacturing. Geographic concentration in a few countries, mainly China and India, has made supply chains vulnerable to the effects of international disputes or conflicts, natural disasters, and other risks. Issues with quality arise frequently and it is challenging to provide the oversight needed to prevent such issues. Finally, a system-wide lack of transparency makes it difficult for regulators to track vulnerabilities at the national level and for individual purchasers or manufacturers to assess or invest in resiliency.

This brief then proposes **three types of policy solutions** that should be included in upcoming legislative and regulatory reforms and private-sector actions that aim to improve resilience:

TABLE 1: Three Policy Solutions to Improve Resilience

PROPOSED SOLUTIONS

| Policy Solutions to Improve Resilience | Chronic Shortage Products | Public Health Emergency Products |
|--|---|--|
| <p>Changing Financial Incentives</p>  | <ul style="list-style-type: none"> • Establish targeted subsidies and tax incentives and tie these incentives, along with CMS reimbursement and federal purchase contracts, to specific manufacturer actions in the areas of Geographic Concentration, Quality Oversight, and Increased Transparency. • Promote guaranteed purchase contracts in the public sector and private sector to increase predictability. | <ul style="list-style-type: none"> • Establish targeted subsidies and tax incentives and promote guaranteed federal purchase contracts, virtual stockpiles, and surge capacity for advanced biologics and other therapies that are targeted towards emerging threats. • Establish targeted subsidies and tax incentives and promote guaranteed federal purchase contracts, virtual stockpiles, and surge capacity for essential medicines for which disruptions would be particularly harmful. |
| <p>Implement New Technologies Manufacturing</p>  | <ul style="list-style-type: none"> • Support the development of advanced manufacturing technologies such as continuous manufacturing that can improve the quality and reliability of manufacturing processes. • Streamline regulatory pathways to facilitate the implementation of modernized manufacturing technologies and processes. | <ul style="list-style-type: none"> • Coordinate internationally to enhance biologic and vaccine manufacturing in order to increase global manufacturing response capabilities. • Streamline regulatory pathways to promote the use of on-demand and distributed manufacturing techniques. |
| <p>Promote Transparency</p>  | <ul style="list-style-type: none"> • Require reporting of key information on supply chain resiliency, and translate nonproprietary findings based on the data to the market to empower purchasers to partner with stable and reliable suppliers, via FDA or an independent nonprofit. | <ul style="list-style-type: none"> • Identify biologics, essential medicines, and other therapies that should be offered incentives or guaranteed federal contracts for timely and sufficient emergency capacity using information collected by FDA or other federal agencies. |

These policy interventions will improve incentives and supports around clear measures of supply chain resilience and quality, so that the market will reward investments in reliable and robust supply chains and manufacturing.

INTRODUCTION

A resilient drug supply chain ensures that patients have safe and effective medications, in adequate quantities, when they're needed. Unfortunately, shortages of life-saving and life-sustaining medications have severely affected many aspects of patient care for years, in large part because of the lack of resilience in drug supply chains. COVID-19 has exacerbated these challenges, involving products ranging from the generic drugs critical for intubated patients to the difficulties of massively scaling up vaccine production. These problems have led to increased policymaker interest in examining drug supply chain resilience critically in order to avoid further disruptions in the current pandemic and reduce the risk of shortages in the future. With growing interest in legislative and regulatory reforms to improve the reliability and robustness of U.S. drug supply chains, it will be crucial to achieve a common understanding of how to enhance supply chain resilience.

In this white paper, we describe the components of modern drug supply chains and the implications of these components for supply chain resilience. We then assess current issues with U.S. drug supply chains and propose policy solutions to those issues. The CARES Act of 2020 introduced several reforms to drug supply chains, most notably requiring manufacturers to report more information to FDA and ordering the Department of Health and Human Services (HHS) and the National Academies of Sciences, Engineering, and Medicine (NASEM) to conduct a comprehensive review of medical supply chains. The White House's recently released "100-Day Review" on Building Resilient Supply Chains proposes additional worthwhile steps related to supply chain mapping and resilience and quality assessments.

However, the "100-Day Review" report does not propose a methodology to measure supply chain resilience or translate critical supply chain information to purchasers, and it does not focus as extensively on the importance of preparing for future public health emergencies by ensuring availability of advanced biologics such as vaccines and monoclonal antibodies. Further steps are needed to correct a lack of effective market incentives, underinvestment in manufacturing quality and supply chains, intense geographic concentration, and a general lack of transparency that have made drug supply chains less resilient in America. Our assessment identifies a set of policy actions to address these issues: new financial incentives to increase resilience; support for investments in new manufacturing technologies like continuous manufacturing, on-demand manufacturing, and modernized inspection and sterilization equipment; and greater transparency to avoid and respond to shortages.

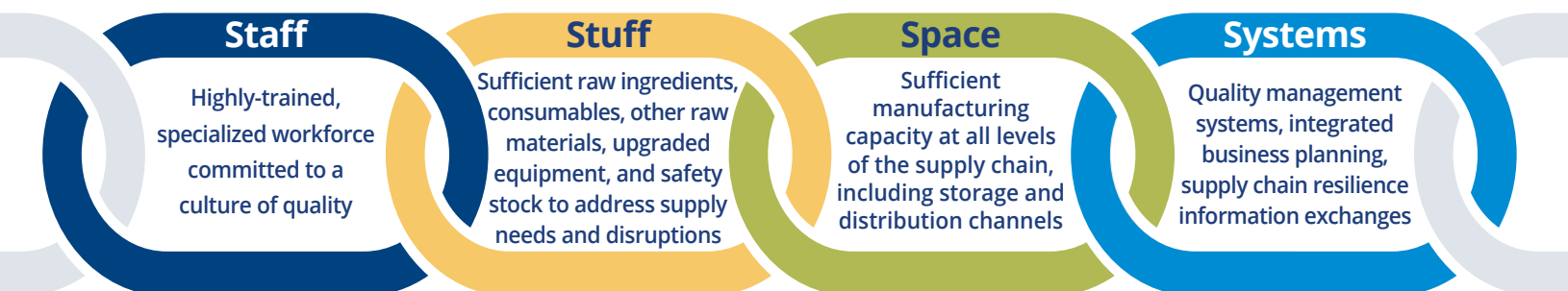
Components of the US Drug Supply Chain

The U.S. drug supply chain is vast and complex, supplying thousands of different products produced from a broad variety of facilities across the globe. Pfizer's COVID-19 vaccine alone [contains 280 components](#) produced by suppliers in 19 different countries. In a complex supply chain, a network of reliable suppliers is necessary at every stage, from early inputs and raw materials to finished dosage forms and distribution. These suppliers must produce drugs that consistently meet high-quality standards, including specifications for purity and potency.

Supply chain resilience is not simply about the existence of facilities that can consistently produce high-quality products. Ultimately, to ensure that high-quality, critical medications are available for patients in the right

quantities and at the right times, the supply chain must have consistency and reliability in four key components:

- Staff: Highly-trained, specialized workforce committed to a culture of quality
- Stuff: Sufficient raw ingredients, consumables, other raw materials, upgraded equipment, and safety stock to address supply needs and disruptions
- Space: Sufficient manufacturing capacity at all levels of the supply chain, including storage and distribution channels
- Systems: Quality management systems, integrated business planning, supply chain resilience information exchanges, and other practices, policies, and procedures that support supply chain resilience.



What Does it Mean for a Supply Chain to be Resilient?

Supply chains are complex, but must ensure that patients have safe and effective drugs, in adequate quantities, when they're needed. A resilient supply chain is able to avert shortages when experiencing supply shocks or demand shocks, when supply of a drug or raw material is disrupted, or demand for a drug suddenly spikes. In addition, when shortages do occur, resilient supply chains effectively mitigate their duration and severity.

Supply chain resilience has become a high-priority issue in part because the country is experiencing a large and sustained spike in demand for certain medical products due to the COVID-19 pandemic. But demand shocks take a variety of other forms as well. Natural disasters or bioterrorist events could cause rapid surges in demand for certain drugs or medical supplies. Even the perception of a potential shortage can cause a demand shock: fearing a potential shortage, individuals or organizations may stockpile essential medicines, leading to a real shortage.

Some of these same factors may contribute to supply-side shocks. For example, if a pandemic, natural disaster, or bioterrorist event affects a major manufacturing facility, supply could be disrupted. Supply shocks also can result from issues with manufacturing quality or geopolitical conflict, including trade restrictions or changes to prices of exports or imports from countries where manufacturing takes place.

All these factors pose ongoing risks to drug supply chains. Each type of risk may require different targeted mitigation measures, and what these measures should be may depend on whether risks are systemic or individualized. Certain problems, like manufacturing quality, could be addressed by policies directed at activities of individual manufacturers, including through private responses such as contract modifications, or policy reforms such as incentives to influence manufacturer actions. Other issues, like geopolitical conflicts or large-scale pandemics, have system-wide effects that may require different kinds of government intervention.

Pandemic
Bioterrorism
Demand Shocks
Natural disasters
Behavioral responses

Manufacturing quality
Natural disasters
Supply Shocks
Cybersecurity
Geopolitical disruptions



Why Does the U.S. Drug Supply Chain Have Resilience Problems?

For years, the U.S. has dealt with common, persistent shortages of numerous critical drugs, and the COVID-19 pandemic has exacerbated these challenges. Several factors drive a lack of resilience in the U.S. drug supply chain: market incentives that contribute to shortages, rising geographic concentration, issues with oversight of manufacturing quality, and limited transparency.

Market Incentives Contribute to Shortages

The 2019 [FDA Drug Shortages Task Force Report](#) identified key root causes of shortages, especially shortages of older generic drugs: a lack of incentives for manufacturers to produce less profitable drugs and that the market does not recognize and reward manufacturers for sustained quality manufacturing. Outside of times of disruption, the lack of differentiation among competing suppliers creates intense downward pressure on market prices, encouraging manufacturers to streamline their supply chains and processes in order to remain cost competitive. When competition focuses on the lowest, short-term price, streamlining can often mean cutting investments in quality and contingency plans. The median per unit price for drugs in shortages is less than \$9, with many priced at less than \$1. While manufacturers understand that these [prices do not represent the true value of their products to public health](#), they often struggle to invest in resilient manufacturing processes when facing low profit margins and uncertain market reward for those investments. These market factors cause many generic markets to support only a very limited amount of competition: [a recent study](#) found that 40% of generic markets are supplied by only one manufacturer and the median number of manufacturers per drug market is two. When more robust competition does exist, significant manufacturer churn occurs where manufacturers frequently enter and exit the market.

Rising Geographic Concentration Creates Risks

When one manufacturer, or a group of manufacturers located within one region, is responsible for an outsized portion of the supply for pharmaceutical drugs or their precursor ingredients, the supply chain is more vulnerable to localized disruptions leading to shortages. The U.S. drug supply chain is increasingly reliant on foreign manufacturers, and those manufacturers are increasingly

concentrated in a few areas of the globe. A 2019 FDA review found [72% of registered active pharmaceutical ingredient manufacturing facilities are located outside the U.S.](#), with a large proportion of those being in China or India. In turn, Indian manufacturers receive many of their raw materials for pharmaceuticals from China as well. When accounting for actual volume produced, as opposed to number of registered facilities, production is likely even more concentrated overseas, with [as much as 80% of Active Pharmaceutical Ingredients \(APIs\) being supplied from abroad by some estimates](#). Supply being concentrated in these areas makes certain supply risks more dire, including geopolitical conflicts. If the countries responsible for much of the U.S. drug supply were to restrict or halt exports, shortages would be inevitable. Other regional risks are amplified, too. For example, if the COVID-19 pandemic had affected China more severely, production would have slowed more significantly, and shortages might have ensued. The severe surge in cases in India in the second quarter of 2021 [sparked concerns of drug shortages](#) in the U.S. and other nations that rely heavily on imported APIs from India.

Quality Manufacturing and Oversight is Challenging

A majority of drug shortages have resulted from [manufacturing quality issues](#). However, predicting and preventing these quality issues is challenging, especially in the absence of standardized evaluation methods. FDA regularly inspects manufacturing facilities, but these inspections provide only limited information about facilities, and current areas of inspection focus may not be a reliable predictor of quality problems. FDA is aiming to implement a more modernized approach by assessing companies' "quality management maturity," i.e., their ability to not only comply with regulations, but also to take sustained and systemic science-based steps to measure and address quality issues that could lead to shortages. Manufacturer compliance with CGMP (Current Good Manufacturing Practices) and precautions like quality checks on traditional manufacturing processes are important, but quality maturity can be best achieved through the implementation of modern manufacturing processes that are more efficient and reliable. FDA's voluntary "quality management maturity" pilots announced in October 2020 are planned to lead to a broader roll-out of new facility-level assessment programs. But it is not yet known whether the information that will be generated through these programs will

help FDA, manufacturers, and others anticipate and preemptively address quality problems that could lead to supply disruptions.

Assessing manufacturing quality across all components of the broader and increasingly complex pharmaceutical supply chains also is challenging. To date, efforts to assess pharmaceutical quality and reliability have focused on active pharmaceutical ingredients and finished products, but proactive approaches to manufacturing quality oversight also are needed upstream in the supply chain, including for raw materials and ingredients. To ensure quality and reliability of finished products, manufacturers must assess the quality of all of a product's components and have contingencies in place to reduce the shortage impacts resulting from delays due to quality issues. Manufacturers of high margin, branded products often have extensive risk mitigation plans in place that include redundant capacity and qualifying backup suppliers for all raw materials and ingredients. While these risk mitigation plans have been very successful at preventing shortages, implementing them is challenging for low margin products.

Additional challenges are posed by the complexities inherent in new technologies and treatments. These complexities can vary significantly from one product to the next. For example, it has recently become important to assess the quality and reliability of the production of lipid nanoparticles used in COVID-19 mRNA vaccines, along with specific types of bioreactors and other types of new production equipment.

Limited Transparency Makes It Difficult to Assess And Address Risks

No stakeholder in the drug supply chain has a clear and comprehensive view of the entire supply chain, allowing them to fully account for the risks of disruptions or to actively anticipate and mitigate shortages. Even the FDA and other government agencies are limited in their ability to understand the entire U.S. drug supply chain and assess systemic vulnerabilities. Much of the information FDA receives about the supply chain comes from manufacturing facility registrations and inspections. While this allows FDA to see where individual facilities that manufacture APIs or finished dosages are located, the scope of that information is limited. For example, it does not account for the production volume at each facility, so it is difficult to say how severe the effects on

supply might be if a facility or group of facilities from a region were to go offline. [FDA's guidance recommends but does not require](#) that active pharmaceutical ingredient manufacturers track sources for their raw materials, meaning that in practice the agency's ability to understand the upstream supply chain is limited.

[The CARES Act](#) amended reporting requirements to begin to alleviate these regulatory blind spots by making manufacturers report more information to FDA. But FDA is still in the process of designing an electronic reporting system for this new information, and even with these expanded reporting requirements, FDA still will not have access to important information. The agency lacks comprehensive information on raw materials, fungibility of production, production capacity constraints, and inventory practices, all of which are key to ensuring a reliable drug supply.

The lack of transparency in the supply chain, aside from hindering regulatory efforts, also makes it difficult for purchasers to recognize and reward supply chain resilience. Many purchasers likely are interested in rewarding resilience – their priority is ensuring that they have reliable access to quality drugs – but the opacity of the current system makes it harder for them to find those reliable suppliers and make commitments to purchase from them. Purchasers making agreements with manufacturers have limited information on the likelihood of disruptions to supply, quality assurance measures on the part of manufacturers, or contingency plans if disruptions do occur. They may know where the finished dosage form and API are being produced, but they have extremely limited visibility into the complexities of the upstream supply chain, where many disruptions occur.

Important recent examples exist of market responses toward rewarding resiliency to create incentives for manufacturers to overcome these limitations. Organizations like Civica and Premier have focused on longer-term, committed contracts with manufacturers, with explicit financial rewards for reliable production over time. This removes some pressure for manufacturers to concentrate solely on lowest price and frees them to invest in greater resiliency. But for many purchasers, experience with such contracts is limited, and they still lack good information on manufacturers' production and supply chain practices, making it difficult for them to identify capable manufacturers to sign to longer-term, committed contracts.

Policy Solutions

The Biden Administration and Congress are considering further policy steps to address these issues that affect supply chain resiliency

The Administration released its [100-Day Review](#) on Building Resilient Supply Chains on June 8th, 2021, pursuant to Executive Order 14017 in February, with a full review of risks to supply chains for essential goods to be completed by February 2022. The Executive Order called for contributions from all “federal Departments and Agencies” on “ways to secure U.S. supply chains” for four critical product categories, one of which was pharmaceuticals and active pharmaceutical ingredients. The 100-Day Review identifies generic drugs facing adverse market incentives as the most likely to go into shortage, an issue also covered here. This white paper’s scope also expands beyond those routine market issues to address critical system-wide shocks like public health emergencies.

The Administration’s focus on pharmaceutical supply chains has been coupled with growing momentum in Congress for legislative reforms to address the key issues contributing to drug shortages and disruptions. Congress has already begun to take some important steps toward greater transparency in the supply chain through the CARES Act, and further initiatives to strengthen supply chains are the subject of many legislative proposals.

In the context of the global pandemic and tensions with China, recent Congressional proposals have focused largely on reducing dependency on China and reinvesting in domestic manufacturing capacity as well as beginning to promote transparency and strengthen emergency response capacity. The Senate has approved bipartisan [legislation](#) based on Senator Chuck Schumer’s Endless Frontier Act, which would establish a “technology directorate” within the National Science Foundation and allocate funding to domestic research into new manufacturing technologies such as continuous manufacturing and on-demand manufacturing. The Biden administration’s [American Jobs Plan](#) takes up these ideas and also provides funding for monitoring systems to track domestic manufacturing capacity for critical goods.




Reps. Buddy Carter (R-LA) and Lisa Blunt Rochester (D-DE) [recently reintroduced legislation from last year](#) that would allow HHS to contract with drug suppliers to maintain a stockpile of essential medicines as well as establish and monitor a list of 50 generic medicines essential in public health emergencies. A variety of Republican proposals also aim to strengthen domestic pharmaceutical manufacturing. For example, in late 2020, Republicans on the Ways and Means Committee put forward [a set of bills](#) that focused on using tax credits and deductions to create incentives for manufacturers to “onshore” production to the U.S. In March 2021 [Sen. James Risch \(R-ID\) introduced a bill](#) that would authorize the State Department to contract with experts to help American businesses move their supply chains out of China. Congressional attention to the issue remains high; in late April, the bipartisan leadership of the Senate HELP Committee [released a statement](#) emphasizing their interest in proposals to strengthen medical supply chains in the wake of the pandemic.

The proposals under consideration in Congress and the Administration seek to address important challenges to supply chain resilience, including the need to reduce U.S. dependence on China, modernize pharmaceutical manufacturing, and bolster domestic manufacturing capacity. But assuring continued supply chain resilience will require a comprehensive effort that addresses not only our dependence on China but the underlying factors that drive supply chain resilience and prepares us to respond to public health emergencies.

To achieve this, proposals should focus on three key aims: providing financial incentives to encourage quality and resiliency, implementing new technologies that can more efficiently and reliably produce quality pharmaceuticals, and increasing transparency to enable better oversight and market competition. These proposals are summarized in Table 1.

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Providing Financial Incentives

Routine issues that lead to chronic shortages in particular generic drug markets can, in many cases, be resolved through greater transparency and improved contracting practices (as described in greater detail below). However, these practices may benefit from federal government support via new financial incentives and resilience policies. Defining the most essential products to focus on is a crucial step. While the [FDA Essential Medicines List](#) is a great starting point, the 100-Day Review also calls for a public-private consortium to identify the 50-100 drugs that are most critical to have available at all times for US patients.

For routine shortages of such essential medicines, carefully-targeted subsidies and tax incentive approaches could be implemented if and when private market solutions are insufficient. In addition, receiving CMS reimbursement and federal contracts, for example through the Federal Supply Schedule (FSS), Department of Defense (DoD), or Strategic National Stockpile (SNS), could be contingent on improved quality and resiliency practices. For example, manufacturers receiving CMS reimbursement or federal contracts could be required to provide metrics on manufacturing line readiness, production capacity and

fungibility, inventory levels, and other supply chain areas. For inpatient drugs that have been in chronic shortage and are not individually reimbursed, a separate Medicare Part B category or add-on payments could be created to compensate providers for the extra cost associated with purchasing products with more reliable supply chains. Increasing resiliency may also entail onshoring production to the U.S. if geographic location is a contributor to shortages.

In addition, federal support may also be necessary to mitigate shortages in the event of another pandemic, a major international conflict, or other unforeseen emergency circumstances.

To prepare for such emergencies, Congress should authorize an appropriate agency (for example, the Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response), to better track surge capacity in the supply chains most likely to be needed in the case of a public health emergency. The past year's pandemic response has indicated this likely includes production of vaccines using multiple platforms and monoclonal antibodies. It could also include essential medicines for chronic conditions that tend to be produced overseas and may be at risk of disruption in an emergency. For manufacturers of these critical goods, the federal government should offer targeted subsidies and tax incentives or arrange contracts to ensure sufficient supply will be available in the case of emergencies. This preparedness effort could entail manufacturers' maintaining extra supplies of existing products so that advanced biologic manufacturing lines could be shifted rapidly to meet new response needs, operating with excess utilization capacity, designing production processes and supply chains that can scale rapidly, and preparing contingency plans to respond to potential disruptions. Incentives should support emergency response capacity in existing, proven manufacturing sites, as the COVID pandemic has highlighted [difficulties](#) that can occur in attempting to scale-up idle capacity not routinely used in pharmaceutical production.

Incentives and contracts for emergency preparedness should be tied to manufacturers' performance. The manufacturers involved could be subject to additional reporting requirements to ensure their production processes are scalable or their reserve capacity is sufficient. They also could be stress-tested and assessed in a simulated emergency scenario. The E.O. 100-Day Review discusses stockpiling strategies, including virtual stockpiling,

which could be coupled with steps to improve stockpiling efficiency. For example, any stockpiling effort should be coupled with efforts to review whether a longer shelf life may be appropriate for essential products. Pharmaceutical manufacturers are currently responsible for gathering data to support the expiration dating for their products, yet they often face a disincentive to seek a longer shelf life in the form of reduced sales. The joint [DoD/FDA Shelf Life Extension Program \(SLEP\)](#) should expand to proactively review the expiration dating of all essential medicines, along with those in the SNS, an entity under HHS that stores essential medicines and medical supplies for use in emergencies.

Implementing New Manufacturing Technologies

Policymakers should ensure that adequate incentives and regulatory pathways are available to implement new manufacturing technologies, which can improve quality and reliability of routine supply and improve the ability to scale up for emergency response. These incentives should be made contingent on performance wherever possible, including in the areas mentioned in the above section. The Endless Frontier Act, for example, makes investments in domestic research and development in advanced manufacturing, among other areas, a priority. These investments could enhance domestic manufacturing capacity through both the expanded use of existing technologies and the development of entirely new ones. One such technology is [continuous manufacturing](#). In continuous manufacturing, materials are moved non-stop through an integrated equipment train, eliminating hold times between processing steps, minimizing active pharmaceutical ingredient usage, and increasing control over manufacturing parameters. Though the process cannot be applied for all types of pharmaceutical products, it can be useful in increasing capacity, quality, and scalability for many. Development of new manufacturing technologies also could be supported, such as small-scale, flexible manufacturing processes that allow for quick deployment during a shortage and more efficient production of low-volume products, as well as production methods and equipment that enable longer product shelf life to increase the efficiency of inventory stockpiles.

However, manufacturers that have already received FDA approval using older technologies often face a disincentive to upgrade due to cost and regulatory risk. Upgrading to the most modern technology for efficient and reliable manufacturing, such as automated visual inspection

equipment or updated autoclaves for sterilization, presents a large up-front cost. Manufacturers may not be willing to take the risk of upgrading when they know that their current process will probably remain viable (and FDA-approved) in the short-term. In addition to streamlining these regulatory processes, policymakers may want to consider tying financial incentives mentioned in the previous section to upgrades in technology to overcome short-term cost pressures. FDA must also closely collaborate with other regulatory bodies globally to ensure consistency in approaches to advanced technology implementation. This is especially true in the emerging areas of advanced biologics and vaccines to ensure scalability and quality of production on a global scale.

Increasing Transparency

Increased supply chain information sharing is clearly helpful, but identifying what types of information can be effectively assessed and shared while avoiding costly reporting burdens is critically important. Current initiatives, such as requirements in the CARES Act and proposals in the E.O. 100-Day Review, aim to improve the ability to map supply chains and determine how much production is occurring in particular manufacturing facilities, especially for essential medicines and those that might be needed in response to a public health emergency. A better understanding of what drugs are made where can enable quicker response to threats. For example, if a natural disaster takes one plant offline, a comprehensive map of the supply chain would allow for rapid identification of what drugs are likely to be affected, and where alternative sources of those drugs exist.

However, using supply chain mappings to help avoid shortages is only one aspect of a holistic supply chain resilience evaluation. Other criteria must also be considered, such as:

- Fungibility of finished dosage form and raw material production – can production be quickly ramped up or shifted between various products?
- Types of production equipment used – is the equipment upgraded and modernized?
- Production capacity constraints – are manufacturing lines running 24x7 or is excess capacity available?
- Inventory levels, distribution timelines, and backorder metrics – are patients receiving medicines when they need them?

The three most important users of supply chain resilience information are government agencies, purchasers, and manufacturers. These groups have very different levels of supply chain expertise and use cases.

Government agencies could use better information about supply chains to [perform comprehensive supply chain resilience evaluations at the national level](#). Congress should first authorize a federal agency such as FDA, possibly with the support of an independent nonprofit, to collect more detailed production process information from manufacturers in the areas listed above, to assess systemic risks to supply chains for critical drugs. This information then would be used to inform federal government actions to provide financial incentives for supply chain resilience and emergency preparedness, as described above. It also could be used to improve the routine functions of pharmaceutical supply chains. FDA or an independent, nonprofit third-party could publicly release key measures of the resiliency and quality of manufacturers' production processes for use by purchasing organizations (see the Duke-Margolis Center's report in collaboration with the Healthcare Leadership Council for more on how this effort would strengthen public health emergency response). Any disclosures should be carefully tailored to avoid sharing proprietary information while still ensuring utility for purchasers, possibly via a high-level rating system for both quality and resiliency. The E.O. 100-Day Review recommends one viable approach to this process: an FDA rating of robustness in manufacturing quality processes that would be shared with manufacturers, giving the manufacturers the option to publicize their own ratings.

Providing purchasers with more comprehensive information on supply chains can harness market forces to promote resilience. Purchasers already have a strong incentive to partner with manufacturers who have robust supply chain management practices, but they often lack the resources and expertise to perform supply chain evaluations themselves. Already, some purchasing organizations have shifted toward longer-term, committed contracts based on the best information available to them, in hopes of ensuring a more stable drug supply. If they were provided reliable, useful information on high-level metrics through a rating system, that trend would be accelerated and purchasers would be able to make more informed contracting decisions, reducing the likelihood of shortages. For example, the E.O. 100-

Day Review suggests that purchasers might require information on their suppliers' quality or resiliency as a condition of a contract with a supplier.

Manufacturers also sometimes lack comprehensive information on their suppliers. For example, manufacturers of finished dosage forms often face challenges in obtaining adequate information on suppliers of active pharmaceutical ingredients and other ingredients to inform their own purchasing decisions. Key performance data collected by a federal regulator or independent entity could help manufacturers address risks and ensure that sales of their products are not disrupted.



CONCLUSION

The private sector is taking encouraging steps toward valuing resiliency, with some purchasers and manufacturers engaging in longer-term contracts designed to guarantee stable supply, not just lowest price. But many of the major factors contributing to drug shortages are systemic and cannot be fully resolved at the level of individual manufacturers. Current private incentives are inadequate for investment in supply chain resilience for major but critically important disruptions, like public health emergencies or geopolitical challenges. Critical information gaps are inhibiting the ability of manufacturers and purchasers to implement contracts that deliver more resilient supply, and the ability to prevent and respond rapidly to major supply disruptions. And though there are emerging technologies with promising potential for making manufacturing more efficient and reliable, few manufacturers have strong incentives or sufficient resources to invest in them. Meaningful, long-term progress will require policy interventions to introduce clear measures of supply chain resilience and quality and to align incentives to support improvements in these measures, so that the market will reward the investments needed to achieve resilient pharmaceutical manufacturing.