

Essential Medicines Supply Chain and Manufacturing Resilience Assessment

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nextfab

a program of  **armi**

NEXIGHT GROUP

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About This Report

To ensure better preparedness for future pandemics and a more resilient and stable U.S. manufacturing environment in general, the White House issued an [Executive Order on supply chain resilience in February 2021](#).

This Executive Order included a directive for key federal agencies, including the U.S. Department of Health & Human Services' (HHS) Office of the Assistant Secretary for Preparedness and Response (ASPR) and the U.S. Food & Drug Administration (FDA), to conduct a 100-day supply chain review and develop a report of the findings.

Led by ASPR and the Advanced Regenerative Manufacturing Institute (ARMI) / the Next Foundry for American Biotechnology (NextFAB), the National Forum to Secure America's Supply Chain for Essential Medicines set out to develop this **action plan to address pharmaceutical supply chain vulnerabilities** identified in the Biden-Harris Administration's 100-day supply chain review report, **Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth: 100-Day Reviews under Executive Order 14017**, specifically those affecting critical medicines on the **FDA's Essential Medicines List**.

With the assistance of Nexight Group, the team conducted the following activities to ensure the greatest variety of inputs and perspectives from across the pharmaceutical supply chain for this important national effort:



Interviews

Met with about 40 key pharmaceutical supply chain stakeholders to capture perspectives from not only government health authorities but also from the industry and clinical care perspectives, including:

- + Material Suppliers
- + Pharmaceutical Manufacturers
- + Group Purchasing Organizations (GPOs)
- + Wholesale Distributors
- + Healthcare Providers/ Pharmacies



Surveys and Workshops

Conducted a series of extensive surveys and workshops with groups of both clinicians and industry stakeholders

- Surveys:** More than 80 completed and analyzed
- Workshops:** Two with a clinical steering committee (40+ participants), Two with an industry steering committee (30+ participants)

- Clinical:** Downselected and prioritized the essential medicines list to reflect those most critical for acute patient care
- Industry:** Vetted the biggest challenges to achieving resilience and prioritized potential strategies for addressing them



Public Feedback

Evaluated and integrated public feedback on the essential medicines list, provided during a public comment period starting in October 2020 (see **Appendix C**).



Desktop Research

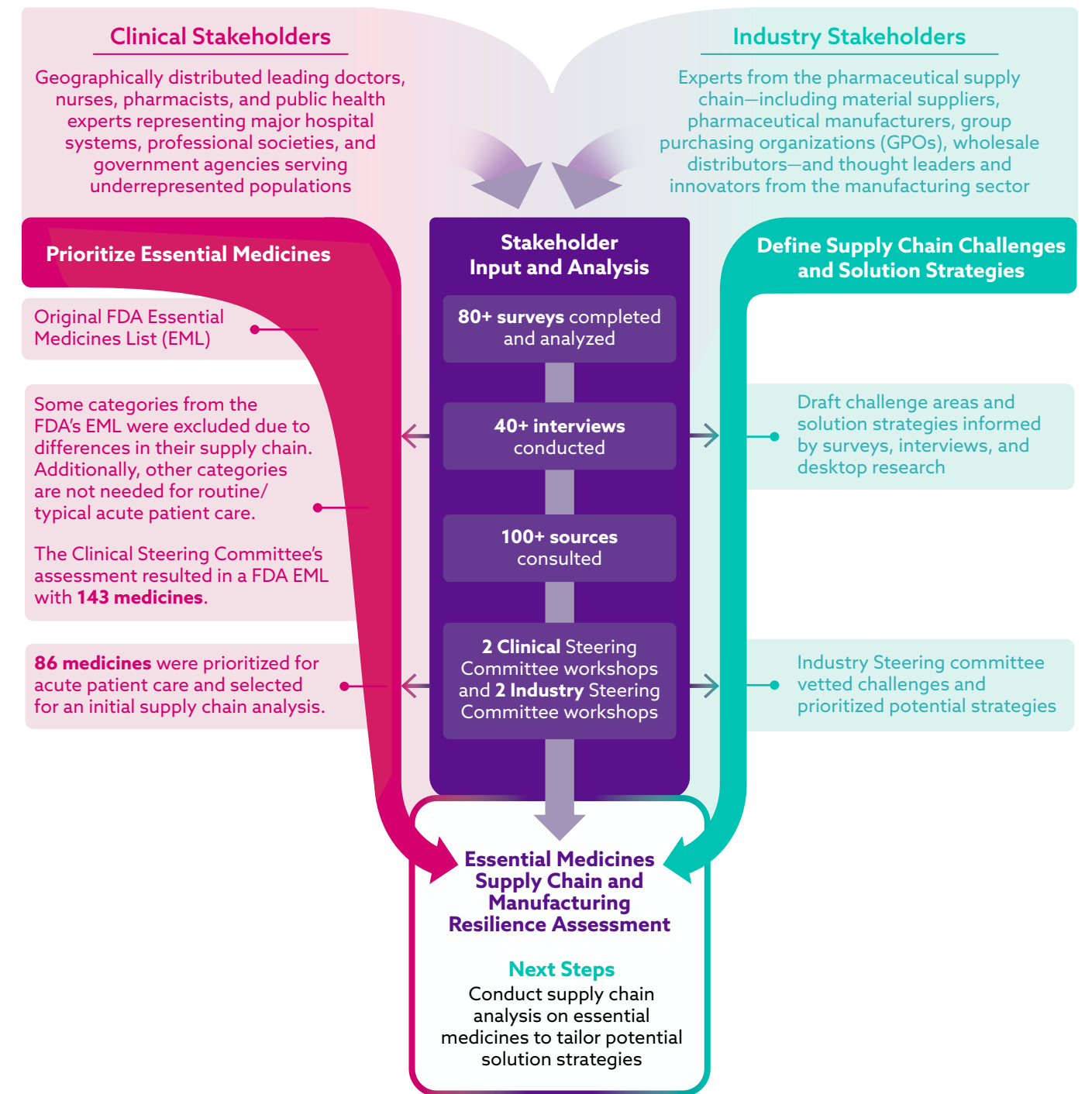
Conducted extensive review and evaluation of more than 100 sources, which were used to clarify inputs from interviews, surveys, and workshops



This report comprises the findings of this work—a **prioritized list of medicines that the government can target for increased resilience, using a set of industry-vetted strategies to overcome current pharmaceutical supply chain challenges and vulnerabilities**. The report has been developed specifically for the Biden-Harris Administration to help inform its investments in domestic pharmaceutical manufacturing capacity and supply chain resilience.

REPORT DEVELOPMENT PROCESS

Expert input and perspectives from clinicians, industry, and government agencies informed the development of a downselected and prioritized essential medicines list and a set of supply chain challenges and potential solution strategies. Together, these parallel efforts informed the development of this report.



Executive Summary



**COVID-19 UNDERSCORES THE NEED
FOR SUPPLY CHAIN PREPAREDNESS**



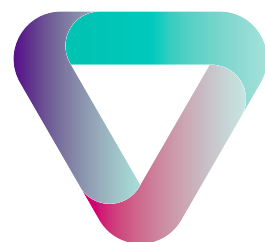
The COVID-19 pandemic illustrates the vulnerabilities of the U.S. pharmaceutical supply chain and how dramatically a crisis can impact its integrity. Spikes in demand for critical medicines coupled with global supply chain disruptions left the United States struggling with shortages and distribution challenges that had direct implications on patient care.

Unfortunately, global pandemics are not the only events that affect the pharmaceutical supply chain. In 2017, Hurricane Maria devastated the island of Puerto Rico, including many facilities that produce injectable saline for the United States; supplies remained critically impacted for several years.¹ Even in the absence of crises, the U.S. pharmaceutical supply chain can be impacted by market and economic factors, such as decisions to close manufacturing facilities.

To ensure better preparedness and a more resilient and stable U.S. manufacturing environment in general, the White House issued an [Executive Order](#) on supply chain resilience in February 2021.

This Executive Order included a directive for key federal agencies, including a [100-day supply chain review and report](#). Specifically, the U.S. Department of Health and Human Services (HHS), Office of the Assistant Secretary for Preparedness and Response (ASPR), was tasked with identifying risks in the supply chain for pharmaceuticals and active pharmaceutical ingredients (APIs), as well as policy recommendations to address these risks. This effort leverages work completed in response to an August 2020 [Executive Order \(13944\)](#), which directed the U.S. Food and Drug Administration (FDA), in consultation with federal partners, to identify a [list of essential medicines](#), medical countermeasures, and critical inputs that are medically necessary to have available at all times in an amount adequate to serve patient needs and in the appropriate dosage forms and delivery methods.

VISION: A RESILIENT PHARMACEUTICAL SUPPLY CHAIN

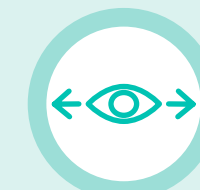


A **resilient and robust U.S. supply chain** can ensure that essential medicines are available in the event of a pandemic or crisis as well as for typical acute patient care. The reliable availability of these medicines can help to alleviate strains on hospital resources, resulting in more lives saved and improved patient care.

¹ "Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth," The White House, June 2021, <https://www.whitehouse.gov/wp-content/uploads/2021/06/100-day-supply-chain-review-report.pdf>.

RESILIENT PHARMACEUTICAL SUPPLY CHAINS

To be more resilient and reliable, the U.S. pharmaceutical supply chain of the future must achieve levels of quality, diversification, and redundancy needed for preparedness—particularly for acute patient care.



Anticipate

issues quickly to ensure safety, quality, and predictability

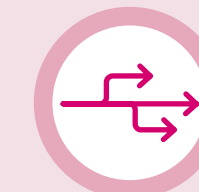
- + Maintain a robust, centralized control tower platform, with a dashboard of integrated data and business metrics networks from across the supply chain²
- + Forecast supply and demand and manage capacity accordingly
- + Develop strategic alliances and partnerships to improve resilience



Prepare

for potential risks and develop strategies for mitigation

- + Maintain supply redundancy and multi-sourcing
- + Maintain sufficient emergency inventory
- + Establish clear distribution logistics
- + Establish contingency measures and continuity plans



Respond

to challenges and shifting demand and swiftly adapt to minimize disruptions

- + Enable source shifting and increased flexibility
- + Maintain appropriate workforce and distribution capacity

VISION

A resilient, reliable U.S. pharmaceutical supply chain that ensures essential medicines are available where and when they are needed, and in the appropriate amounts and dosage forms

² The Control Tower maintains a 24-hour watch function for situational awareness of any emerging situation within the pharmaceutical supply chain, nationally or internationally, that may require a coordinated federal response.

PROJECT MISSION AND OBJECTIVES

To build upon the initial 100-day response and develop a coordinated action plan for achieving improved pharmaceutical supply chain resilience, ASPR tasked ARMI / NextFAB with performing a more in-depth analysis.

The team conducted two parallel efforts—soliciting expert input and perspectives from clinicians, industry, and other government agencies—to achieve the following:

1. **Downselect and prioritize the essential medicines list** to identify the most critical medicines needed for acute patient care
2. **Identify specific supply chain and manufacturing vulnerabilities** for the most critical downselected medicines, characterize the biggest cross-cutting **challenges** impacting supply chain resilience, and develop **strategies** for achieving a robust, resilient pharmaceutical supply chain that offers unfettered access to those essential medicines

PATHWAYS TO INCREASING PREPAREDNESS

1. Prioritized Essential Medicines

The team conducted a series of exercises—with significant input (workshops, surveys) from clinical stakeholders—to narrow the medicines on the initial essential medicines list³ down to the 50–100 considered by consensus to be most critically needed for typical acute patient care. In this context, acute patient care is defined as:

- + Rescue and/or lifesaving use (i.e., Intensive Care Units [ICU], Cardiac/Coronary Care Units [CCU], and Emergency Departments)
- + Stabilizing patients in hospital continued care to enable discharge
- + Urgent or emergency surgery

This exercise resulted in a downselected list of 86 critical medicines—provided in [Appendix A](#).

This list of medicines will inform medicine-specific next steps the government should focus on to increase resilience in the U.S. pharmaceutical supply chain, building on the broader solution strategies outlined in this report. The strategies for ensuring a resilient supply of these medicines will need to be tailored for each medicine based on its unique supply chain and manufacturing challenges and vulnerabilities, if any.

³ This exercise focused on assessing the clinical criticality and supply chains of small molecules and therapeutic biologics. As a result, some categories from FDA's Essential Medicines List—including Blood and Blood Products, Fractionated Plasma Products, Vaccines, and Volume Expanders—were excluded from this exercise due to differences in their supply chains. Additionally, other categories are not needed for routine/typical acute patient care (i.e., Biological Threat Medical Countermeasures, Burn and Blast Injuries, Chemical Threat Medical Countermeasures, COVID-19, Pandemic Influenza Medical Countermeasures, Radiologic-Nuclear Threat Medical Countermeasures) and were therefore out of scope of this exercise.

2. Supply Chain Challenges and Solution Strategies

CHALLENGES

According to industry input,⁴ the pharmaceutical supply chain faces a number of challenges and vulnerabilities in key areas that impact its robustness and make it vulnerable to disruption:



Market Structure

Market influences that contribute to shortages of essential medicines, such as downward pressures on costs for generic medicines and the common use of just-in-time inventory practices that magnify the effects of upstream supply interruptions



Global Competition

Factors that put U.S.-manufactured pharmaceuticals at a competitive disadvantage, including foreign government investments, lower offshore operating costs and labor rates, and dependency on offshore sources for raw materials



Labor/Workforce

Difficulty in maintaining an adequate workforce for pharmaceutical manufacturing due to a lack of specialized knowledge and wage competition from other U.S. STEM fields



Manufacturing Processes

Technological limitations, such as reliance on outdated and inefficient equipment and processes, that make it difficult for pharmaceutical manufacturers to respond to supply disruptions and shifts in demand rapidly and effectively



Supply Chain and Distribution

Issues with communication, transparency, and coordination throughout the supply chain that impede efficiency and strategic decision-making



Regulatory

Aspects of U.S. regulations that are perceived as limiting flexibility or cost effectiveness for U.S.-based pharmaceutical manufacturers

⁴ While other challenges exist—such as the difficulty of managing wastewater and other industrial waste from pharmaceutical manufacturing, these challenges were only discussed within the context of these six key challenge themes.

SOLUTION STRATEGIES

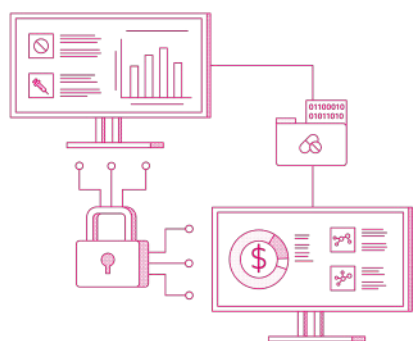
To achieve increased supply chain resilience, industry contributors indicated that the United States must develop a balanced approach to global diversification of essential medicine materials sourcing and manufacturing, increase investment in manufacturing innovation and excellence, and improve its strategies and efficiencies related to essential medicine manufacturing capacity, supply, and distribution.

This report offers prioritized strategies for making impactful progress toward achieving such resilience—by addressing challenges and vulnerabilities—for the essential medicine supply chain:

➔ *Bold denotes high-priority strategies*

Increased Supply Chain Coordination, Security, and Transparency

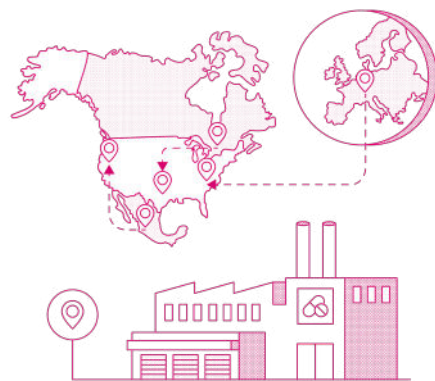
Improving end-to-end supply chain visibility will offer a greater ability to anticipate, prioritize, and respond to critical issues, demands, and potential disruptions.



1. **Improve data- and information-sharing, integration, and standardization across the entire supply chain**
2. **Strengthen collaboration and coordination between the government and all participants in the pharmaceutical supply chain**
3. Develop and utilize predictive tools and conduct risk assessments
4. Establish a more comprehensive centralized control tower platform
5. Increase both physical and cyber security posture throughout the supply chain

Expanded Onshore or Nearshore Production Capacity

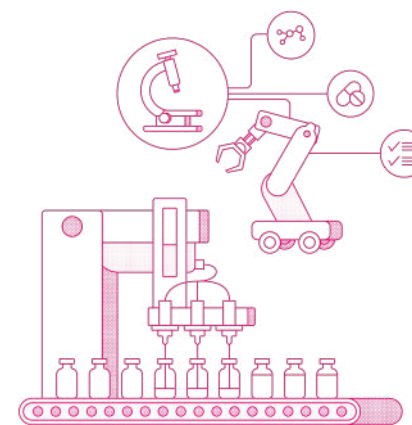
A balanced, diversified approach to capacity and sourcing that avoids single-source points of failure can decrease the risk of essential medicine shortages and reduce U.S. reliance on materials or manufacturing from competitor nations.



1. **Ensure stable, long-term demand for generic medicines at a sustainable price to encourage manufacturers to expand domestic production**
2. **Incentivize manufacturers to add/expand domestic production by offsetting capital investment**
3. Develop a complete essential medicine supply chain and manufacturing model—from precursor materials to finished products—that more fully leverages both on- and ally-shored resources and suppliers
4. Streamline implementation and communication around regulatory procedures to make adding new facilities or capacity faster and easier

Advanced Manufacturing Capabilities and Innovative Research and Development

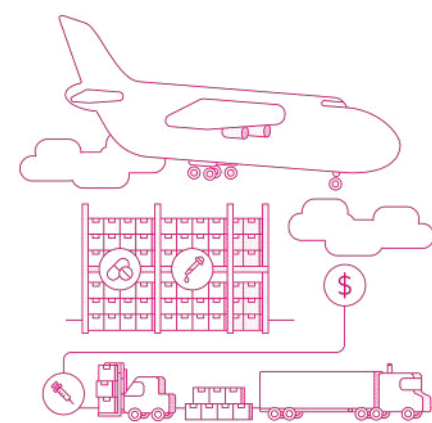
Advanced technologies and processes can improve the quality and safety of essential medicines, increase manufacturing efficiency and cost effectiveness, and strengthen the manufacturing competitiveness of both the United States and its allies and partners.



1. **Identify, promote, and invest in innovative and sustainable manufacturing paradigms that can facilitate U.S. self-sufficiency**
2. **Develop strategies for targeted workforce investment (e.g., training, access, partnerships) that will enhance U.S. competitiveness**
3. Support and invest in innovative drug research and development
4. Promote smart manufacturing through increased automation and other digital solutions
5. Encourage widespread adoption of new manufacturing technologies and approaches through increased standardization and greater regulatory certainty, while ensuring quality

Purchasing, Stockpiling, and Distribution Approaches

Improved national strategies around purchasing and stockpiling will enable more targeted and efficient handling and distribution of supplies of essential medicines in response to demand fluctuations or shortages.



1. **Leverage the federal government's collective buying power to reform procurement protocols**
2. **Revise purchasing models to increase emphasis on product quality and supply chain resilience, not simply lowest cost**
3. Regionalize the Strategic National Stockpile (SNS) for better prepositioning of essential medicines and other critical materials
4. Develop a distributed stockpile of APIs and precursor materials
5. Incentivize pharmaceutical manufacturers and wholesale distributors to hold buffer stock, rotate stock, and manage distribution, or develop other similar strategies or models
6. Develop mandates or explore mechanisms, such as pursuing statutory authority, for maintaining stock reserves
7. Proactively develop comprehensive essential medicine distribution logistics plans



Challenges

Various market pressures and economic drivers have created challenges to the resilience of the U.S. pharmaceutical supply chain, increasing risks and vulnerabilities.⁵ Low margins have driven a significant amount of production offshore as well as reduced redundancies necessary for supply chain resilience. As a result, the industry faces an overdependence on foreign producers and suppliers, some of whom implement anti-competitive actions that limit the United States' access to medicines and supplies in times of crisis, as witnessed during the COVID-19 pandemic.

Low margins have driven a significant amount of production offshore as well as reduced redundancies necessary for supply chain resilience. As a result, the industry faces an overdependence on foreign producers and suppliers, some of whom implement anti-competitive actions that limit the United States' access to medicines and supplies in times of crisis, as witnessed during the COVID-19 pandemic.

These vulnerabilities are magnified when coupled with other pharmaceutical production complexities and challenges, including a lack of data sharing and transparency across the supply chain, technology limitations that inhibit responsiveness and agility in times of surge or crisis, and an increasing inability to secure and maintain an adequate skilled workforce.

Challenges outlined in this section are based on industry input obtained through interviews, surveys, and workshops.

⁵ Drug Shortages: Root Causes and Potential Solutions, U.S. Food and Drug Administration, October 2019, <https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions>.



Market Structure

Market influences that contribute to shortages of essential medicines, such as downward pressures on costs for generic medicines and the common use of just-in-time inventory practices that magnify the effects of upstream supply interruptions

1) Most essential medicines are generics, which offer low return on investment when not offset by external incentives

- + **Originator brand manufacturers often elect not to manufacture** essential medicines for which innovator patents and exclusivities have been exhausted.
- + Low margins can drive current manufacturers to leave the market. **Those who remain have more difficulty consistently meeting demand.**
- + The slim margins for generic medicines present a **high-risk, low-reward outlook for new players** considering investing in development of these medicines, including building new facilities or maintaining and upgrading existing facilities.
- + This issue also impacts **drug accessories** (e.g., sterile injectable packaging) which are capital-intensive to manufacture, low margin, and tend to be produced in facilities at near full capacity with little room for error if there is a disruption (e.g., equipment downtime).

2) Pressure to continually lower costs can drive manufacturers to de-emphasize quality management maturity and continuous manufacturing improvements

- + Various pressures—including foreign competition and inconsistent reimbursement for medical providers—**drive prices lower and make it difficult for manufacturers to maintain profitability** in the generic market.
- + **Thin margins inhibit investment in quality management maturity**, including redundant supply and new manufacturing facilities and equipment, which makes production of generics more susceptible to disruptions.

3) Just-in-time inventory practices limit safety stocks and on-hand inventory, which can significantly reduce the agility and flexibility of the supply chain if disrupted

- + Just-in-time inventory practices—characterized by **rapid production of small batches of products and relatively low levels of on-hand inventory**—are widely used in pharmaceutical manufacturing to lower storage costs and improve efficiency.
- + This approach to manufacturing may be **vulnerable to disruption—if not coupled with appropriate risk and quality management—and can quickly result in shortages** if issues occur at any upstream step in the supply chain.
- + **The COVID-19 pandemic illustrated the risks of the just-in-time approach**, creating major supply chain disruptions for pharmaceuticals and critical medical supplies because of sudden spikes in demand, facility closures, and import delays.



Global Competition

Factors that put U.S.-manufactured pharmaceuticals at a competitive disadvantage, including foreign government investments, lower offshore operating costs and labor rates, and dependency on offshore sources for raw materials

1) U.S.-based manufacturing of generics is at a disadvantage against global competitors due to foreign government investment

- + Some key **non-U.S. countries** (e.g., China and India) have **invested heavily in subsidizing** the manufacturing of medicines and active pharmaceutical ingredients (APIs).
- + This creates an environment that **makes it difficult for U.S.-based manufacturers to compete** without similar external support or incentives.

2) Offshore pharmaceutical manufacturing facilities have lower labor rates and operating costs

- + Overseas manufacturers often have a **competitive advantage over the United States due to lower labor costs.**
- + Less stringent environmental and safety regulations in many countries also contribute to **lower overall operating costs.**
- + In the case of China, the **ability to manufacture APIs at lower costs through economies of scale** has allowed China to force various foreign competitors out of the market.⁶

3) U.S. dependence on foreign pharmaceutical manufacturers has increased as many U.S.-based manufacturing centers close or relocate overseas

- + As of March 2021, **87 percent of manufacturing sites making APIs and 63 percent producing finished dosage forms** were located overseas.⁷
- + Currently, a single country—China—**controls most of the fermentation-based API production in the world** and has pursued strategies such as dumping products at a price below the production cost to disrupt markets and increase China's market share.⁸
- + Foreign countries may **face localized supply disruptions or restrict exports in times of crisis**, which threatens U.S. access to essential medicines and the overall resilience of the supply chain.

4) Domestic manufacturers of pharmaceuticals are dependent on raw materials produced in China or India

- + Even for APIs with onshore or nearshore sources, the **raw materials** (i.e., chemical components) **of most APIs are overwhelmingly produced in China or India.**
- + A shortage in a specific precursor material could **impact manufacturing of medicines that use common ingredients**, even if they are otherwise seemingly unrelated.
- + Producing all precursor materials in the United States may be unrealistic; **some require rare components that may only be sourced from other countries** due to the location of natural deposits.

⁶ Jerin Jose Cherian et al., "India's Road to Independence in Manufacturing Active Pharmaceutical Ingredients: Focus on Essential Medicines," *Economies* 9, no. 2 (March 2021): p. 71, <https://doi.org/10.3390/economies9020071>.

⁷ "Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth," The White House, June 2021, <https://www.whitehouse.gov/wp-content/uploads/2021/06/100-day-supply-chain-review-report.pdf>.

⁸ Jerin Jose Cherian et al., "India's Road to Independence in Manufacturing Active Pharmaceutical Ingredients: Focus on Essential Medicines," *Economies* 9, no. 2 (March 2021): p. 71, <https://doi.org/10.3390/economies9020071>.



Labor/Workforce

Difficulty in maintaining an adequate workforce for pharmaceutical manufacturing due to a lack of specialized knowledge and wage competition from other U.S. STEM fields

1) The United States faces a shortage of workers with specialized knowledge for pharmaceutical manufacturing

- + An estimated **60 percent of U.S. manufacturing jobs will go unfilled between 2015 and 2025** due to shortages in talent.⁹
- + The **U.S. workforce lags behind international competitors in the number of students pursuing the STEM-related degrees** necessary to participate in most pharmaceutical manufacturing roles, including both lower-skilled manufacturing positions and research and development.
- + Many pharmaceutical manufacturing **positions require additional specialized training**, particularly areas of innovation such as biologics, formulation, and advanced manufacturing.
- + **Training new employees for pharmaceutical manufacturing roles is time consuming** and difficult to accomplish quickly enough to meet urgent essential medicine needs.

2) Competition from other U.S.-based STEM fields drives up wages for pharmaceutical manufacturing jobs beyond what the market can bear

- + **Highly competitive wages in other U.S.-based STEM fields** put upward pressure on wage structures for domestic manufacturers of generics.
- + Comparatively high U.S. wage expectations **encourage manufacturers to move operations offshore** to remain competitive in the marketplace.

⁹ "Enhancing Today's Stem Workforce to Ensure Tomorrow's New Medicines," Phrma, June 2017, <http://phrma-docs.phrma.org/files/dmfile/TEconomy-PhRMA-STEM-Report-Final.pdf>.



Manufacturing Processes

Technological limitations, such as reliance on outdated and inefficient equipment and processes, that make it difficult for pharmaceutical manufacturers to respond to supply disruptions and shifts in demand rapidly and effectively

1) Traditional manufacturing methods may make it more difficult to detect product quality issues that can be time-consuming and disruptive to correct

- + At least **63 percent of U.S. drug shortages between 2013 and 2017 could be traced back to quality issues**.¹⁰
- + **When contamination is detected** on a traditional aseptic processing line in products required to be sterile, the **line must be shut down and cleaned**, which can take weeks to months and often results in shortages.
- + Generic medicines often use one production line for multiple products as a cost efficiency measure. **In addition to limiting a manufacturer's ability to increase production to meet surges in demand, if there is a quality or cross-contamination concern, the whole line must be shut down.**

2) The U.S. generics market generally lacks sufficient incentives and broad current support for technological innovations such as continuous manufacturing

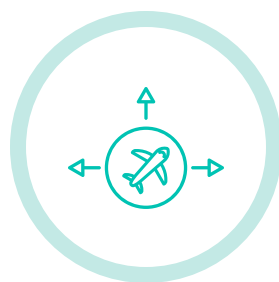
- + Continuous manufacturing and inline monitoring offer potential solutions to manufacturing quality issues, but **the generic market is not generally able to attract the high level of investment needed to set up cutting-edge technologies**.
- + There is also a **gap in government funding for supporting technologies through the transition** from development in academic laboratories to commercial-scale production.
- + Information about the facilities where medicines were manufactured is usually unavailable to purchasers along with measures of quality maturity that might lead purchasers to favor manufacturers with mature quality management systems. As a result, **manufacturers lack incentives to invest in improving manufacturing quality practices to achieve sustainable compliance**.¹¹

3) Pharmaceutical manufacturers have difficulty providing surge capacity due to resource constraints and technological limitations

- + **Manufacturers must operate close to full capacity** to be financially viable, which limits their ability to offer surge capacity to address short-term needs such as shortages or spikes in demand.
- + **Manufacturing equipment cannot easily be switched on and off as demand changes**—some equipment (e.g., melting tanks) must run continuously, while other equipment may break down or become obsolete during long periods of disuse.
- + **Increasing capacity also requires additional staff**, along with the time investment needed for hiring and training.

¹⁰ "Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth," The White House, June 2021, <https://www.whitehouse.gov/wp-content/uploads/2021/06/100-day-supply-chain-review-report.pdf>.

¹¹ "FDA Drug Shortages: Root Causes and Potential Solutions, 2019." U.S. Food and Drug Administration, February 2020.



Supply Chains and Distribution

Issues with communication, transparency, and coordination throughout the supply chain that impede efficiency and strategic decision-making

1) Pharmaceutical supply chains are complex, with many factors that make it difficult to diversify suppliers and control costs

- + Intermediaries in the supply chain (e.g., wholesale distributors) **may introduce a markup and increase medicine costs.**
- + **Insurance and purchasing practices** by insurance companies, pharmacy benefit managers (PBMs), pharmacy services administrative organizations (PSAOs), and Group Purchasing Organizations (GPOs) **may also affect supply or availability of medicines.**
- + While **GPOs indicate that they help to reduce costs of drugs to hospitals** by consolidating operations, their use can **create unintended consequences such as limiting the number of suppliers** available for hospitals to choose from and driving down margins for manufacturers.
- + Maintaining multiple redundant sources for products is one approach to improving resilience but carries **additional costs for keeping suppliers qualified and conducting audits.**

2) Lack of data and information sharing prevents pharmaceutical supply chain transparency

- + Companies are **often protective of their supply chain data.** For example, the volume of a given medicine produced by different companies is often not publicly available, which makes it unclear if capacity and supply is balanced across different companies.
- + Companies are **often not transparent about the sources of their raw materials,** which can create the impression of more diversity of supply sources than actually exists.
- + There is a **lack of standardization in the names of companies across manufacturing sites and geographic locations,** which makes it difficult to track data and detect connections (e.g., a company with multiple names in different countries may appear to be multiple companies and make a supply chain seem more resilient than it is).

3) Limited pharmaceutical supply chain transparency prevents strategic decision making related to supply chain security

- + The lack of information sharing between stakeholders across the supply chain **limits the ability to predict and prevent shortages,** making it more difficult to track product allocations.
- + Purchasers **lack the information needed to evaluate the supply chain resilience risks** of one manufacturer over another.
- + Clinicians often **do not know why a medicine or supply is on backorder,** which limits their ability to respond strategically.
- + **Uncoordinated responses to shortages or other unanticipated market events** result in hoarding behaviors, which increase waste from expired products and exacerbate the shortage by sending conflicting supply and demand signals up and down the supply chain, often creating the bullwhip effect.

4) Lack of coordination and strategy around stockpiling makes it difficult to determine what to stockpile and what parties should be responsible for stockpiling specific items

- + There is uncertainty and lack of coordination around what items should be stockpiled at the federal level versus regionally or by individual organizations.
- + Some pharmaceutical components such as vials are difficult to stockpile due to a **lack of standardization** in sizes and associated manufacturing equipment.

5) Stockpiles are challenging to maintain due to their infrequency of use and the limited shelf life of finished dosage forms

- + Because stockpiles are only used in the event of an emergency, they are **challenging to maintain and often lack necessary supplies when they are needed.**
- + The limited shelf life of finished dosage forms means that stockpiles of these products **must be rotated at a pace that is often not practical.**
- + Rotation of stockpile products can be difficult for those products that may only be needed in the event of an emergency (e.g., Botulism vaccine) because there is **no active market for the product.**
- + **Excess inventory requires additional space and staff** to manage supply, making maintenance expensive.

→ CASE STUDY: INJECTABLE DEXAMETHASONE

Injectable dexamethasone, a versatile medicine used to treat a variety of conditions, was discovered as an effective therapeutic for COVID-19, resulting in a **610 percent increase in demand and multi-month delays in its availability.**¹²

WHY IS INJECTABLE DEXAMETHASONE ESSENTIAL?

Dexamethasone is a corticosteroid used to treat inflammation of the joints, lungs, skin, and other organs.¹³ It has a **wide range of uses in emergency settings**, including treatment of severe allergic reactions and other inflammatory conditions (e.g., swelling of the brain). Intravenous dexamethasone is typically needed by sicker patients (e.g., those on ventilators) because the oral form is more difficult to administer in critically ill populations. In addition, dexamethasone is a therapeutic option for critically ill COVID-19 patients.

THE SHORTAGE

After a June 2020 U.K. study showed that dexamethasone had the potential to reduce deaths in patients with COVID-19 receiving respiratory support,¹⁴ demand dramatically increased, leading to shortages in the injectable form of the drug.



610 percent increase in hospital orders for dexamethasone in June 2020¹⁵

137 percent increase in dexamethasone's price in October 2020, further threatening its availability and affordability¹⁶



THE IMPACT



Most manufacturers were forced to backorder the drug, causing multi-month delays in its availability.¹⁷

The WHO advised healthcare providers to **prioritize the most serious cases**,¹⁸ limiting doctors' ability to use it for hospitalized COVID-19 patients on oxygen or mechanical ventilation.¹⁹ However, treatment guidelines recommended that if dexamethasone was not available, alternative glucocorticoids (e.g., prednisone, methylprednisolone, hydrocortisone) could be used.²⁰

MITIGATION STRATEGIES

FDA worked closely with all manufacturers and offered assistance, including expediting any applications related to increasing supply.

To increase supply, FDA added dexamethasone sodium phosphate to its approved list of medications permitted to be **temporarily compounded by outsourcing facilities and pharmacy compounders** during the pandemic.²¹



Regulations

Aspects of U.S. regulations that are perceived as limiting flexibility or cost effectiveness for U.S.-based pharmaceutical manufacturers

1) Lack of flexibility within certain regulatory processes may limit pharmaceutical manufacturers' ability to make rapid changes to operations

- + The rigorous regulatory environment in the United States promotes a high standard of medicine quality and safety but can **result in unintended constraints on manufacturers who wish to make changes to partnerships or processes.**
- + Manufacturers often find it easier to continue relationships with **the suppliers** (e.g., for container closures) **they used at the time of regulatory approval**, reducing their flexibility if a supplier has a shortage or becomes tied up in emergency production.
- + **Gaining regulatory approval for updated production processes can also be time consuming and expensive**, which may inhibit manufacturers from incorporating more efficient processes as technology advances.

2) More stringent U.S. environmental regulations can make it more cost effective to manufacture pharmaceutical products overseas

- + Some processes for manufacturing APIs and finished dose antibiotic products **release high levels of pollutants** that can increase localized health risks such as antimicrobial resistance and negatively affect local ecosystems.²²
- + **The U.S. Environmental Protection Agency (EPA) has established strict regulations to help minimize these issues**, but manufacturers often move operations to other countries with less stringent environmental requirements rather than seek technological solutions to minimize waste.

3) Long lead times for setting up new pharmaceutical manufacturing facilities can limit ability to respond to market demands

- + **Setting up a new plant can take 5-7 years, and adding a single line in an existing plant can take 3-5 years.** This includes time needed to meet Current Good Manufacturing Practice (CGMP) regulatory requirements.
- + Companies deciding whether to manufacture new products internally must make a tradeoff between the **cost and time of setting up a new facility or the potential loss in supply resilience** of sourcing the product from a contract manufacturer.

12 Ed Silverman, "Hospitals See Shortages of a Cheap Steroid That One Study Says Helps Covid-19 Patients," Stat, June 25, 2020, <https://www.statnews.com/pharmalot/2020/06/25/covid19-coronavirus-dexamethasone-shortages/>.

13 "Dexamethasone Injection," Cleveland Clinic, <https://my.clevelandclinic.org/health/drugs/20480-dexamethasone-injection>.

14 "Dexamethasone in Hospitalized Patients with Covid-19," New England Journal of Medicine 384, no. 8 (2021): 693-704, <https://doi.org/10.1056/nejmoa2021436>.

15 Ed Silverman, "Hospitals See Shortages of a Cheap Steroid That One Study Says Helps Covid-19 Patients," Stat, June 25, 2020, <https://www.statnews.com/pharmalot/2020/06/25/covid19-coronavirus-dexamethasone-shortages/>.

16 Maia Anderson, "Dexamethasone Price Has Increased 137% in Recent Months," Becker's Hospital Review, October 7, 2020, <https://www.beckershospitalreview.com/pharmacy/dexamethasone-price-has-increased-137-in-recent-months.html>.

17 "Critical Drug Shortages Caused by COVID-19," MDLinx, August 21, 2020, <https://www.mdlinx.com/article/critical-drug-shortages-caused-by-covid-19/1yrBAMojw6N6vw7s1czB7c>.

18 "Coronavirus Disease (Covid-19): Dexamethasone," World Health Organization, October 16, 2021, <https://www.who.int/news-room/q-a-detail/coronavirus-disease-covid-19-dexamethasone>.

19 Dian Zhang, "Demand for Dexamethasone Rises after Study Finds COVID-19 Benefits, FDA Data Shows," USA Today, July 2, 2020, <https://www.usatoday.com/story/news/2020/07/02/coronavirus-drug-cheap-steroid-shortage-after-increased-demand/5355016002/>.

20 "Corticosteroids," The National Institutes of Health, December 16, 2021, <https://www.covid19treatmentguidelines.nih.gov/therapies/immunomodulators/corticosteroids/>.

21 "List of Drugs Used for Hospitalized Patients with COVID-19," U.S. Food and Drug Administration, December 17, 2021, <https://www.fda.gov/drugs/coronavirus-covid-19-drugs/compounding-activities-covid-19>.

22 Adela Maghear and Maja Milkowska, "The Environmental Impact of Pharmaceutical Manufacturing: How Does Industry Address Its Own Waste?" Health Care Without Harm Europe, December 2018, https://noharm-europe.org/sites/default/files/documents-files/5731/2018_PharmaceuticalIndustryReport_WEB.pdf.

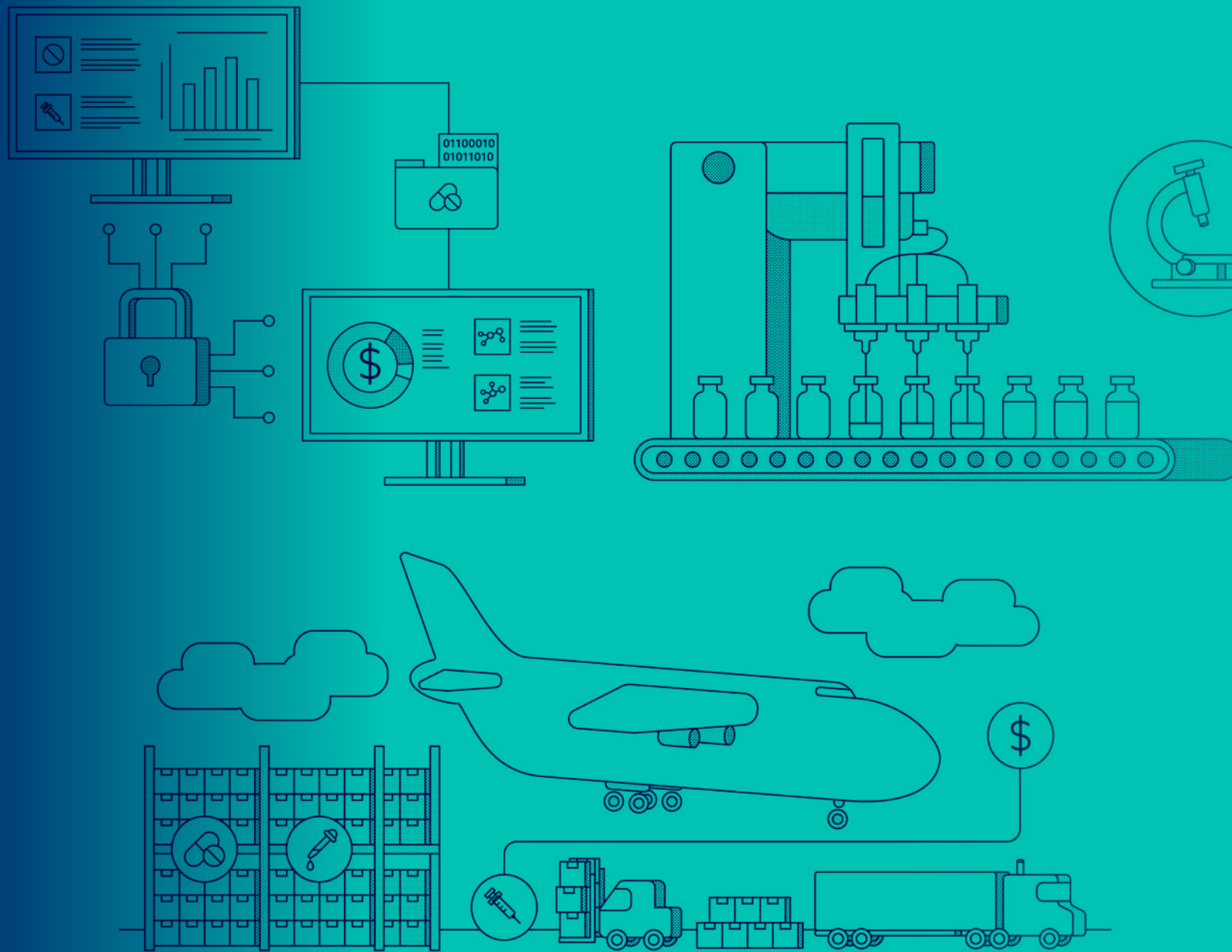


Solution Strategies

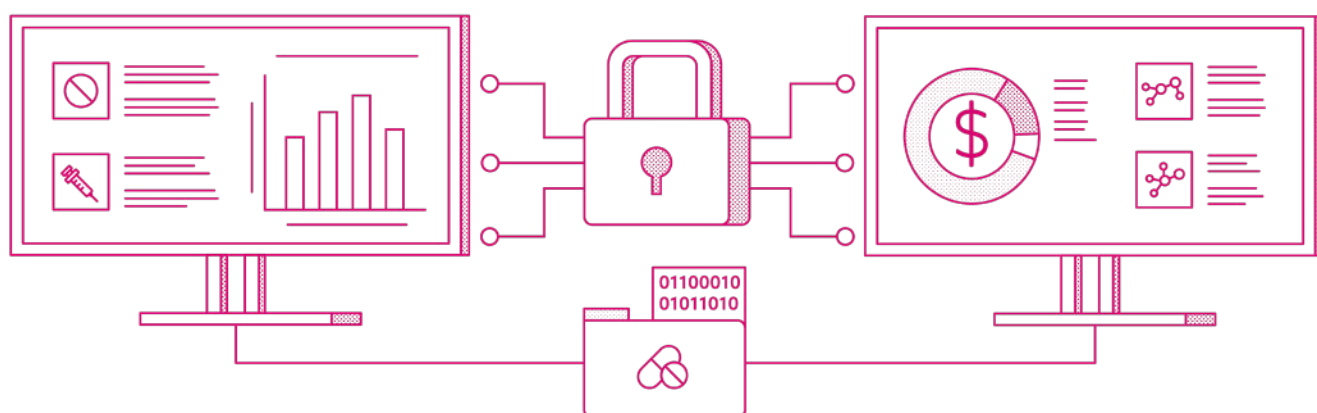
A key element of this report is to identify strategies that can be employed across the essential medicines supply chain to address the identified challenges and vulnerabilities.

Many of the solutions proposed will need to be combined into an integrated strategy to achieve the end goal of a more resilient pharmaceutical supply chain. A long-term commitment from the government, through budgetary, regulatory, or policy actions, is needed to change the current paradigm. Such a commitment should involve strategies that leverage the government's collective buying power to ensure stable demand, secure the fidelity of the supply chain and incentivize an increase in domestic manufacturing, and encourage and incentivize collaborative partnerships with an emphasis on increasing the United States' competitive global position and leadership in advanced manufacturing, innovative research, and workforce development.

Solutions outlined in this section are based on industry input obtained through interviews, surveys, and workshops. Next steps may include assessing the feasibility and impact of these solutions, and identifying specific action plans, including roles and responsibilities, for their implementation.



Increased Supply Chain Coordination, Security, and Transparency



Improving supply chain visibility will offer a greater ability to anticipate, prioritize, and respond to critical issues, demands, and potential disruptions. This level of supply chain integrity can best be ensured by:

- + Improving coordination and communication among supply chain stakeholders (e.g., by leveraging Manufacturing USA Institutes)
- + Expanding use of data, analytics, and predictive tools to mitigate and manage risk
- + Increasing traceability of all products and materials
- + Ensuring that proprietary and sensitive supply chain data is secure and inaccessible to emerging threats and malicious actors

➔ = strategies prioritized by the industrial steering committee

➔ 1) Improve data- and information-sharing, integration, and standardization across the entire supply chain

Implementation Actions

- + Leverage public-private partnerships to create a shared data infrastructure/network for both government agencies and supply chain stakeholders to collectively respond to supply and demand challenges
 - Implement regionally based focus groups to define data needs for improved decision making
- + Create mechanisms for companies to share data and analytics while ensuring IP protection
- + Establish consistent standards and processes for data transparency and harmonization to improve integration
- + When possible, leverage existing data resources (e.g., healthcare provider inventory and usage; wholesale distributor data; and aggregate data from electronic health record systems, excluding personal identifiable information)
- + Require reporting of key information (e.g., inventory levels) to the U.S. government, and consider increasing the reporting frequency (i.e., monthly or quarterly rather than annually) of data that is currently required
- + Strengthen oversight of foreign drug manufacturing processes by improving data sharing with the Food and Drug Administration (FDA) and enhancing collaboration with international stakeholders

Challenge Areas Addressed



Supply Chain and Distribution

➔ 2) Strengthen collaboration and coordination between the government and all participants in the pharmaceutical supply chain

Implementation Actions:

- + Improve interagency coordination: clearly define roles for FDA, the Federal Emergency Management Agency (FEMA), Centers for Disease Control and Prevention (CDC), etc. and create a National Command Center or Federal Health Authority to which they report
- + Monitor for over-consolidation of GPO options to prevent monopolistic practices within the market or reduced choices for hospitals and care facilities
- + Maintain the currency and relevance of the essential medicine list by conducting a regular comprehensive review (e.g., every 2 years) with sufficient time for industry to adjust to any new priorities
 - The list is the foundation for other policies so obsolescence must be monitored
 - Two years is in alignment with the World Health Organization (WHO) cycle
 - An update schedule that is not overly frequent will help maintain manufacturing cycle stability
- + Establish an essential medicine consortium / public-private partnership with membership representing all supply chain stakeholders, including clinicians and public health experts, so that the private sector can better inform, complement, and support government efforts through a continuous feedback loop
 - Establish an open capacity consortium to maintain visibility into which manufacturers have open capacity to develop which product in the event of a demand surge
 - Leverage consortium to advise those looking to build domestic capacity

Challenge Areas Addressed



Supply Chain and Distribution

3) Develop and utilize predictive tools and conduct risk assessments

Implementation Actions:

- + Assess the global supply chain for essential medicines that covers source location, volume, and the number of facilities involved in production of APIs, finished dosage forms, and other required components (e.g., filters, stoppers, vials)
 - Provide resources to the Department of Commerce to update Harmonized Systems (HS) Codes to monitor imports and exports of raw materials, APIs, and medicines separately
- + Create a map of the supply chain for essential medicines that includes information such as fungibility of finished dosage form and raw material production; types of production equipment used; production capacity constraints; inventory levels, distribution timelines, and backorder metrics
 - Develop an index of APIs that assigns “resilience scores” based on demonstrated quality management maturity, country of origin, business continuity of supply, etc.
 - Mandate transparency on inventories of APIs and finished dosage forms in the pipeline—which would need to be aggregated and reported at an anonymized industry level to avoid exposing trade secrets—to create a “virtual stockpile” inventory of all essential medicines
- + Develop broad surveillance into common quality standards and controls for all precursor materials, APIs, and finished products for essential medicines, regardless of country of origin, to ensure integrity of raw materials, CGMP, etc.
 - Congress should authorize and provide appropriate appropriations to enable FDA to publish metrics for quality management maturity of facilities and manufacturing processes and to assess facilities based on these metrics.
- + Work with manufacturers and distributors to identify the greatest risks for shortages and create interim measures to stabilize those classes of drugs
- + Assess and mitigate sourcing risk / diversify sources of supply, leveraging methods such as dual- or multi-sourcing (for redundancy) and distributed regionalization/ geographic diversity, to avoid single points of failure

Challenge Areas Addressed



Supply Chain and Distribution

4) Establish a more comprehensive centralized control tower platform

Implementation Actions:

- + Leverage integrated data analytics to identify key risk indicators and improve both demand forecasting and capacity management
- + Develop a national critical drug tracking, monitoring, and alert system, with regional coordination and inputs, to monitor manufacturer and distributor inventory of essential medicines and identify and respond to signals of supply disruption to adapt to demand and capacity fluctuations more flexibly
 - Create a federal mandate for quarterly reporting of supplies of essential medicines to the government
 - Establish an early alert system for API shortages
 - Leverage expertise of those in the supply chain who have built or employ similar computational models

Challenge Areas Addressed



Supply Chain and Distribution

5) Increase both the physical and cyber security posture throughout the supply chain

Implementation Actions:

- + Designate the pharmaceutical industry and its supply chain as a specific, high-priority critical U.S. infrastructure sector to allow the government to coordinate during times of crisis
- + Deploy technologies that segregate manufacturing functions to better protect them from vulnerabilities in networked operational systems
- + Require that all companies are, at a minimum, in compliance with existing government cybersecurity protocols (e.g., [National Institute of Standards and Technology \[NIST\] Cybersecurity Framework](#)) and industry-developed cyber protection standards (e.g., [IEC 62443](#) and [ISO 27001](#)), and should be considering regular threat assessments
- + Increase government support to help protect against theft of competitive IP that could result in increased counterfeiting
- + Consider mandating the reporting of detected threats that could cause vulnerabilities and supply chain disruptions
- + Leverage serialization and product tracing required by the Drug Supply Chain Security Act to better protect against illegitimate product, such as counterfeits

Challenge Areas Addressed



Supply Chain and Distribution

➔ CASE STUDY: INCREASED ALBUTEROL INHALER DEMAND

During the COVID-19 pandemic, albuterol inhalers became a common alternative to nebulizers in hospitals, resulting in a shortage that impacted the nearly **25 million people**²³ in the United States who suffer from asthma, in addition to patients with other lung diseases.

WHY IS ALBUTEROL ESSENTIAL?

Albuterol is a bronchodilator used to open the air passages in patients' lungs to treat or prevent bronchospasm.²⁴ It is **critical for patients with asthma, emphysema, chronic bronchitis, chronic obstructive pulmonary disease (COPD), and other lung diseases** as well as bronchospasm caused by exercise. It can be prescribed to children under 4 years, and it works slightly faster and is more affordable than any alternative medications available.²⁵

DEMAND INCREASES

After the use of nebulizers was identified as a potential source of airborne spread of COVID-19,²⁶ albuterol inhalers became a common alternative to nebulizers in hospital settings for patients suffering from respiratory distress. This use resulted in shortages of albuterol asthma inhalers in hospitals and retail pharmacies.²⁷

400 percent increase in demand for inhalers early in the pandemic²⁸

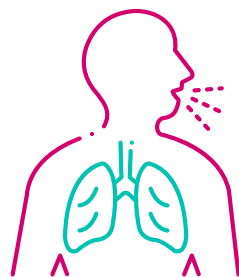


CDC recommendations further exacerbated shortages by encouraging asthma sufferers to seek extended supplies of their medication²⁹



THE IMPACT

According to an Asthma and Allergy Foundation of America (AAFA) survey, **46 percent of survey respondents had trouble accessing prescription asthma or allergy medication** during the COVID-19 pandemic.³⁰



Asthma sufferers having trouble obtaining refills during the shortage were advised to adopt measures such as:

- + Using partially effective expired inhalers
- + Rationing the use of their inhalers³¹

MITIGATION STRATEGIES

- + **FDA approved the use of generic albuterol inhalers** for the first time in April 2020, which helped alleviate shortages.³²
- + **Expansion of formularies** by pharmacy benefit managers and payers was used to expand patient access to branded and generic albuterol inhalers.³³
- + **AAFA sent a letter to the FDA proposing a collaborative effort** to identify and resolve problems to mitigate and prevent shortages and alleviate supply chain vulnerabilities.³⁴

23 "Asthma Facts and Figures," Asthma and Allergy Foundation of America, <https://www.aafa.org/asthma-facts/>.

24 "Albuterol (Inhalation Route) Description and Brand Names," Mayo Clinic. Mayo Foundation for Medical Education and Research, July 1, 2021, <https://www.mayoclinic.org/drugs-supplements/albuterol-inhalation-route/description/drg-20073536>.

25 Ibid.

26 G. Reychler, L. Vecellio, and J.C. Dubus, "Nebulization: A Potential Source of Sars-Cov-2 Transmission," *Respiratory Medicine and Research* 78 (2020): 100778, <https://doi.org/10.1016/j.resmer.2020.100778>.

27 Christopher Rowland and Joanna Slater, "Spikes in Demand from Coronavirus Patients Are Creating Shortages of Asthma Drugs and Sedatives for Ventilator Patients," *The Washington Post*, April 12, 2020, <https://www.washingtonpost.com/business/2020/04/12/drug-ventilator-shortage-coronavirus/>.

28 Aislinn Antrim, "Generic Albuterol Inhalers Are Key to Minimizing Shortages Early in Pandemic," *Pharmacy Times*, May 18, 2021, <https://www.pharmacytimes.com/view/generic-albuterol-inhalers-are-key-to-minimizing-shortages-early-in-pandemic>.

29 Kenneth Mendez, "AAFA Comment Letter to FDA on COVID-19 Asthma Drug Shortages," Asthma and Allergy Foundation of America, April 7, 2020, <https://www.aafa.org/media/2653/aafa-comment-letter-to-fda-on-covid-19-asthma-drug-shortages.pdf>.

30 Ibid.

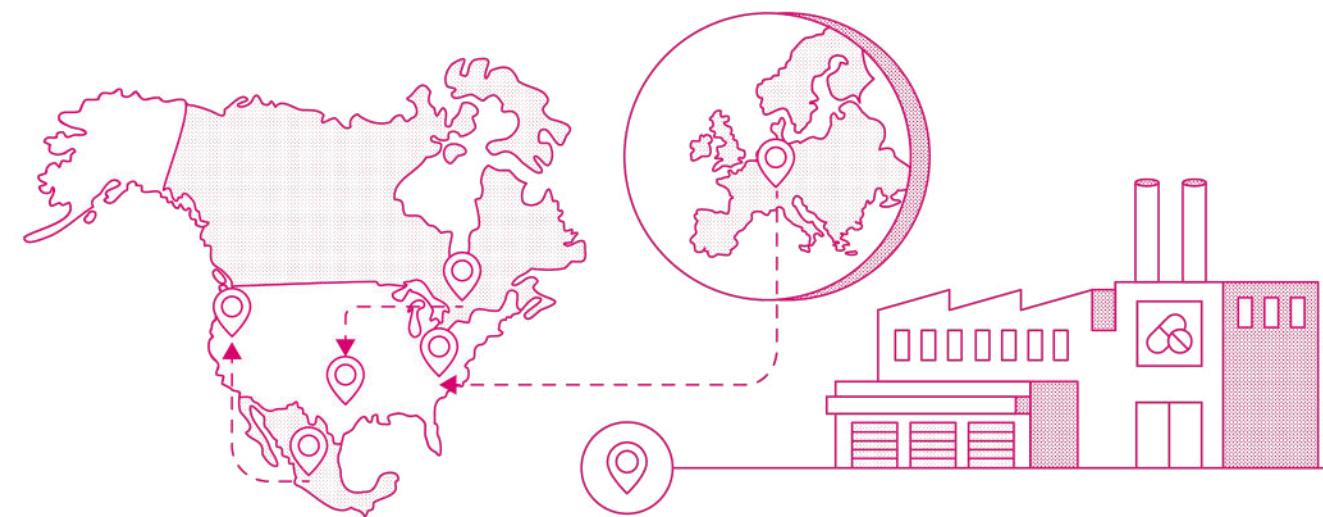
31 "A Message to Asthma Sufferers about a Shortage of Albuterol Metered Dose Inhalers," ACAAI Public Website, June 23, 2020, <https://acaai.org/news/message-asthma-sufferers-about-shortage-albuterol-metered-dose-inhalers>.

32 "FDA Approves First Generic of a Commonly Used Albuterol Inhaler to Treat and Prevent Bronchospasm," U.S. Food and Drug Administration, April 8, 2020, <https://www.fda.gov/news-events/press-announcements/fda-approves-first-generic-commonly-used-albuterol-inhaler-treat-and-prevent-bronchospasm>.

33 "Albuterol Inhalers in Short Supply: Here's What to Do," Allergy & Asthma Network, May 17, 2020, <https://allergyasthmanetwork.org/news/albuterol-inhalers-in-short-supply-heres-what-to-do/>.

34 Kenneth Mendez, "AAFA Comment Letter to FDA on COVID-19 Asthma Drug Shortages," Asthma and Allergy Foundation of America, April 7, 2020, <https://www.aafa.org/media/2653/aafa-comment-letter-to-fda-on-covid-19-asthma-drug-shortages.pdf>.

Expanded Onshore or Nearshore Production Capacity



A balanced, diversified approach to capacity and sourcing that avoids single-source points of failure can decrease the risk of essential medicine shortages and reduce U.S. reliance on materials or manufacturing from competitor nations. This onshore resilience can be achieved by:

- + Leveraging the capacity of and agreements with ally-shore resources and suppliers
- + Encouraging market commitments for generics to reduce risk and add certainty for manufacturers
- + Providing mechanisms and incentives to make it more viable for new players to enter the generic market or existing players to increase their commitment to domestic production
- + Increasing the efficiency of the regulatory review and approval process—leveraging methods demonstrated during the COVID-19 pandemic—to encourage manufacturers to increase regular capacity or prepare for surge-based capacity

➔ = strategies prioritized by the industrial steering committee

➔ 1) Ensure stable, long-term demand for generic medicines at a sustainable price to encourage manufacturers to expand domestic production

Implementation Actions

- + Establish guaranteed, diversified markets through long-term price and volume guaranteed contracts for essential medicines to protect manufacturers' investments from low-priced foreign imports of the same medicines
- + Work with policymakers to devise multi-stakeholder strategies to address the lack of incentives to produce less profitable drugs
 - Establish a pricing floor for generic medicines on the essential list to prevent unsustainable price erosion

Challenge Areas Addressed



➔ 2) Incentivize manufacturers to add/expand domestic production by offsetting capital investment

Implementation Actions

- + Provide incentives for domestic essential medicine production using U.S. government loans, grants, direct investment, and partnership/cost-share for critical medical infrastructure
- + Pass long-term tax incentives that encourage U.S. pharmaceutical companies to relocate manufacturing back to the United States, build new manufacturing sites, refurbish existing onshore facilities, and/or repurpose existing production lines to focus on essential medicines—with an emphasis on developing and deploying advanced manufacturing platform technologies that enable more efficient and sustainable manufacturing
- + Perform risk analyses to identify essential medicines (including precursors and components) with the greatest offshore dependence and prioritize establishing incentives for the on- or ally-shoring of their production, if feasible
- + Incentivize manufacturers to add capacity for essential medicine surge production; offer subsidies and/or tax incentives to manufacturers that:
 - Maintain extra supplies of existing products so that manufacturing lines could be shifted rapidly to meet new response needs
 - Operate with excess utilization capacity
 - Prepare contingency plans to respond to potential disruptions, including leveraging standby capacity (e.g., qualified equipment, processing lines) that can be brought online in the event of a disruption
 - Develop cost-share programs to design new production processes and supply chains that can scale rapidly

Challenge Areas Addressed

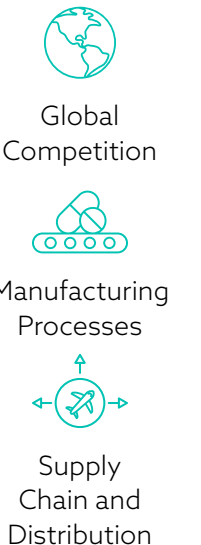


3) Develop a complete essential medicine supply chain and manufacturing model—from precursor materials to finished products—that more fully leverages both on- and ally-shored resources and suppliers

Implementation Actions

- + Incentivize domestic manufacturing of essential medicine APIs, precursor materials, and components, with particular focus on those with no U.S. source, a limited number of offshore sources, and/or offshore sources concentrated in one geographic area
- + Strengthen partnerships and trade agreements with nearshore allies (e.g., Latin America and Central America) to bolster their own domestic manufacturing
 - Create contractual agreements / mechanisms for directly sourcing the Strategic National Stockpile (SNS)
- + Work with off- and nearshore U.S. allies (e.g., Canada, Europe, Mexico, Japan) to develop a cooperative approach to expanding and securing the U.S. supply chain, ensuring supply diversity, economies of scale, and a coordinated approach to global pandemics
 - Establish Pharmaceutical Supply Chain Trade Agreement with allied countries who would commit to not implementing trade restrictions during public health emergencies
 - FDA should revisit the current mutual recognition agreement between the United States and Europe to identify further opportunities

Challenge Areas Addressed

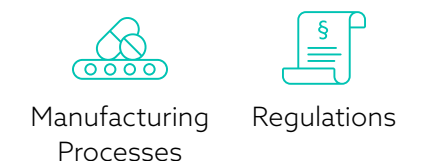


4) Streamline implementation and communication around regulatory procedures to make adding new facilities or capacity faster and easier

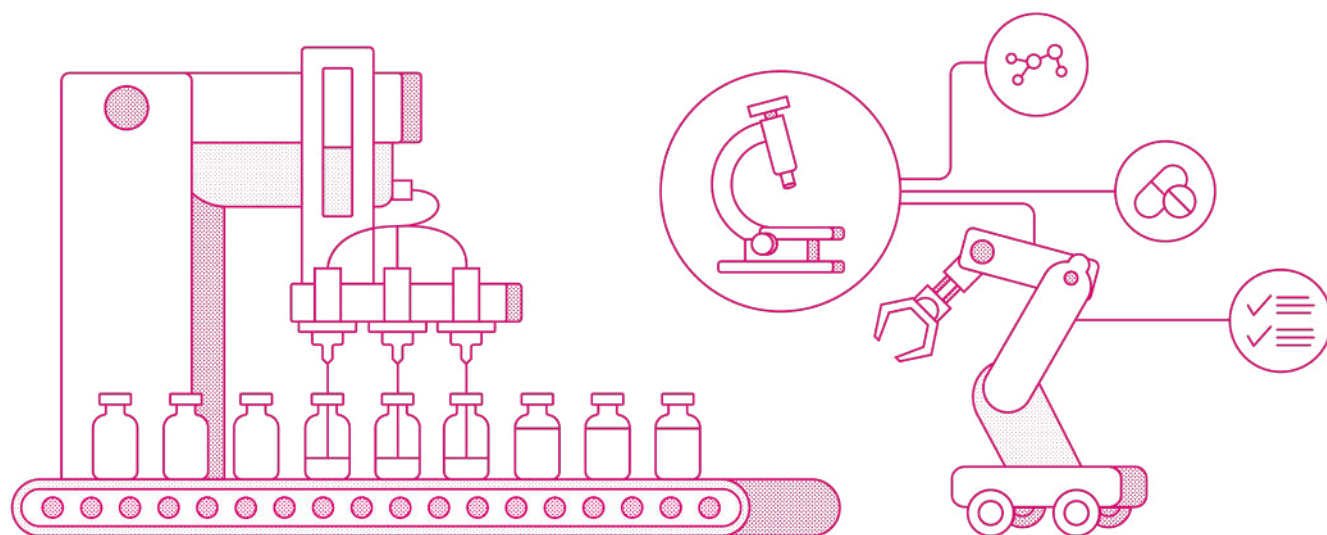
Implementation Actions

- + Provide manufacturers with earlier opportunities for regulator input on process development and validation, including facility design and utilities, technology transfer processes, quality management systems, and equipment qualification
- + Strengthen communication channels between FDA and manufacturers to ensure industry stakeholders are aware of resources and support the FDA provides for rapidly qualifying new suppliers
- + Develop “shortage manufacturing establishments” by pre-qualifying existing facilities for dosage manufacturing so new lines could be more quickly ramped up when demand arises; examine what economic incentives may be needed to influence shifts in production

Challenge Areas Addressed



Advanced Manufacturing Capabilities and Innovative Research and Development



New formulation and production technologies can strengthen the manufacturing competitiveness of both the United States and its allies and partners. To increase the efficiency and product quality, safety, and security needed to more rapidly deliver critical essential medicines, the United States should:

- + Promote the use of more efficient and innovative manufacturing techniques that will enable the United States to increase/expand production capabilities and competitively produce high-quality essential medicines at scale
- + Create fit-for-purpose regulatory pathways to facilitate the use of on-demand and distributed manufacturing techniques to reduce demand on legacy manufacturing
- + Ensure the domestic workforce of the future is adequately prepared, trained, and competitively compensated to keep pace with the industry's rapidly changing processes and technologies

➔ = strategies prioritized by the industrial steering committee

➔ 1) Identify, promote, and invest in innovative and sustainable manufacturing paradigms that can facilitate U.S. self-sufficiency

Implementation Actions

- + Augment a centralized manufacturing model with decentralized, regionally based, on-demand manufacturing (e.g., distributed / modular manufacturing, managing across sites to ensure quality and consistency)
 - Supports smaller-scale production and targeted medicine production
 - Reduces reliance on complex logistics and stockpiling
 - Regionally positioned for more targeted, rapid response, including point-of-care production
 - Reduces current geographical disparities in drug distribution
- + Sustain and increase investment in platform technologies to ensure agility, flexibility, and installed capacity
- + Incentivize distributed networks of manufacturing capabilities based on flexible platform technologies to avoid single points of failure (e.g., shutdown of a single large centralized production facility)

Challenge Areas Addressed



Global Competition



Manufacturing Processes

➔ 2) Develop strategies for targeted workforce investment (e.g., skills and experiential training, equipment access, partnerships) that will enhance U.S. competitiveness

Implementation Actions

- + Establish training centers where new STEM graduates or biopharma employees wanting to re-train for higher-skilled roles can receive short-course practical skills training and application management in the areas of engineering, data analytics, and process development
- + Create opportunities to increase pharmaceutical company partnerships with educational institutions to donate equipment and/or provide access to life sciences equipment and techniques as well as hands-on experiential learning for both educators and students
- + Increase biopharmaceutical company partnerships with educational institutions throughout the country using demonstrated successful models:
 - Participate in program advisory capacity to provide educational programs with perspective on industry's STEM needs
 - Offer industry internships for students and/or pathways to hiring for program graduates

Challenge Areas Addressed



Labor/Workforce

3) Support and invest in innovative drug research and development

Implementation Actions

- + Develop a comprehensive database of essential medicine substitutions / similar formulations of a medicine that do not rely as heavily on hard-to-get APIs
- + Invest in technologies, including novel advanced platforms (e.g., cell-free/ biochemical-driven systems, miniaturization), that streamline production of essential medicine APIs, precursor materials, and components
- + Invest in regional development hubs or "incubators," geographically distributed throughout the United States (i.e., follow the model of the research park) for collaborations among industry, academia, and regulators

Challenge Areas Addressed



Global Competition



Manufacturing Processes

4) Promote smart manufacturing through increased automation and other digital solutions

Implementation Actions

- + Perform an assessment of the critical prioritized drugs from the Essential Medicines List to qualify essential medicines best suited for batch, automated, continuous, on-demand, or regionally distributed manufacturing techniques
- + Provide incentives to help manufacturers upgrade to a more efficient manufacturing process (e.g., continuous manufacturing, automated batch execution), while ensuring continued quality based on the type of essential medicine
- + Leverage data analytics and continuous monitoring processes to make continuous manufacturing more efficient and better able to respond to unexpected process disruptions
- + Leverage the benefits of advanced manufacturing technologies to reduce manufacturing footprint and environmental impacts (e.g., less waste, fewer emissions)

Challenge Areas Addressed



Global Competition



Manufacturing Processes

5) Encourage widespread adoption of new manufacturing technologies and approaches through increased standardization and greater regulatory certainty, while ensuring quality

Implementation Actions

- + Increase the efficiency of regulatory review and approval, particularly around manufacturing process changes, to assist in adoption of new technologies; to the extent that such pathways already exist (e.g., ICH Q12 and Emerging Technology Program), examine ways to maximize awareness and use among industry stakeholders
- + Identify a standardized approach for applications using advanced manufacturing processes such as continuous manufacturing
- + Establish standards and best practices around continuous manufacturing that allow for agility while ensuring quality (e.g., preventing cross-contamination)

Challenge Areas Addressed

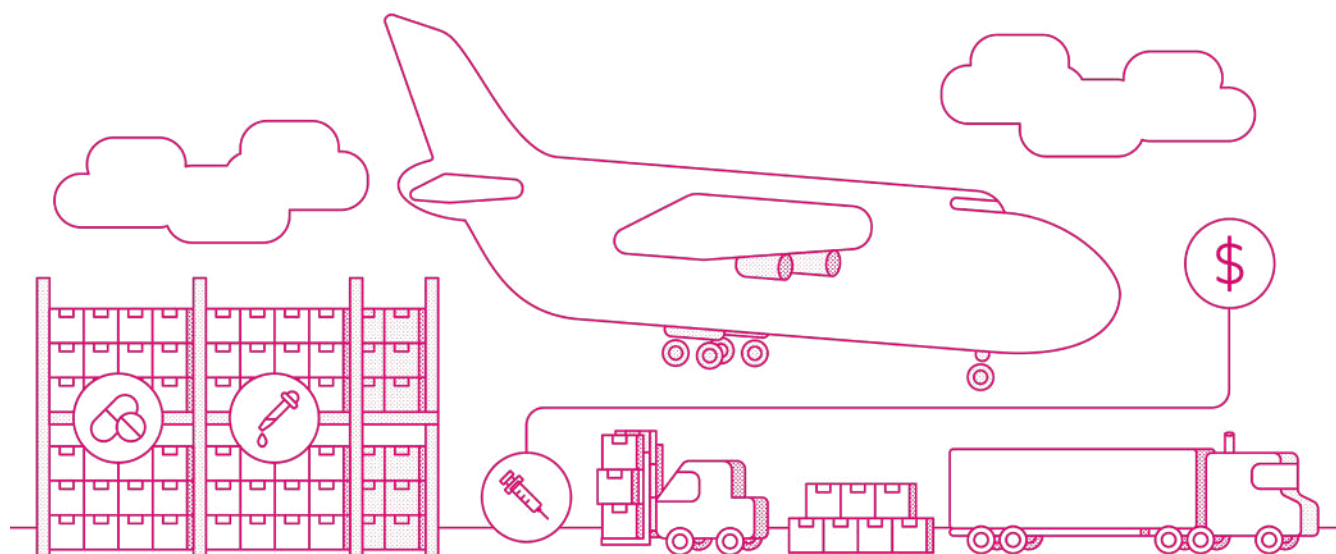


Manufacturing Processes



Regulations

Purchasing, Stockpiling, and Distribution Approaches



Improved national strategies around purchasing and maintaining supply reserves will enable more targeted and efficient handling and distribution of essential medicines in response to demand fluctuations or shortages. This increased resilience can be achieved by:

- + Signaling the government's commitment to domestic products to help provide the predictability and economic stability needed to increase domestic production capacity
- + Increasing flexibility to allow purchasing based on supply chain resilience, diversification of supply, recognized investment in quality, and compliance status and history
- + Virtually stockpiling APIs and other materials used to produce essential medicines to allow the United States to better respond to surge events and short-term spikes in demand, as well as manage market imbalances
- + Exploring new methods for maintaining a just-in-case rather than just-in-time inventory approach—including leveraging commercial mechanisms or models

➔ = strategies prioritized by the industrial steering committee

➔ 1) Leverage the federal government's collective buying power to reform procurement protocols

Implementation Actions

- + Implement more predictable purchasing by including targets in purchase agreement programs (e.g., CMS) for domestically produced or finished products, and diversify supply by awarding more than one contract for essential medicines
- + Establish preference for domestically produced essential medicines, procured either directly by the government (e.g., VA, Department of Defense [DOD]) or through CMS (i.e., similar to the Berry Amendment for DOD); to the extent that such preferences already exist, reexamine their impact and that of any waiver processes
- + Form a non-profit consortium / public-private partnership composed of key stakeholders in drug development, manufacturing, distribution, and end users (e.g., hospital systems) to negotiate reimbursement rates directly with CMS and Medicare, Tricare, etc., considering increased reimbursement rates for products that are produced domestically in facilities with demonstrated quality management maturity

Challenge Areas Addressed



Market Structure

➔ 2) Revise purchasing models to increase emphasis on product quality and supply chain resilience, not simply lowest cost

Implementation Actions

- + Create a rating system to encourage drug manufacturers to invest in achieving quality management system maturity
- + Utilize existing data reporting requirements from the supply chain to develop nonproprietary information that can be disseminated (via FDA or an independent nonprofit) among relevant stakeholders to empower partnerships with stable and reliable suppliers
- + Receiving CMS reimbursement and federal contracts—for example, through the Federal Supply Schedule (FSS), DOD, or SNS—could be contingent on quality and resilience practices
 - Require manufacturers receiving CMS reimbursement or federal contracts to provide metrics on quality manufacturing maturity, including manufacturing line readiness, production capacity, and risk management

Challenge Areas Addressed



Market Structure

3) Regionalize the SNS for better pre-positioning of essential medicines and other critical materials

Implementation Actions

- + Develop local/regional stockpiles of essential medicines managed by individuals neutral in the supply chain but reporting to a consortium of supply chain stakeholders
- + Create opportunities for partnership between large academic medical centers and smaller community hospitals for a medicine sharing system
- + Limit stockpiling to one major academic medical center in an area to address fairness, vulnerability, etc.

Challenge Areas Addressed



4) Develop a distributed stockpile of APIs and precursor materials

Implementation Actions

- + Increase safety stock of critical materials and products with high supply chain risk
- + Establish preference for domestically produced APIs and precursor materials for the stockpile

Challenge Areas Addressed

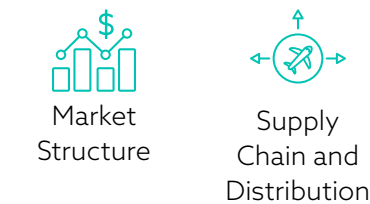


5) Incentivize pharmaceutical manufacturers and wholesale distributors to hold buffer stock, rotate stock, and manage distribution, or develop other similar strategies or models

Implementation Actions

- + Consider a vendor-managed inventory (VMI) "stockpile" model or other perpetual inventory model to actively manage and cycle stock to avoid expiration waste and ensure committed buying to incentivize increased manufacturing capacity
 - Managed by pharmaceutical manufacturers and wholesale distributors, rather than hospitals, to address capacity, storage, etc.
- + Connect Defense Production Act rated orders to the total vendor capacity to ensure continuity of supply

Challenge Areas Addressed

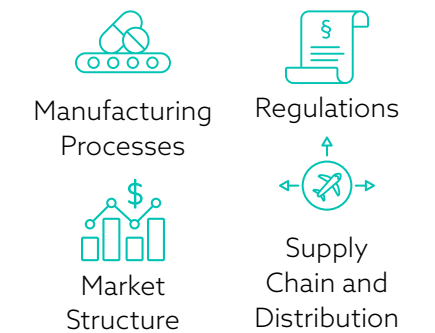


6) Develop mandates or explore mechanisms, such as pursuing statutory authority, for maintaining stock reserves

Implementation Actions

- + Require producers to maintain a reserve of supply stock for emergency orders instead of shipping all product coming off production lines
- + Investigate potential for FDA to require stability data from manufacturers to enable drug expiration date extensions—a strategy which has been used in the past on a limited basis
 - Leverage the CDC's CHEMPACK model to develop guidelines for supplies of critical medicines beyond listed expiration with testing/validation of effectiveness so they can be used in cases of extreme shortage
 - Create buy-back programs for stockpiled essential medicines nearing expiration, preventing frequently used medicines from being wasted

Challenge Areas Addressed



7) Proactively develop comprehensive essential medicine distribution logistics plans

Implementation Actions

- + Create a federal mechanism for mandatory reporting of stock levels by each supplier to the government in time of crisis
- + Develop federal mechanism/allocation program to channel needed essential medicines to "hot zones," underserved areas, or areas experiencing shortages
- + Develop clear guidelines on prioritization criteria to establish equitable and efficient "fair share allocation" of available quantities of shortage medicines
- + Develop logistics contingency plans for disruptions with nearshore and offshore producers

Challenge Areas Addressed



→ CASE STUDY: FENTANYL INJECTION

During the COVID-19 pandemic, **fentanyl became critical for treating patients placed on ventilators** that were experiencing respiratory failure.

WHY IS FENTANYL ESSENTIAL?



Fentanyl is a **powerful synthetic opioid** that works by binding to the body's opioid receptors to help control pain.³⁵ It is **critical for patients with severe pain** (particularly after surgery, as well as severe chronic pain)³⁶ and can be used as a short-term analgesia during induction, maintenance, and recovery from general or regional anesthesia.³⁷ Fentanyl is similar to morphine, but it is **50 to 100 times more potent** and is associated with a risk of addiction and abuse.³⁸

THE SHORTAGE

Hospitals in regions experiencing a **surge of COVID-19 cases** and hospitalizations saw an increased use of fentanyl for **patients experiencing respiratory failure** who were placed on ventilators for up to two weeks.³⁹

Demand for fentanyl rose in April 2020 as **hospitals required:**



“**large, 50-milliliter vials of fentanyl to treat ventilated patients humanely.**”⁴⁰

THE IMPACT

The use of fentanyl to treat COVID-19 patients was constrained due to lack of supply.

When Colorado-based SCL Health Hospitals & Clinics could not find fentanyl vials large enough to fill a bedside drip bag in one shot, they bought any size available, including syringe-sized ampules.

Pharmacy techs then cracked as many as 25 thumb-size glass bottles to draw out the clear liquid to make a single 50 milliliter intravenous bag for one ventilator patient.⁴¹



A COVID patient may need two or more bags a day.

MITIGATION STRATEGIES

- + Before the pandemic, the DEA called for **cutting authorized production of fentanyl by 31%**.⁴² However, the **DEA reversed that in early April 2020** by ordering a **15% increase** in the production of fentanyl used for COVID-19 treatments.⁴³
- + **A potential mitigation strategy to address future shortages** would be to **allow batches to ship pending sterility testing results**, and allow final release of the product if results meet sterility criteria.

35 "Fentanyl Drug Facts," National Institute of Abuse, <https://www.drugabuse.gov/publications/drugfacts/fentanyl>.

36 "Fentanyl," Drug Bank, <https://go.drugbank.com/drugs/DB00813>.

37 Ibid.

38 "Fentanyl Drug Facts," National Institute of Abuse, <https://www.drugabuse.gov/publications/drugfacts/fentanyl>.

39 Christopher Rowland and Joanna Slater, "Spikes in demand from coronavirus patients are creating shortages of asthma drugs and sedatives for ventilator patients," The Washington Post, April 12, 2020, <https://www.washingtonpost.com/business/2020/04/12/drug-ventilator-shortage-coronavirus/>.

40 Ibid.

41 Lisa Girion, Dan Levine and Robin Respaut, "Special Report: COVID Deepens the other Opioid Crisis - A Shortage of Hospital Painkillers," Reuters, June 9, 2020, <https://www.reuters.com/article/us-health-coronavirus-opioids-specialrep-idUSKBN23G1GM>.

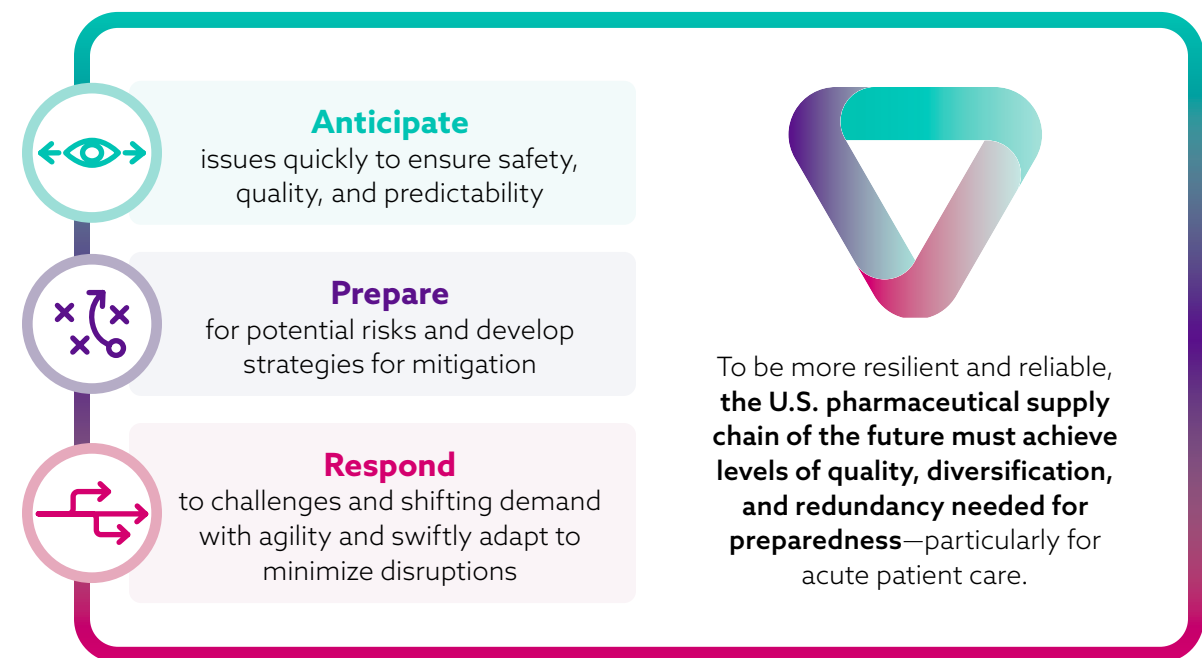
42 "DEA proposes to reduce the amount of five opioids manufactured in 2020, marijuana quota for research increases by almost a third," U.S. Drug Enforcement Administration, September 11, 2019, <https://www.dea.gov/press-releases/2019/09/11/dea-proposes-reduce-amount-five-opioids-manufactured-2020-marijuana-quota>.

43 Ed Silverman, "DEA moves to fight shortages of medicines needed for Covid-19 patients," STAT, April 7, 2020. <https://www.statnews.com/pharmalot/2020/04/07/dea-covid19-coronavirus-ventilators-shortages/>.

→ Next Steps

By analyzing manufacturing and supply data for the prioritized essential medicines, the U.S. government can better identify those with supply chain vulnerabilities that require the most targeted focus and actions to ensure their continued availability.

The strategies outlined in this report aim to move toward a more coordinated and prepared pharmaceutical supply chain. The result—the more reliable availability of medicines when and where they are needed—can strengthen the United States' ability not only to respond to crisis- or market-based demand fluctuations but also to ensure economic and national security.



Appendices

Appendix A: Downselected Essential Medicines Needed for Acute Patient Care

➔ Summary

RANKING TYPE

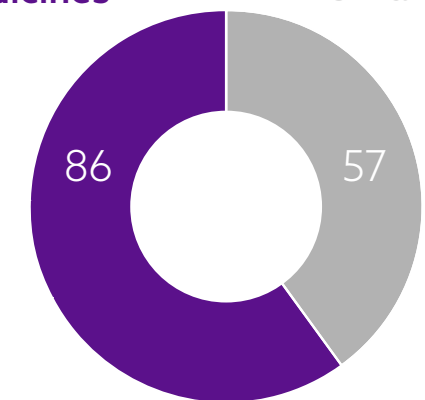
86 Total Prioritized Medicines

57 Unranked Medicines

143 Total Medicines

Total Prioritized Medicines

Unranked



Appendix A: Downselected Essential Medicines Needed for Acute Patient Care

★ 86 medicines in the following table were identified as either critical for minimum patient care in acute settings or important for acute care, with no comparable alternative available.

Medicine Prioritization Status	Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Additives			
Calcium Gluconate (IV)	★ Often	❗ Current Shortage (Since December 2021)	❗ Current Shortage (Since March 2021)
Cyanocobalamin 1000 mcg ml (IM)	- Sometimes	-	-
Magnesium Sulfate (IV)	★ Often/Sometimes	❗ Current Shortage (Since March 2011)	-
Potassium Chloride (Oral/IV)	★ Often	❗ Current Shortage (Since September 2021)	❗ Current Shortage - IV (Since November 2021)
Sodium Bicarbonate Injection (IV)	★ Often/Sometimes	-	❗ Current Shortage (Since March 2017)
Sodium Phosphate (IV)	★ Often/Rarely	❗ Current Shortage (Since August 2021)	❗ Current Shortage (Since September 2021)
Thiamine (IV)	★ Sometimes/Rarely	✅ Resolved Shortage	-
Analgesics			
Fentanyl (IV)	★ Often	❗ Current Shortage (Since May 2017)	❗ Current Shortage (No Date Available)
Hydromorphone (Oral/IV)	★ Often/Sometimes	❗ Current Shortage (Since June 2017)	❗ Current Shortage - IV (Since October 2017)
Lidocaine/Epinephrine (Solution for SQ Local)	★ Often/Rarely	❗ Current Shortage (Since June 2015)	❗ Current Shortage (Since February 2012)
Morphine (IV/Oral Solution)	★ Often	❗ Current Shortage (Since June 2009)	❗ Current Shortage - IV (Since October 2017)

Please note that the FDA shortage list contains drugs that are confirmed to be in a national shortage. The FDA considers a shortage to be "the period of time when the demand for the drug within the United States exceeds the supply of the drug." In contrast, the ASHP shortage list contains "all drug and biologic shortages reported and confirmed with manufacturers that are national in impact."

In addition, the FDA shortage list removes drugs with resolved shortages from the list after six months ("FDA Drug Shortages Frequently Asked Questions," U.S. Food and Drug Administration, https://www.accessdata.fda.gov/scripts/drugshortages/dsp_faq.cfm).

Learn more about the differences between the two shortage lists at:

<https://www.ashp.org/drug-shortages/current-shortages/fda-and-ashp-shortage-parameters?loginreturnUrl=SSOCheckOnly/>.

Medicine Prioritization Status	Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Anesthetic			
Isoflurane (Gas)	★ Often	-	-
Animal-Derived IG Products			
Anti-Thymocyte Globulin Products (IV)	- (Rare)	Sometimes/Rarely	-
Black Widow Spider Anti-Venin (Latrodectus mactans) (IV)	- (Rare)	Sometimes/Rarely	❗ Current Shortage (Since October 2021)
Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) Equine (IV)	- (Rare)	Rarely	-
Centruroides Immune Fab (Scorpion) (IV)	- (Rare)	Rarely	-
Coral Snake Antivenom (Antivenin) (Micrurus Fulvius) (IV)	- (Rare)	Rarely	-
Crotalidae Immune Fab (North American Rattlesnakes) (IV)	- (Rare)	Rarely	-
Crotalidae Polyvalent Immune Fab (Rattlesnake, Water Moc, Cottonmouth) (IV)	- (Rare)	Rarely	-
Digi Immune Fab (Digoxin) (IV)	- (Rare)	Rarely	-
Anticholinergic Secretions			
Glycopyrrolate (IV)	-	Sometimes/Rarely	-

Medicine Prioritization Status	Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Anticoagulants/Antiplatelets			
Alteplase (IV)	★ Sometimes	❗ Current Shortage (Since November 2021)	–
Apixaban (Oral)	★ Often/Sometimes	–	–
Argatroban (IV)	★ Sometimes	❗ Current Shortage (Since November 2018)	–
Aspirin (Oral)	★ Often	✅ Resolved Shortage	–
Enoxaparin (SQ)	★ Often	✅ Resolved Shortage	–
Heparin (IV)	★ Often	❗ Current Shortage (Since October 2017)	❗ Current Shortage (Since November 2017)
Ticagrelor (Oral)	★ Often	–	–
Vitamin K (IV)	★ Often/Sometimes/Rarely	✅ Resolved Shortage	–
Anticonvulsants			
Levetiracetam (Oral/IV)	★ Often	❗ Current Shortage (Since May 2015)	✅ Resolved Shortage - Oral
Phenytoin (IV)	★ Often/Sometimes/Rarely	✅ Resolved Shortage	✅ Resolved Shortage
Antiemetics			
Ondansetron (IV)	★ Often/Rarely	❗ Current Shortage (Since March 2018)	❗ Current Shortage (Since April 2018)
Antihistamines			
Diphenhydramine (Oral/IV)	★ Often/Sometimes	✅ Resolved Shortage	–

Medicine Prioritization Status	Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Antihypertensives/Cardiovascular			
Adenosine (IV)	★ Often/Sometimes/Rarely	✅ Resolved Shortage	–
Amiodarone (IV)	★ Often	❗ Current Shortage (Since January 2018)	–
Amlodipine (Oral)	– Often/Sometimes	–	–
Atropine (IV)	★ Often/Sometimes/Rarely	❗ Current Shortage (Since August 2011)	❗ Current Shortage (No Date Available)
Diltiazem (Oral/IV)	★ Sometimes	❗ Current Shortage (Since June 2015)	❗ Current Shortage - IV (Since February 2018)
Dobutamine (IV)	★ Sometimes/Rarely	❗ Current Shortage (Since March 2017)	❗ Current Shortage (Since November 2017)
Furosemide (Oral/IV)	★ Often	❗ Current Shortage (Since May 2017)	❗ Current Shortage - IV (Since April 2020)
Hydralazine (Oral/IV)	★ Often/Sometimes	❗ Current Shortage (Since June 2018)	✅ Resolved Shortage - IV
Hydrochlorothiazide (Oral)	– Often/Sometimes	❗ Current Shortage (Since 2017)	–
Labetalol (IV)	★ Often/Sometimes	✅ Resolved Shortage	–
Mannitol (IV)	– Sometimes/Rarely	❗ Current Shortage (Since September 2021)	❗ Current Shortage (Since September 2021)
Metoprolol (Oral/IV)	★ Often	❗ Current Shortage (Since November 2017)	✅ Resolved Shortage - IV
Nitroglycerin (Oral/IV)	★ Often/Sometimes	✅ Resolved Shortage	–
Phenoxybenzamine (Oral)	– Rarely	–	–

Medicine Prioritization Status	Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Anti-Malarial			
Artesunate (IV)	– (Rare)	Rarely	❗ Current Shortage (Since September 2021)
Antimetabolite			
Hydroxyurea (Oral)	–	Sometimes/ Rarely	–
Anti-Microbial			
Amikacin (IV)	–	Sometimes/ Rarely	✅ Resolved Shortage
Amphotericin B (IV)	–	Sometimes/ Rarely	❗ Current Shortage (Since November 2021)
Ampicillin (IV)	★	Often/ Sometimes/ Rarely	❗ Current Shortage (Since June 2011)
Azithromycin (IV)	★	Often	✅ Resolved Shortage ✅ Resolved Shortage
Cefepime (IV)	★	Sometimes/ Rarely	❗ Current Shortage (Since April 2015)
Ceftazidime (IV)	–	Often/ Sometimes/ Rarely	–
Ceftazidime-Avibactam (IV)	★	Rarely	✅ Resolved Shortage ✅ Resolved Shortage
Ceftriaxone (IV)	★	Often	✅ Resolved Shortage
Daptomycin (IV)	★	Sometimes/ Rarely	✅ Resolved Shortage
Doxycycline (Oral/IV)	★	Sometimes/ Rarely	–
Fluconazole (Oral/IV)	★	Sometimes	✅ Resolved Shortage
Levofloxacin (Oral/IV)	★	Often	–
Linezolid (IV)	★	Often	–

Medicine Prioritization Status	Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Meropenem (IV)	★	Often/ Sometimes/ Rarely	✅ Resolved Shortage
Metronidazole (Oral/IV)	★	Often/ Sometimes	❗ Current Shortage (Since October 2021) ✅ Resolved Shortage - IV
Micafungin (IV)	★	Often	–
Penicillin G (IV)	★	Often/ Sometimes/ Rarely	✅ Resolved Shortage
Piperacillin/Tazobactam (IV)	★	Often	✅ Resolved Shortage
Rifampin (IV)	–	Sometimes/ Rarely	❗ Current Shortage (Since December 2021) ❗ Current Shortage (Since February 2021)
Tobramycin Ophthalmic Solution 0.3% (Solution/Topical)	–	Sometimes/ Rarely	–
Trimethoprim/Sulfamethoxazole (Oral)	★	Often/ Sometimes	–
Vancomycin (Oral/IV)	★	Sometimes	❗ Current Shortage (Since September 2015)
Voriconazole (IV)	★	Sometimes	–
Antipyretics			
Acetaminophen (Oral)	★	Often	–
Ibuprofen (Oral)	★	Often	–
Antiseptics/Disinfectants			
Chlorhexidine (Solution/Topical)	★	Often	–
Povidone-Iodine 10% Solution (Solution)	–	Sometimes	–
Topical/Surface Alcohol-Based Sanitizers (Topical)	★	Often	–

Medicine Prioritization Status	Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Antivirals			
Acyclovir (IV)	★ Sometimes/Rarely	❗ Current Shortage (Since December 2021)	–
Bictegravir/ Emtricitabine/ Tenofovir Alafenamide (Oral)	★ Sometimes	–	–
Oseltamivir (Oral)	– Often/ Sometimes/ Rarely	✅ Resolved Shortage	–
Peramivir (IV)	– Rarely	–	–
Valganciclovir (Oral)	★ Sometimes/ Rarely	✅ Resolved Shortage	–
Chemotherapeutic			
Cyclophosphamide (IV)	– Rarely	–	–
Chemotherapy/Immunosuppressants/Immunomodulators			
Mycophenolate Mofetil (Oral/Suspension)	– Sometimes/ Rarely	❗ Current Shortage (Since July 2018)	–
Tacrolimus (Oral)	★ Sometimes/ Rarely	✅ Resolved Shortage	❗ Current Shortage (Since May 2019)
Dialysis Agents			
Continuous Renal Replacement Solution (Solution)	★ Often/Rarely	–	❗ Current Shortage (Since April 2020)
Endocrine			
Desmopressin Acetate (IV)	– Sometimes/ Rarely	✅ Resolved Shortage	–
Levothyroxine (Oral/IV)	★ Often/ Sometimes/ Rarely	✅ Resolved Shortage	–
Propylthiouracil (Oral)	– Rarely	–	–
Zoledronic Acid (IV)	– Sometimes/ Rarely	–	–

Medicine Prioritization Status	Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Gastrointestinal Agents			
Famotidine (Oral/IV)	– Often	❗ Current Shortage (Since December 2019)	✅ Resolved Shortage
Lactulose (Liquid)	★ Often/ Sometimes/ Rarely	–	–
Loperamide (Oral)	– Sometimes/ Rarely	–	–
Pantoprazole (IV)	★ Often	❗ Current Shortage (Since March 2019)	❗ Current Shortage (Since May 2019)
Glycemic Control			
Dextrose 50% Injection (IV)	★ Often/Rarely	❗ Current Shortage (Since December 2021)	–
Glargine (SQ)	– Often	–	–
Insulin Regular (IV)	★ Often	–	–
Hormones			
Oxytocin (IV)	★ Often	✅ Resolved Shortage	✅ Resolved Shortage
Human Granulocyte Colony-Stimulating Factor			
Filgrastim (SQ)	– Often/Rarely	–	–
Hyperimmune Globulins			
Botulism Immune Globulin (IV)	– Rarely	–	–
Rabies Immune Globulin (IV)	– Rarely	✅ Resolved Shortage	–
Tetanus Immune Globulin (IV)	– Sometimes/ Rarely	–	–
Immune Globulins			
Immune Globulin (IV/IM/Subcutaneous)	★ Sometimes/ Rarely	❗ Current Shortage (Since February 2019)	❗ Current Shortage (Since October 2018)

Medicine Prioritization Status	Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Malignant Hyperthermia			
Dantrolene (IV)	★ Rarely	–	–
Nutrition			
Cupric Chloride (IV)	– Sometimes/Rarely	–	–
Intralipid 20% (IV)	★ Sometimes/Rarely	❗ Current Shortage (Since August 2021)	❗ Current Shortage (Since October 2021)
Trophamine (AA for Infants) (IV)	– Sometimes	–	–
Zinc (IV)	– Sometimes/Rarely	✅ Resolved Shortage	–
Ophthalmic/Glaucoma			
Timolol Maleate Ophthalmic Solution 0.5% (Solution)	– Often/Sometimes	❗ Current Shortage (Since June 2020)	✅ Resolved Shortage
Other			
Anticoagulants in Blood Bags and Storage Solutions (IV)	– Often	–	–
Hemin for Injection (IV)	– Rarely	–	–
Octreotide (IV)	– Sometimes/Rarely	❗ Current Shortage (Since March 2016)	–
Paralytics			
Cistracurium (IV)	– Often/Sometimes/Rarely	❗ Current Shortage (Since April 2020)	✅ Resolved Shortage
Rocuronium (IV)	★ Often	❗ Current Shortage (Since February 2017)	✅ Resolved Shortage
Succinylcholine (IV)	★ Often	✅ Resolved Shortage	–
Vecuronium (IV)	– Often/Sometimes	❗ Current Shortage (Since September 2015)	❗ Current Shortage (Since May 2020)

Medicine Prioritization Status	Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Psychiatric Agents			
Haloperidol (IM)	★ Often	❗ Current Shortage (Since December 2020)	–
Olanzapine (Oral)	– Often	–	–
Pulmonary			
Albuterol (MDI/NEB)	★ Often	❗ Current Shortage (Since March 2020)	–
Ipratropium Bromide (MDI/NEB)	★ Often	✅ Resolved Shortage	–
N-acetylcysteine (IV Solution)	– Sometimes	–	–
Surfactant (Solution)	★ Sometimes/Rarely	–	–
Reversal Agents			
Flumazenil (IV)	– Sometimes/Rarely	❗ Current Shortage (Since September 2021)	–
Fomepizole (IV)	– Rarely	✅ Resolved Shortage	–
Methylene Blue (IV)	– Sometimes/Rarely	✅ Resolved Shortage	–
Naloxone (IV)	★ Often/Sometimes	–	–
Sugammadex (IV)	– Often/Sometimes/Rarely	–	–

Medicine Prioritization Status		Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Sedatives/Hypnotics				
Dexmedetomidine (IV)	–	Often/Sometimes	⚠️ Current Shortage (Since November 2018)	⚠️ Current Shortage (Since April 2020)
Etomidate (IV)	★	Often/Rarely	✅ Resolved Shortage	✅ Resolved Shortage
Ketamine (IV)	–	Often/Sometimes	⚠️ Current Shortage (Since February 2018)	⚠️ Current Shortage (Since February 2018)
Lorazepam (IV)	★	Often	⚠️ Current Shortage (Since June 2015)	⚠️ Current Shortage (Since May 2018)
Midazolam (IV/IM)	★	Often	⚠️ Current Shortage (Since June 2019)	⚠️ Current Shortage (Since April 2020)
Propofol (IV)	★	Often	⚠️ Current Shortage (Since April 2020)	⚠️ Current Shortage (Since April 2020)
Steroids				
Dexamethasone (IV)	★	Often	⚠️ Current Shortage (Since March 2011)	⚠️ Current Shortage (Since February 2019)
Hydrocortisone (Oral/IV)	–	Sometimes	⚠️ Current Shortage (Since March 2020)	⚠️ Current Shortage (Since April 2020)
Methylprednisolone (IV)	★	Often	⚠️ Current Shortage (Since August 2021)	⚠️ Current Shortage - Methylprednisolone acetate (Since December 2021)
Unapproved Drug Initiative				
Potassium Iodide - OTC for Radiation Emergency but also could be used for thyroid storm (Oral Solution)	–	Sometimes/Rarely	✅ Resolved Shortage	–
Selenium (IV)	–	Often/Rarely	✅ Resolved Shortage	–

Medicine Prioritization Status		Frequency of Use for Acute Patient Care	ASHP Shortage Status (as of Dec. 17, 2021)	FDA Shortage Status (as of Dec. 17, 2021)
Vasopressors				
Epinephrine (IV/Prefilled Syringe)	★	Often/Sometimes	⚠️ Current Shortage (Since May 2018)	⚠️ Current Shortage (Since April 2020)
Norepinephrine (IV)	★	Often	⚠️ Current Shortage (Since February 2017)	–
Phenylephrine (IV)	★	Often/Sometimes	⚠️ Current Shortage (Since December 2021)	–
Vasopressin (IV)	★	Often/Sometimes	–	–

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The views in this document represent the perspectives of the individual report contributors and authors and not necessarily those of their respective agency, organization, or institution.

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Appendix C: Summary of Public Comments on the FDA Essential Medicines List

The August 2020 Executive Order (EO) on Ensuring Essential Medicines, Medical Countermeasures, and Critical Inputs Are Made in the United States directed the U.S. Food and Drug Administration (FDA) to identify a list of essential medicines, medical countermeasures, and critical inputs that are medically necessary to have available at all times in an amount adequate to serve patient needs and in the appropriate dosage forms (the Essential Medicines List). In January 2021, FDA released a preliminary version of the Essential Medicines List and gathered feedback from the public on the following:

- + The criteria for inclusion of essential medicines, medical countermeasures, or their critical inputs in the Essential Medicines List
- + Suggested additions to the Essential Medicines List, including rationale for their inclusion
- + The frequency and process by which the list should be maintained

This appendix provides an overview of the input FDA received and the common themes from stakeholder feedback.

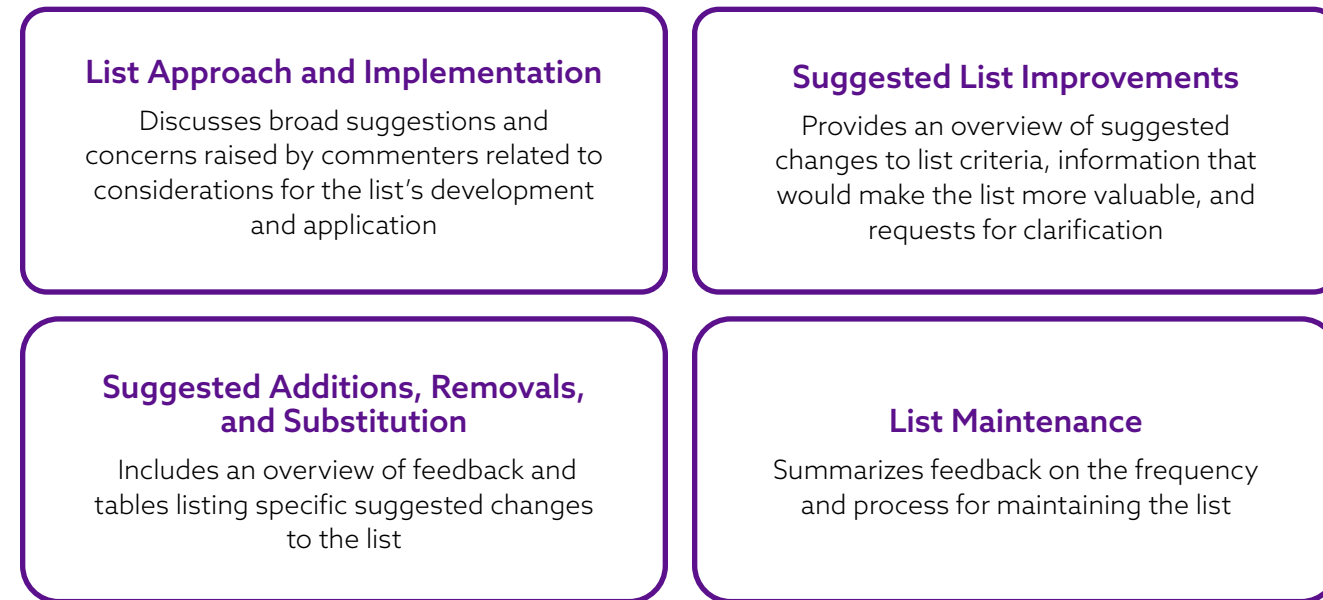
Comments by Stakeholder Type

COUNT, STAKEHOLDER TYPE

2	Academia
5	Professional Associations (e.g., professional, healthcare, or medical)
1	Researchers
1	Clinicians/Health Providers
15	Industry (e.g., pharmaceutical manufacturer, medical device manufacturer, consulting)
1	Non-profit Organizations
8	Individual or Affiliation Unknown
33	Total

Structure of Content

The stakeholder feedback is organized as follows:



List Approach and Implementation

Some stakeholders—particularly manufacturers—raised concerns that the supply chain of items in the Essential Medicines List could be disrupted in the short term by its implementation, due to the time- and resource-intensive process of onshoring manufacturing capabilities, as well as potential negative impacts on international trade. For instance, Sanofi suggested conducting a risk analysis and narrowing the list only to products with confirmed supply chain vulnerabilities for which the potential benefits of onshoring manufacturing would outweigh the risks. Other common concerns included potential issues with onshoring feasibility and the need to ensure that the list adequately covers the needs of vulnerable populations (e.g., children and the elderly). In addition, there were recommendations to leverage existing work done by industry to develop robust supply chains.

The major themes from stakeholder feedback and their supporting points are summarized below.

NARROWLY FOCUS THE LIST TO AVOID SUPPLY CHAIN DISRUPTION

- + Globally diversified supply chains are more resilient, and **many manufacturers of medicines have already established robust systems** to avoid major disruptions in their supply chains.
- + **The list should be narrowly tailored to foreign-manufactured products with specific quality or supply issues** warranting some degree of onshoring of their manufacture
- + Inclusion of items in the list should be based on **individualized risk analyses**, describing:
 - + Rationale for including a product on the list based on quality, supply, or shortage issues
 - + Analysis of the global and domestic supply chains
 - + Product-specific critical inputs, components, and other upstream or downstream operations or supplies that are within scope
 - + Risk that patients would be forced to switch to therapies that are less effective for them
- + **Stakeholders estimate that it would take 5–10 years and billions of dollars to develop and validate a new U.S. manufacturing facility**; sourcing restrictions adopted in the interim could be disruptive for patients and the health system and potentially make U.S. patients more vulnerable to drug shortages (Pfizer, PhRMA, Sanofi)

DESIGN LIST TO MINIMIZE DISRUPTION TO INTERNATIONAL TRADE

- + Because a significant share of pharmaceutical spending in non-U.S. markets is from direct government procurement, **retaliatory actions by U.S. trading partners could harm the competitiveness of American pharmaceutical companies**; this risk should be factored into the list design (Pfizer, PhRMA, Sanofi)
- + Before designing the prioritized list, FDA should consider the potential impact of each list item on **trade agreements, relationships with trading partners, and the costs and pricing of medical items** (Pfizer, PhRMA, Sanofi)

EXCLUDE PRODUCTS USED TO TREAT SYMPTOMS OF COVID-19 FROM THE LIST

- + Excluding medicines used to treat COVID-19 from the list would **help ensure continuity in supply of these critical products** (PhRMA, Pfizer, Sanofi)
- + The EO establishes a general exemption for items necessary to respond to a public health emergency, but **agencies have not yet established clear guidance on the application of this exception**; more time is needed to allow development of this guidance

IMPLEMENTATION FEASIBILITY CONCERNS

- + The EO does **not sufficiently consider the feasibility of producing the active pharmaceutical ingredients (APIs) and critical inputs (CIs)** included in their entirety in the United States. (EPCOT International, PhRMA)
- + FDA has not adequately addressed how it will handle the **sharing of highly sensitive information on API and CIs** with federal partners and others publicly. (EPCOT International, PhRMA)
- + It is likely that **many of the needed raw materials for APIs are not manufactured in the United States** and the necessary and adequate equipment and trained personnel may not be present. (EPCOT International, PhRMA)
- + Companies who opt to produce APIs in the United States may not have the needed processes to retain their margins while meeting **price constraints from Pharmacy Benefit Managers (PBMs)**. (EPCOT International, PhRMA)
- + **Some advanced manufacturing technologies have not yet been tested at a commercial scale** and may not be feasible. (EPCOT International, PhRMA)
- + The EO is likely to prompt many new FDA applications and submissions, which **may overburden the FDA and slow review and approval of new medicines**. (EPCOT International, PhRMA)

ENSURE VULNERABLE POPULATIONS ARE ADEQUATELY COVERED BY THE LIST

- + The current list does **not appear to fully address conditions common with older adults** or to consistently consider whether items in the list are inappropriate in older adults (e.g., diphenhydramine). (Center for Health Equity Research and Promotion [CHERP] and Geriatric Research and Education and Clinical Center [GRECC] at VA Pittsburgh Healthcare System/University of Pittsburgh)
- + There are opportunities to leverage existing essential medicine lists to **better target pediatric populations**. (Vizient)

Suggested List Improvements

Stakeholders offered various suggestions on ways to **enhance the selection criteria** and **make the list more useful and informative**. These suggestions are summarized below.

CRITERIA SUGGESTIONS

- + Include **medicines that may prevent morbidity and mortality of chronic and mental health conditions** (e.g., diabetes, hypertension, heart disease, cancer, asthma, and depression). (University of Southern California)
- + Include **preventative and emergency hormonal contraceptives**. (University of Southern California)
- + Avoid **duplicative essential medicines associated with serious adverse effects**. (University of Southern California)
- + Ensure the selected medicines are the **safest and most effective**. (University of Southern California)
- + Consider the availability of **long-term vascular access devices and technologies to place them in crisis situations**, including resuscitative medications, monitoring, dialysis, etc. (AngioDynamics)
- + Consider **care delivery models and technologies that keep patients out of common procedural areas** such as interventional radiology (IR). (AngioDynamics)
- + Consider additional factors such as **site of care and affected population** (e.g., pediatrics, oncology), clinical circumstance, number of available alternatives, and shortage vulnerability. (Healthcare Supply Chain Association)
- + Include products that **facilitate treatment of patients in private facilities** to help keep them out of hospital emergency rooms and reduce transmission risks. (American Association of Oral and Maxillofacial Surgeons)
- + **Consider adding items related to packaging**, which can impact quality and safety of a drug. (Corning Incorporated)

POTENTIAL FEATURES TO IMPROVE THE LIST'S USEFULNESS

- + **Add priority tiers**, as essential medicines may vary depending on emergency. (Health Care Association)
- + **Include information on the source and location of product manufacturing**; limited sources of API may suggest supply chain vulnerabilities. (Vizient)
- + Include information on **which products are interdependent**, and the situations in which they are **most likely to be utilized**. (Vizient)
- + Add information on the **quantities needed for each API**. (EPCOT International)
- + Consider **organizing categories alphabetically or by human body system** to aid navigation. (American College of Emergency Physicians)
- + **Add search functionality** within the list to allow users to locate medications more easily. (American College of Emergency Physicians)
- + The FDA should implement a process to **track whether the United States or specific regions develop shortages** of any essential medications and recommend appropriate solutions. (Health Care Association)

Suggested Additions, Removals, and Substitutions

The most common suggestions received on the Essential Medicines List were requests to add new products. The rationale for these suggestions most frequently focused on **major clinical care needs for high-impact diseases, conditions, or other healthcare priorities (e.g., trauma)**. In some cases, stakeholders suggested substitutions for existing list items based on factors such as cost or frequency of use. Several stakeholders also suggested removing specific groups of items from the list, such as those without confirmed supply chain vulnerabilities or products used for the treatment of COVID-19. The **List Approach and Implementation** section discusses these concerns in more detail.

The following tables list the suggested additions, removals, and other changes (e.g., substitutions) and their rationale.

SUGGESTED ADDITIONS

Drug or Drug Critical Input	Rationale	Source Comment
Allergy drugs: Nasal steroids (e.g., flunisolide) Fexofenadine	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Allopurinol (gout drug)	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Antibiotics: Cleocin (oral) Clindamycin (oral) Penicillin VK	Oral Cleocin is a first-line antibiotic agent for patients with penicillin allergies when treating severe head and neck odontogenic infections (rationale for other items not given).	American College of Emergency Physicians American Association of Oral and Maxillofacial Surgeons
Bone marrow transplant drugs: Busulfan Melphalan Fludarabine Immunosuppression drugs (tacrolimus and sirolimus)	Bone marrow transplant is a curative therapy for certain leukemias and cannot be delayed. We've already seen impacts that shortages of these medicines have in the recent past after Hurricane Maria hit Puerto Rico.	An individual clinician
Bovine Serum Albumin (BSA)	Critical input for essential drugs	American Regents, Inc.

Drug or Drug Critical Input	Rationale	Source Comment
Chemotherapy agents:		
Daunorubicin and cytarabine for treatment of adult acute myeloid leukemia (AML)		
Vincristine for acute lymphocytic leukemia (ALL) and other childhood leukemias	Should be included based on criteria of treatment for acute conditions inside the hospital Clinician	Children's Oncology Group An individual clinician
The medications listed in the Children's Oncology Group (COG) essential medicines list for children with cancer	Children's Oncology Group	
Constipation drugs:		
Polyethylene glycol Senna	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Coronary artery disease drugs:		
Statins (e.g., pravastatin) Isosorbide	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Depression drugs:		
Bupropion Citalopram	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Donepezil (dementia drug)	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Dopamine hydrochloride (blood pressure support)	Needed to maintain blood pressure of patients who are in shock	American Regent, Inc.

Drug or Drug Critical Input	Rationale	Source Comment
Ferrous sulfate (anemia medication)	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Glaucoma treatments:		
Latanoprost Other prostaglandin analogs	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Heart failure with reduced ejection fraction drugs:		
Angiotensin converting enzyme inhibitors (e.g., Lisinopril) Angiotensin receptor blockers (e.g., losartan)	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
HIV/AIDS drugs	Needed for treatment of a high-impact disease	American College of Emergency Physicians
Lamotrigine (seizure drug)	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Metformin (type 2 diabetes drug)	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Metoclopramide (antiemetic and gut motility stimulator)	None given	American College of Emergency Physicians
Neuropathic pain drugs:		
Gabapentin Tramadol	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh

Drug or Drug Critical Input	Rationale	Source Comment
Osteoporosis treatments: Alendronate Calcium Vitamin D	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Oxytocin (start/control labor and reduce bleeding)	None given	American College of Emergency Physicians
Packaging components for pharmaceuticals (e.g., glass vials)	Critical input for essential medicines; needed for secure storage, transport, and administration	Corning Incorporated
Pantoprazole (gastroesophageal reflux disease drug)	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Parkinson's Disease drugs: Levodopa Carbidopa	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Phenobarbital (anticonvulsant)	None given	An individual (affiliation unknown)
Prednisone , oral (polymyalgia rheumatica/temporal arteritis)	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Promethazine (antihistamine and antiemetic)	None given	American College of Emergency Physicians
Remdesivir/Veklury (COVID-19 treatment)	While we do not have final conclusive evidence of its utility in SARS-CoV2 infection, we are using this antiviral under an Emergency Use Authorization (EUA), and it initially appears to show some benefit.	An individual clinician

Drug or Drug Critical Input	Rationale	Source Comment
Salsalate (osteoarthritis drug)	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Sodium azide	Key critical building block for essential medicines (e.g., Sartans, antimicrobials, and antihistamines containing tetrazole rings) with supply chain concerns due to offshoring to China	American Pacific AMPAC Fine Chemicals
Supplements: Pyridoxine (Vitamin B6) Potassium Phosphate Tralement Calcium chloride (alternative to calcium gluconate) Magnesium chloride (alternative to magnesium sulfate) Potassium acetate (alternative to potassium chloride)	Important for providing electrolyte additives in critical care and parenteral nutrition support for patients on ventilators	American Regent, Inc.
Tolterodine (incontinence drug)	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh
Tranexamic acid (clotting promoter)	Carried by military medics for treatment of severe bleeding and should be available in the event of a terrorist attack	American Regent Inc. American College of Emergency Physicians
Urinary tract symptom treatments: Finasteride Tamsulosin	Intended to address chronic conditions experienced by older adults	CHERP and GRECC at VA Pittsburgh Healthcare System and the University of Pittsburgh

Drug or Drug Critical Input	Rationale	Source Comment
Vaccines: Tdap, MMR All other essential childhood vaccines	Essential to promote public health	American College of Emergency Physicians
Xylocaine, carpule (anesthetic)	Relied on in dental emergencies to provide targeted local anesthetic blocks	American Association of Oral and Maxillofacial Surgeons
Respiratory therapy supplies: Flexible inhalation bags Sterile water	None given	Healthcare Supply Chain Association
Tubing for IV medicines and their pumps	This may be intended to be included under "MRZ Accessories, Pump, Infusion," but should potentially be made explicit.	An individual (affiliation unknown)

Device or Device Critical Input	Rationale	Source Comment
Diagnostic testing consumables: Sample Collection: screw cap tubes, nasal and nasopharyngeal swabs Sample Preparation: filtered pipette tips, storage blocks, microcentrifuge tubes Sample Analysis: PCR plates, PCR tubes	Needed for rapid development and processing of diagnostic tests	Corning Incorporated
Kaolin-based hemostatic devices (e.g., QuikClot)	Hemorrhage is the most common cause of preventable death in trauma patients.	Z-Medica, LLC.
High Flow Nasal Cannula (HFNC) systems	Important alternative form of respiratory support for patients critically ill with COVID-19	Vapotherm, Inc.
Nitrile Latex raw material supply	A critical input for polymer patient examination gloves (LZA). None of the raw materials needed to produce any of the listed glove devices, other than the OPC and OIG items, are made in the United States, and the OPC and OIG items also have domestic supply concerns.	American Performance Polymers

SUGGESTED REMOVALS, REPLACEMENTS, AND OTHER CHANGES

Product	Suggested Change	Rationale	Source Comment
Andexanet alfa (anticoagulation reversal agent)	Remove from list Replace with four-factor prothrombin complex concentrate (4F-PCC) (Kcentra)	The trials leading to its approval were based on surrogate endpoints, sponsored by the manufacturer, and did not include data on patient outcomes. It is also expensive (\$30,000-\$50,000 per dose). 4F-PCC (Kcentra) is preferentially used by many health systems for both cost and efficacy reasons.	American College of Emergency Physicians An individual clinician
Doxycycline (antibiotic)	Add to additional applicable categories	Doxycycline can be used in cases of bioterrorism as well as endemic treatment of pneumonic tularemia.	American College of Emergency Physicians
Mannitol (diuretic)	Recategorize from Antihypertensive/ Cardiovascular based on most common use cases	While the medication can have effects on blood pressure, that is not typically its intended use.	American College of Emergency Physicians
Nitroprusside (antihypertensive infusion)	Replace with Nicardipine	Nicardipine is used more regularly.	American College of Emergency Physicians
Potassium iodide (radioactive iodide poisoning treatment)	Consider replacing with an alternative such as perchlorate	Potassium iodide has a very narrow therapeutic window for treatment in the aftermath of a nuclear event. Also, many people have adverse drug reactions and dosing for children is difficult to gauge based on age.	An individual clinician
Rabies Immunoglobulin and rabies vaccine	Group these items together	These related items are currently in different areas.	American College of Emergency Physicians
Sanofi products	Consider removing all products manufactured by Sanofi	These products are supplied via demonstrably robust and secure supply chains, even during the COVID 19 pandemic, that do not implicate the risks or concerns cited in the EO.	Sanofi
Selenium (supplement)	Recategorize to Drug Category: Additives	Selenium was FDA approved on April 30, 2019. The NDA number is 209379, the NDC# is 0517-6560-05.	American Regent, Inc.
Tigecycline/ TYGAGIL (antibiotic)	Consider recategorization or removal	This is not a COVID-19 specific agent and has a black box warning of increased mortality. It should be used only when other antibiotics are ineffective.	An individual clinician

Product	Suggested Change, Rationale, Source Comment
COVID-19 Treatments	
Anticoagulant: Heparin	
Antimicrobials: Amikacin, Ampicillin, Azithromycin, Cefepime, Ceftazidime, Ceftriaxone, Clindamycin, Fluconazole, Linezolid, Levofloxacin, Meropenem, Piperacillin/Tazobactam, Penicillin G, Trimethoprim/Sulfamethoxazole, Voriconazole	
Analgesics: Fentanyl	
Gastrointestinal Agent: Pantoprazole	
Paralytics: Cisatracurium, Rocuronium	
Sedatives: Dexmedetomidine, Ketamine, Midazolam, Propofol	
Steroids: Hydrocortisone, Methylprednisolone	
Vasopressors: Epinephrine, Norepinephrine	
Volume Expanders: Dextrose 5% Water, Sodium Chloride 0.45%, Sodium Chloride 0.9%	
Additives: Magnesium Sulfate, Potassium Chloride	
	<p>Products used to treat symptoms of COVID-19 should be excluded from the list</p> <p>Removing these items from the initial list will ensure that implementation of the policy does not interfere with supply of these critical products and will allow agencies time to establish clear guidance on the application of the exception set forth in the EO for products necessary to respond to a federally declared national emergency (such as the COVID-19 pandemic). This will minimize disruption, ensure a consistent approach to the exception's application in any future national emergency, and reduce the impact of retaliation overseas on U.S. manufacturing.</p> <p>Pfizer</p>

List Maintenance

Stakeholders suggested that updates to the Essential Medicine List should be transparent, predictable, and allow industry time to adjust. Specific approach suggestions included publishing draft versions in the Federal Register consistent with the Administrative Procedures Act and ensuring that revisions are open to public comment.

REVIEW TIMING

Recommended Timing	Related Comment	Source Comment
Every 5 Years	Conduct a comprehensive review of the list every five years to include new, critical medications.	American College of Emergency Physicians
Every 2 Years	A 2-year cycle is used for the World Health Organization (WHO)'s Essential Medicine List. A longer update cycle will mitigate regulatory burdens for stakeholders and help manufacturers with products on the list maintain manufacturing cycle stability and continue to manufacture products in the United States to ensure an ongoing and reliable supply. Since the list is going to be the foundation of other policies across the government, frequent deletions from the list would have a regulatory ripple effect.	Pfizer
Semi-annually	Allow stakeholders to review the list every 6 months through the notice-and-comment rulemaking process	American Association of Oral and Maxillofacial Surgeons
Semi-annually or Quarterly	FDA should update its list on a semi-annual basis at minimum and on a quarterly basis, when possible.	Healthcare Supply Chain Association
Add items quarterly, Remove every 2 years	Products should be added to the list on a quarterly basis, as needed, but only be reviewed and deleted from the list once every two years.	American Regent, Inc.
Add items quarterly, Remove every 5 years	It should be possible to add medicines to the list on a quarterly basis, but a medicine should not be removed from the list sooner than five years after being included on the list.	Association for Accessible Medicines

