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September 7, 2023

Advancing Federal Coordination to Address Drug Shortages

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ACKNOWLEDGEMENTS

The Duke-Margolis Drug Supply Chain Resilience and Advanced Manufacturing Consortium consists of a group of experts in supply chain, manufacturing, regulatory science, national security, and drug shortages from academia, private industry, governmental agencies, and additional relevant stakeholder groups. The Consortium's mission is to identify effective policy solutions that promote a resilient drug supply chain with advanced manufacturing capabilities and, ultimately, reduce the frequency and severity of drug shortages.

The recommendations and analysis in this white paper represent the thinking of Duke-Margolis researchers, which has been informed by Consortium activities and the expertise of its members. As part of Duke University, Duke-Margolis honors the tradition of academic independence on the part of its faculty, researchers, and scholars. Neither Duke nor the Duke-Margolis Center takes partisan positions, but the individual researchers are free to speak their minds and express their opinions regarding important and pertinent issues. This white paper may not represent the opinions of every Consortium member. This publication is not intended to limit the ability of Consortium members to provide their own comments on behalf of their independent organizations.

DISCLOSURES

Mark B. McClellan, MD, PhD, is an independent director on the boards of Johnson & Johnson, Cigna, Alignment Healthcare, and PrognomIQ; co-chairs the Guiding Committee for the Health Care Payment Learning and Action Network; and receives fees for serving as an advisor for Arsenal Capital Partners, Blackstone Life Sciences, and MITRE.

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About the Duke-Margolis Center for Health Policy

The Robert J. Margolis, MD, Center for Health Policy at Duke University is directed by Mark McClellan, MD, PhD, and brings together expertise from the Washington, DC, policy community, Duke University, and Duke Health to address the most pressing issues in health policy. The Center's mission is to improve health, health equity, and the value of health care by developing and implementing evidence-based policy solutions locally, nationally, and globally. For more information, visit healthpolicy.duke.edu.

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EXECUTIVE SUMMARY

A crisis in the drug supply chain is increasingly affecting patients and creating shortages of life-saving and life-sustaining medications in the American health care system. A past shortage of norepinephrine, a drug used to treat septic shock, was estimated to cause hundreds of deaths or more. Alarmingly, some pediatric cancer patients have been forced to delay life-saving care during oncology drug shortages. Providers are left to ration medications that have been the standard of care for years. Staff needlessly dedicate countless hours and dollars to finding treatment alternatives, which may be less effective for patients or unavailable. Every health system, hospital, and patient may be at risk due to this chronic, systemic issue.

This white paper details the root causes of drug shortages in the U.S., highlights new and ongoing federal government efforts to prevent and mitigate drug shortages, and identifies gaps in those efforts. The white paper then proposes the establishment of a new cross-cutting **Prevent Drug Shortages (PDS) Initiative** to coordinate and expand upon the federal government's approach to address drug shortages.

The leading cause of drug shortages is manufacturing quality issues (see **Appendix A** for working definitions of product quality, quality management maturity, and supply chain reliability, along with potential next steps to improve quality management maturity and supply chain reliability). Drug payment policies and limited transparency into manufacturers' supply chains means purchasers choose manufacturers largely based on lowest price, which creates adverse market incentives for manufacturers to keep costs down even at the expense of needed investments in supply chain reliability. These issues are particularly challenging for generic manufacturers, which often operate on slim profit margins compared to branded manufacturers and have limited incentives to invest in their supply chains. Intense competitive pressure for low prices in generic drugs also contributes to significant offshoring of manufacturing to countries where the cost of production may be lower.

A wide range of governmental and non-governmental efforts aim to mitigate or prevent drug shortages. The U.S. Food and Drug Administration (FDA), Administration for Strategic Preparedness and Response (ASPR), White House Office of Science and Technology Policy (OSTP), Department of Defense (DOD), and Department of Commerce (DOC) all oversee various offices or programs intended to address drug shortages from various angles--supporting innovative manufacturing methods, stockpiling certain medicines, promoting onshoring of manufacturing, and more. Non-governmental organizations also have undertaken productive efforts to improve manufacturing processes, reshape contracting practices, and introduce more transparency into drug supply chains.

While these various efforts are commendable and have attempted to reduce the frequency and severity of drug shortages, significant strategic and tactical gaps persist that should be filled by new efforts, and further strategic planning and coordination could increase the impact of existing programs and initiatives. The numerous relevant federal government strategies and plans issued rarely incorporate Specific, Measurable, Achievable, Relevant, and Timebound (SMART) goals or identify accountable government entities with the authorities, funding, and expertise needed to accomplish such goals.

RECOMMENDATIONS

We recommend that the Administration and Congress take urgent action to establish a new coordinating effort, the Prevent Drug Shortages Initiative, with requisite authorities and funding to lead a cross-cutting effort to improve drug supply chain reliability, including producing measurable reductions in the frequency and severity of shortages of critical drugs, bringing together relevant federal agencies and private-sector entities, establishing SMART goals, and addressing the following four Tactical Gaps and Policy Priorities:

1. **The federal government, in collaboration with the private sector, should support development and implementation of tools that measure supply chain reliability, including quality management maturity, for drugs at high risk of shortages.** A system-wide lack of supply chain reliability insights makes it difficult to assess supply chain vulnerabilities and leaves purchasers to choose suppliers primarily based on price, not reliability of supply chains. The PDS Initiative should lead a cross-cutting government effort to develop and implement a robust toolkit of actionable supply chain reliability measures, including measures of quality management maturity, that are readily available to purchasers, manufacturers, and other stakeholders and enable accurate evaluation of suppliers' reliability and appropriately value and encourage the use of products with reliable supply chains.

2. **The federal government should provide well-targeted incentives and support purchasing approaches that increase supply chain reliability.** Current payment structures incentivize health care institutions to choose lower-cost drugs without regard for manufacturers' supply chain reliability, which in turn incentivizes manufacturers to keep costs low even at the expense of needed investments in their supply chains. The PDS Initiative should include participation by the Centers for Medicare & Medicaid Services (CMS), along with other federal agencies and private payers, to explore further steps to encourage health care institutions to identify and contract with more reliable suppliers for drugs at high risk of shortage.

3. **The PDS Initiative should be the keeper of fit-for-purpose lists of medicines used to guide policy and private-sector efforts regarding manufacturing and supply chain reforms to prevent drug shortages.** The PDS Initiative should be tasked with compiling useful existing lists and incorporating additional lists based on different methodologies as needed to ensure policies intended to reduce drug shortages can be targeted toward sets of products for which policy interventions will be most impactful.

4. **The federal government should pursue a proactive, coordinated focus on preventing the most impactful drug shortages, regardless of the cause.** Current governmental efforts focus on mitigating supply-driven shortages after they are imminent, along with working to ensure a reliable supply of public health emergency products and medical countermeasures that experience spikes in demand. The PDS Initiative would ensure adequate, proactive focus on addressing economic and other issues to prevent supply-driven, chronic drug shortages.

The PDS Initiative could be established within one of the several agencies within the Department of Health and Human Services (HHS) already working on supply chain reliability and drug shortage issues, as a new office reporting directly to the HHS Secretary, or into the White House. Regardless of where the PDS Initiative is housed, it should be granted authorities and resources commensurate with the scale and scope of the challenges it will be asked to address.

PROPOSED LEGISLATIVE ACTION

This white paper identifies a number of administrative actions that can and should be undertaken within current law to begin to address major causes of chronic drug shortages. In addition, further legislation focused specifically on drug shortages is needed to advance necessary changes in CMS payment policy, bolster U.S. manufacturing and supply chain capabilities, or some combination of these and other factors.

- As proposed above, Congress should authorize and provide funding to staff and implement the proposed Prevent Drug Shortages Initiative (PDS), with an initial focus on reducing chronic drug shortages.

- Congress should support ASPR coordination and other HHS actions to improve a reliable supply of drugs that are both needed in a public health emergency but also used outside of an emergency and provide appropriate funding for these actions.

- Congress should appropriate the funds requested by ASPR's Industrial Base Management and Supply Chain office (IBMSC) office in the President Biden's FY24 budget.

- Congress should appropriate additional funding to develop and implement FDA's Quality Management Maturity (QMM) program or a similar program, either stood up through FDA or through an independent third party with significant FDA participation.

- The Administration and Congress should develop CMS policy reforms to support more reliable drug supply chains for essential medicines at high risk of shortages, and Congress should provide legislative support for relevant payment changes.

INTRODUCTION

The U.S. needs more reliable drug supply chains to prevent, mitigate, and recover from shortages of life-saving and life-sustaining medications and be prepared for national security threats, public health emergencies, manufacturing quality issues, natural disasters, and other systemic threats and vulnerabilities.

Failures in the drug supply chain have led to critical shortages of essential medicines. Over the past decade, numerous drugs have gone into shortage each year, and as of June 2023, more than 130 drugs are listed as in shortage by FDA. These essential medicines in shortage mainly consist of relatively inexpensive, generic (non-patented) drugs, including many injectable formulations. Research and public attention increasingly indicate that the shortages are affecting a significant proportion of American patients--for example, more than 90 percent of cancer centers may be affected by current oncology drug shortages. Drugs in shortage as of June 2023 also included 50 central nervous system agents (a drug category that includes anesthetics, analgesics, and other widely used medications) and more than 40 antimicrobial drugs.

The impact on patients from drug shortages is broad and far-reaching. A past shortage of norepinephrine, a drug used to treat septic shock, was estimated to cause hundreds of deaths or more. Alarmingly, some pediatric cancer patients have been forced to delay life-saving care during oncology drug shortages. Providers are left to ration medications that have been the standard of care for years. Staff needlessly dedicate countless hours and dollars to finding treatment alternatives, which may be less effective for patients or unavailable. Every health system, hospital, and patient may be at risk due to this chronic, systemic issue.

With programs well targeted to root causes, drug shortages can be relatively inexpensive to resolve. To address these critical drug shortage issues, Duke-Margolis earlier this year launched a new Drug Supply Chain Resilience and Advanced Manufacturing Consortium, which consists of a group of experts in supply chain, manufacturing, regulatory science, national security, and drug shortages from academia, private industry, non-profit organizations, and governmental agencies. The mission of the Consortium is to identify effective policy solutions that promote a reliable drug supply chain with advanced manufacturing capabilities and reduce the frequency and severity of drug shortages.

As we describe below, through our work with the Consortium, we have identified a set of coordinated federal policies for both immediate and sustained action to address the lack of reliability in drug supply chains and help prevent drug shortages.

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Most drugs that experience frequent shortages are relatively inexpensive products that typically sell for only a few dollars per dose, and well-designed and coordinated steps to achieve a reliable supply of those drugs would only add incrementally to that price. For example, the Brookings Institution recently estimated that additional payments of about $3 billion per year would be sufficient to achieve a reliable supply of most essential medicines. While not a trivial amount, $3 billion in additional spending per year only amounts to about 0.5 percent of US prescription drug spending and 2 percent of US physician-administered drug spending. The benefits and cost savings of ensuring American patients have a stable supply of life-sustaining and life-saving drugs--leading to fewer delays in treatment and suboptimal treatment, and in turn, better outcomes and fewer costly disease complications--are substantial relative to the incremental cost needed to support reliable drug supply chains.

The Administration and Congress should act now to create a new, coordinated, and sustained federal initiative that changes the market dynamics that drive chronic drug shortages, in addition to continuing existing efforts to respond to and mitigate shortages on a case-by-case basis.

Root Causes of Drug Shortages

Though federal efforts have helped mitigate or avert some shortages, the root causes remain and are very likely to continue to cause shortages until they are addressed. While the causes of supply chain instability are complex, the following four factors are the leading contributors:

- **Quality Issues are the Single Largest Driver of Drug Shortages**

  Quality issues in manufacturing are the single largest driver of drug shortages, responsible for 62 percent of shortages between 2013-2017. These issues are more prevalent for older, less expensive drugs whose manufacturers operate on slim profit margins relative to manufacturers of newer, branded drugs. These margins may limit investments in reliable manufacturing processes--particularly for older generic sterile injectable drugs, for which manufacturing processes are relatively expensive, complex, and demanding.

A Note on Quality

Different stakeholders intend different meanings when they use the term "quality." The "quality issues" that cause most drug shortages stem from low levels of quality management maturity. If manufacturing processes are identified as not being up to quality standards, production delays may occur while the manufacturer works to resolve the identified issues. Manufacturers with low levels of quality management maturity might also produce drug product that does not meet quality standards and thus is not released into the market, again potentially resulting in a shortfall of supply. Higher levels of quality management maturity can avoid these situations and prevent drug shortages. For clarity, we include our working definitions of product quality, quality management maturity, and supply chain reliability in **Appendix A**. We also note the current state of each of these terms and potential next steps/improvements that the PDS Initiative can lead.

- **Adverse Market Incentives Contribute to Inconsistent Quality and Other Risks**

  Rising health care cost pressures, current payment methodologies, and other factors increase incentives to seek the lowest short-term price in the market for these complex generic drugs, in turn discouraging manufacturers from making needed investments to maintain a reliable supply chain and even leading them to discontinue production in some cases. The previously mentioned Brookings Institution publication describes the lack of incentives for providers, purchasers, and manufacturers to ensure supply chain reliability. Notable exceptions exist, but because purchasers are often unable to sufficiently assess reliability and sustained quality in their contracts for these drugs, manufacturers see little return on investments in the increased reliability that could be achieved through equipment upgrades (including but not limited to adoption of advanced manufacturing technologies), supply chain redundancies, quality management maturity investments, and other risk mitigation steps.

- **Increased Geographic Concentration of Manufacturing Creates Further Risks**

  Incentives for low-cost generic production may contribute to outsourcing of manufacturing to a concentrated group of foreign countries. Another contributing factor is the challenge of locating such production facilities within the U.S. due to environmental concerns and domestic regulatory standards associated with manufacturing involving petrochemicals, as required for many active pharmaceutical ingredients. Increasing foreign manufacturing concentration intensifies geopolitical and trade vulnerabilities. FDA also faces challenges in conducting unannounced inspections at facilities located in some foreign countries compared to inspections at domestic facilities. As of March 2021, 63 percent of FDF (finished dosage form) facilities for generic drugs and 87 percent of facilities making active pharmaceutical ingredients (API) for generic drugs were located outside the U.S. Manufacturing of certain types of pharmaceutical products has become concentrated in China and India, where facilities have had slightly

lower percentages of "acceptable final outcomes" in FDA inspections. Offshoring of manufacturing, and concentration in India and China, has been steadily ongoing since at least 2000.

- **Market Conditions and Limited Transparency Complicate Assessing and Addressing Risks to Reliable Manufacturing**

  An important contributor to purchasing behaviors that lead to shortages for these drugs is that public and private stakeholders generally do not have a clear and comprehensive view of the *reliability* of the entire supply chain for a drug, from key starting materials (KSM), to API, to FDF, to distribution and use. Federal agencies like FDA lack sufficient visibility into upstream aspects of supply chains, such as KSM production, and downstream aspects, such as inventory levels at health care institutions, making it difficult to assess risks of disruptions that result in shortages. In addition, when FDA finds manufacturing compliance issues, affected production lines and drug product lots are often prohibited from being marketed. While this regulatory approach helps to assure safety (akin to flight safety inspections that do not allow flights to proceed if safety or quality issues are identified), it does not assure reliability. Implementation of FDA's Quality Management Maturity (QMM) program has been recommended by an FDA Advisory Committee and others to provide insight to purchasers, manufacturers, and other stakeholders about manufacturers' ability to have consistent, reliable, continually-improving processes that go above and beyond basic CGMP compliance, which could in turn help promote purchasing decisions that better account for reliability. However, FDA has not received dedicated funding for a QMM program, and there is further work yet to be done on several areas of the program.

While some manufacturers have invested more in reliable manufacturing, provided their customers with more transparency, and entered into more sustainable contracts with incrementally higher prices or a greater degree of commitment from providers alongside assurances of more reliable supply, purchasers still face challenges with obtaining transparent, standardized supply chain data. As a result, the default approach is often to prioritize lower prices over reliability. Purchasers also may not devote enough resources to identify potential risks in the supply chains of manufacturers from which they purchase drugs, and manufacturers may be unlikely to disclose sufficient information voluntarily.

Together, these factors have led to pharmaceutical supply chains that are fragile to demand-side and supply-side shocks, resulting in frequent and severe shortages of a growing number of life-saving and life-sustaining medications. In the remainder of this white paper, we review existing federal efforts to reduce drug shortages, highlight persistent gaps in those efforts, and propose policy actions for a coordinated and sustained federal effort to support needed changes in manufacturing reliability--and in drug purchasing to sustain these manufacturing reforms--to achieve more reliable supply chains and avoid drug shortages.

Overview of Ongoing Drug Supply Chain Reliability Programs and Initiatives

In recent years, the federal government has taken many steps to counteract drug supply chain threats and shore up vulnerabilities, including the development of several emerging new programs spearheaded by various agencies. Each of these programs represents a potential piece needed to solve the drug shortage solution puzzle. See the Glossary in **Appendix C** for a more comprehensive overview of all listed federal programs.

- **U.S. Food and Drug Administration**

  Using its regulatory authority, FDA works to prevent, mitigate, and help resolve drug shortages by working with manufacturers of drugs in short supply as well as provider and patient groups that may be affected by shortages. FDA Center for Drug Evaluation and Research (CDER)'s Drug Shortage Staff (DSS), QMM pilot program, Emerging Technologies Program (ETP), and Framework

for Regulatory Advanced Manufacturing Evaluation (FRAME) Initiative; together with FDA Center for Biologics Evaluation and Research (CBER)'s Advanced Technologies Team (CATT), and the National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing, and Advanced Manufacturing Technologies Designation Program, all seek or will seek to reduce or prevent drug shortages, among other aims.

In its work to prevent, mitigate, and help resolve drug shortages, the DSS solicits manufacturer reports of supply disruptions and notifies other manufacturers of those products when a shortage is anticipated in an effort to increase supply and avoid a shortage. The DSS also collects and compiles data on shortages and averted shortages, which shows FDA helped to prevent over 200 drug shortages each year in 2021 and 2022.

Other FDA initiatives and programs aim to encourage the adoption of advanced manufacturing technologies, which can increase manufacturing agility, enabling more rapid ramp-up in production if demand spikes, easier changeovers from manufacturing one product to the next, and more efficient, less wasteful production processes with lower unit costs. Advanced manufacturing also can enable improved measurement and monitoring of products as they are manufactured, along with better control over product quality, reducing the cost of more reliable manufacturing. The control systems and associated data also can enable easier identification of manufacturers that are sustaining high quality standards over time. The ETP and CATT provide avenues for drug manufacturers to meet with FDA to discuss advanced manufacturing approaches. These meetings can offer manufacturers greater clarity on FDA's expectations for a submission of a new drug that could be manufactured using advanced manufacturing and offer FDA staff an opportunity to gain familiarity with new manufacturing technologies and approaches, reducing the uncertainty associated with these manufacturing improvements.

These programs have generated engagement and led to some adoption of advanced manufacturing technologies. FDA has approved 19 drug applications using advanced manufacturing technologies since 2015, and CATT received 28 meeting requests and program inquiries between January and May of 2023. However, applications using advanced manufacturing still represent a small proportion of FDA approvals – CDER has in total approved several hundred novel drug applications since 2015. Uptake has been even lower among generic manufacturers, where smaller profit margins and less assurance of demand make it difficult for them to invest in long-term manufacturing upgrade projects.

- **Administration for Strategic Preparedness and Response**

ASPR has long been involved in securing the supply of medical countermeasures and pandemic-related medicines through programs such as the Strategic National Stockpile (SNS) and the Biomedical Advanced Research and Development Authority (BARDA). During the COVID-19 pandemic, ASPR expanded the mission of the SNS to include medical products needed for infectious disease response, rather than its previous focus solely on emergencies such as natural disasters and bioterrorism events.

A number of other ASPR initiatives have expanded or launched to tackle supply chain issues more comprehensively. New funding linked to the COVID-19 response enabled new ASPR efforts, such as the HHS Coordination Operations and Response Element (H-CORE), Supply Chain Control Tower (SCCT), and the Industrial Base Management and Supply Chain office (IBMSC). The primary focus of ASPR during the response to COVID-19 has been to ensure sufficient supply of therapeutics and other products used to treat the virus, as well as medical countermeasures, based on projections of supply and demand. The IBMSC manages Defense Production Act-related activities. Though the IBMSC has thus far remained focused on personal protective equipment (PPE), diagnostics, and domestic manufacturing for certain critical drug substances and drug products, the formal mission of the office is to expand, secure, and build resilience across the entire public health and medical industrial base. Notably, products that may experience demand-driven shortages during public health emergencies may also experience supply-driven issues outside of emergencies, for example, generic sterile injectable painkillers and anesthetics. During the pandemic, BARDA also issued a contract to Phlow and Civica Rx for domestic manufacturing of essential generic APIs and finished dosage forms.

- **Other Governmental Initiatives**

Other federal agencies, departments, and offices with some involvement in these issues include the OSTP, DOD, and DOC. Each of these entities has conducted efforts to promote supply chain reliability across various sectors,

based on their respective missions and authorities, sometimes including drugs and medical products. For example, OSTP is responsible for implementing the Bold Goals for U.S. Biotechnology and Biomanufacturing, which spans several industries and agencies but has important provisions related to assessing drug supply chain vulnerabilities and increasing production capacity for API.

- **Non-Governmental Initiatives**

An increasing number of efforts outside of government directly aim to provide a more reliable drug supply by supporting reliable manufacturing and resilient supply chains. For example, Civica Rx, a non-profit generic drug company founded by a coalition of health systems and private foundations, is focused on using a committed contracting model to provide participating health systems with a more reliable supply of essential generic medicines that have historically experienced chronic shortages. The health systems and Civica Rx use committed, long-term contracting models to support Civica Rx's investments in more robust supply chains and manufacturing processes, enabling Civica Rx to provide assurance of supply to the customer, with meaningful adverse financial consequences if either party does not fulfill their longer-term commitment. This model has the potential to materially reduce the likelihood of drug shortages. Drug purchasers (as defined in **Appendix B**) also have implemented new committed contracting models that are designed to reduce drug shortages. Hospital group purchasing organization (GPO) committed contracting models, including HealthTrust's SIMS, Premier's ProvideGx, and Vizient's Novaplus Enhanced Supply, all have been implemented within the past few years and entail varying levels of supply and demand commitments. However, significant opportunity exists to increase participation in these programs, as most hospitals do not participate in such programs or only purchase a small amount of volume through them. For example, Civica Rx accounts for well under 10 percent of generic sterile injectable drug sales. In addition, less than 15 percent of HealthTrust members' generic injectable purchases went through their SIMS committed contracting program from July 2022 through June 2023.

Other non-governmental efforts aim to provide more transparency and predictability in pharmaceutical supply. US Pharmacopeia's (USP) Medicine Supply Map, which leverages more than 40 different datasets, including insights derived from the use of USP quality standards spanning 92 percent of generic medicines approved in the U.S., aims to map the pharmaceutical supply chain and predict drug shortages. The Resilient Drug Supply Project (RDSP) at the University of Minnesota is focused on mapping supply chains for each drug and creating a platform to assess root causes for critical supply failures.

The pharmaceutical manufacturing industry has taken voluntary steps to further quality management maturity. The International Society for Pharmaceutical Engineering's (ISPE) Advancing Pharmaceutical Quality (APQ) program is a voluntary, industry-led program through which manufacturers can assess and advance their level of quality management maturity and share it independently with their patients, consumers, customers, and health authorities globally. The APQ Program entails quality system assessment, performance measures, improvement tools for advancement, and case studies for robust application. The program was initially piloted in several iterations between 2014 and 2016, and the data and findings from the pilot stages were made public in a series of reports.

Pharmaceutical manufacturers have increasingly begun to use innovative manufacturing technologies, such as continuous manufacturing techniques and real-time monitoring and release, to improve production flexibility and reduce production downtime. The API Innovation Center, a non-profit public benefit corporation, is working to create a reliable, market-competitive domestic supply of API for essential and critical medicines using advanced manufacturing technologies.

Several notable collaborative organizations are working to advance other solutions as well. The End Drug Shortages Alliance (EDSA) and the Healthcare Industry Resilience Collaborative (HIRC) were founded in 2021 by a broad set of industry stakeholders seeking to reimagine medical supply chains. While EDSA focuses on pharmaceutical availability and HIRC focuses on medical supplies and medical device availability, both organizations take similar approaches around best practice sharing, standards development, supply chain research, and improved transparency and communication. EDSA has assembled a rapid response team to publish transparent data that can assist in mitigating the impact of disruptive events such as the Akorn bankruptcy and Rocky Mount tornado. HIRC recently announced the launch of a Resiliency Badging initiative which establishes a standardized and evidence-based assessment to equip manufacturers to better compete on the merits of reliability. EDSA and HIRC have hundreds of member companies between them, including many of the largest pharmaceutical

and medical product manufacturers, group purchasing organizations, wholesalers, providers, and other industry stakeholders. Securing America's Medicines and Supply (SAMS) is another coalition of industry stakeholders, focused more specifically on ensuring a secure domestic supply of medicines through policy action. The National Institute for Pharmaceutical Technology and Education (NIPTE), a non-profit academic organization consisting of 18 universities, is addressing supply chain issues by developing new advanced and continuous manufacturing technologies for domestic industrial adaptation. Notably, two of its pharmaceutical manufacturing research centers, the Center for Structured Organic Particulate Systems (C-SOPS; Rutgers University) and Medicines for All Institute (Virginia Commonwealth University), have been developing such technologies for both drug products and drug substances, respectively, for a long time. Recognizing that implementation of advanced technologies requires an adequately trained industrial workforce, NIPTE has recently initiated the Industrial Consortium for Workforce Development to develop training programs collaboratively with industry.

Through interactions with hundreds of relevant stakeholders, particularly Drug Supply Chain Resilience and Advanced Manufacturing Consortium members, Duke-Margolis has identified several Strategic Gaps and Tactical Gaps in the federal government's efforts to promote and sustain reliable drug supply chains and manufacturing to prevent drug shortages

These governmental and non-governmental initiatives are positive steps that demonstrate progress toward addressing critical shortages. However, much of the federal government approach thus far is siloed, not comprehensive and sometimes duplicative, with each listed federal program only tackling a part of the drug supply chain reliability problem within its existing authorities and resources, reflecting the complex, multifaceted nature of the issues. Many of the federal programs have multifaceted aims and increasing drug supply chain reliability is not always the primary focus. In some cases, the programs' aims and responsibilities overlap, leading to potentially redundant efforts. Finally, the programs mainly provide supply-side incentives with a lack of requisite focus on demand-side incentives.

Some of the private-sector initiatives focus more directly on best manufacturing and supply chain practices for avoiding drug shortages without adding excessive costs, and on providing direct and predictable financial supports for such practices (for example, through longer-term contracts that reward reliability over time, not just safe manufacturing at a point in time). But these programs have not yet been applied to much of the current supply, manufacturing, and contracting for generic drugs that are frequently in shortage.

A pressing need exists for leadership of a coordinated, cross-cutting effort to best determine how these various pieces fit together and address remaining gaps, particularly in widespread uptake of needed reforms. Through interactions with hundreds of relevant stakeholders, particularly Drug Supply Chain Resilience and Advanced Manufacturing Consortium members, Duke-Margolis has identified several **Strategic Gaps** and **Tactical Gaps** in the federal government's efforts to promote and sustain reliable drug supply chains and manufacturing to prevent drug shortages. Further action is needed to achieve sustainable reforms in supply chains and manufacturing of essential drugs that are prone to shortages. Policymakers have increasingly recognized the urgency of these issues over the past several years, and it is critical that momentum doesn't fade. Making meaningful progress in reducing drug shortages will require ongoing focus and additional resources commensurate with the task at hand.

Strategic Gaps in Federal Government Approach

Several national strategies and plans have been created to help improve the reliability of U.S. drug supply chains (see **Glossary in Appendix C** for more details). However, the strategies lack specific focus on drug supply chains because of their multifaceted aims. The complexities and challenges unique to pharmaceutical manufacturing, most notably potentially severe public health impacts, may not be adequately addressed with strategies that consider

supply chains for a broader range of products rather than focusing on pharmaceuticals. The strategies often lack specific metrics for success and do not identify specific parties to be accountable for implementation. While aiming to reduce quality-related drug shortages or increase the usage of advanced manufacturing technologies are, for example, admirable goals, they do not establish concrete thresholds to measure progress and maintain accountability, and are unlikely to achieve concrete improvements without funding and authorities commensurate with the challenge, in the particular context of the generic injectable drugs that are disproportionately involved in essential drug shortages.

Some recent strategies propose more concrete goals, but still lack the specific focus needed for significant impact. The Administration's Bold Goals for U.S. Biotechnology and Biomanufacturing lays out the goal that in five years, the U.S. should "deploy broad synthetic biology and biomanufacturing capabilities to produce at least 25 percent of all APIs for small molecule drugs," and "enable prediction of at least 50 percent of supply chain weaknesses." The American Pandemic Preparedness Plan proposes that the country should be able to design, test, review, and produce enough vaccine for the domestic population within 100 days of the emergence of a new viral pandemic threat but has a less measurable goal for reliable drug supply chains, stating that America should "ensure a stable and secure supply chain" for products used in pandemic response. Unfortunately, specific goal-setting is not the norm among the proposed strategies to enhance supply chain reliability, and often the goals that are set do not include specific steps to address the distinct challenges facing generic drug manufacturing and supply chains.

Most of the strategies and goals laid out for supply chain reliability do not incorporate Specific, Measurable, Achievable, Relevant, and Timebound (SMART) Goals. A more effective national strategy to improve drug supply chain reliability must come from a federal government initiative, in collaboration with non-governmental stakeholder organizations, that meets the following conditions. The initiative should have cross-cutting federal support that includes:

- **A long-term vision and mission** as well as short- and medium-term steps to further it, addressing all key aspects of the issue, from manufacturing quality and regulation to payment and contracting, trade agreements, and accountability for payers, group purchasing organizations, health care organizations, and other drug purchasers;
- **A specific focus on drug supply chain reliability,** particularly for generic drugs and other drugs that are frequently involved in shortages, including demand and supply side factors;
- **The standing and expertise to coordinate meaningful action across HHS** and other departments, including facilitating promising changes to contracting and payment for drugs that are frequently in shortage;
- **An effective channel for engaging private sector stakeholder organizations,** including soliciting input and facilitating collaborative action through public-private partnerships;
- **A coordinated strategy** to develop and implement needed administrative reforms, legislative reforms, and private-sector actions – including economic reforms; and
- **Sufficient resources, funding, and expertise** to confront the challenge

While existing governmental, private sector, and non-profit efforts have made progress toward reducing drug shortages, further strategic planning and coordination are still needed to substantially reduce the risk of shortages of many essential medicines, particularly inexpensive generic medications that are complex to manufacture. Therefore, we propose the establishment of a new coordinating initiative, the Prevent Drug Shortages (PDS) Initiative, with requisite authorities and funding to lead a cross-cutting effort to improve drug supply chain reliability, including measurable reductions in the frequency and severity of shortages of critical drugs, and that brings together relevant federal agencies and private-sector entities, establishes SMART goals, identifies accountable parties for implementation, and continuously identifies gaps and improvements.

RECOMMENDATIONS

Prevent Drug Shortages Initiative

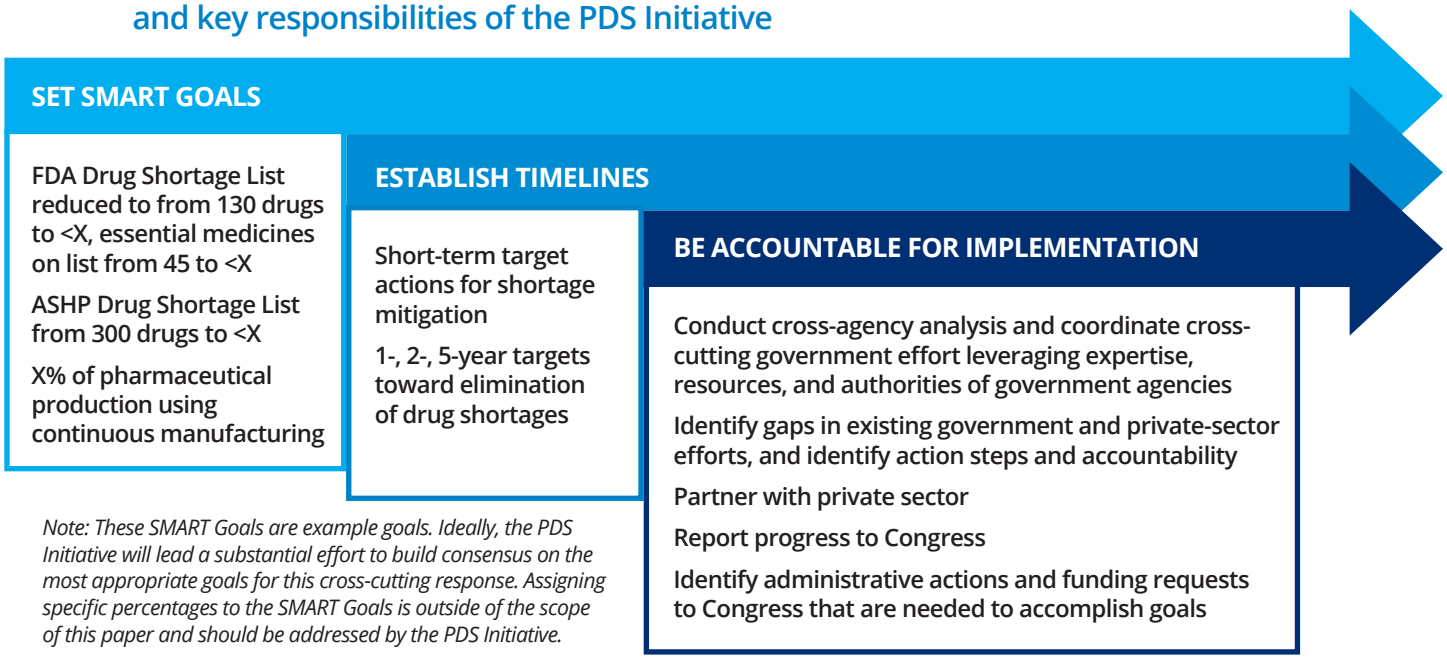
Too frequently, manufacturing quality issues, natural disasters, and other supply chain breakdowns cause patients to suffer the consequences of drug shortages. The ramifications of shortages include the unavailability of standard-of-care medicines, increased risk of medication safety events, delayed and disrupted procedures, and increased cost of care from more expensive alternatives.

To address these challenges, and in collaboration with promising private-sector initiatives, the PDS Initiative should undertake a cross-cutting federal coordination effort to:

- Identify appropriate SMART goals and timelines for improving drug supply chain reliability (examples in **Figure 1**),
- Continually conduct cross-agency analysis of funding, authorities, and information available to federal agencies and non-governmental stakeholders to achieve the SMART Goals in the set timeline. For example, determine if the scope and level of funding deployed is sufficient among relevant government programs to achieve goals in the set timeline, and request additional funding and authorities from Congress as needed, and
- Address the **4 Tactical Gaps**, outlined in the following section and continuously scan for additional gaps.

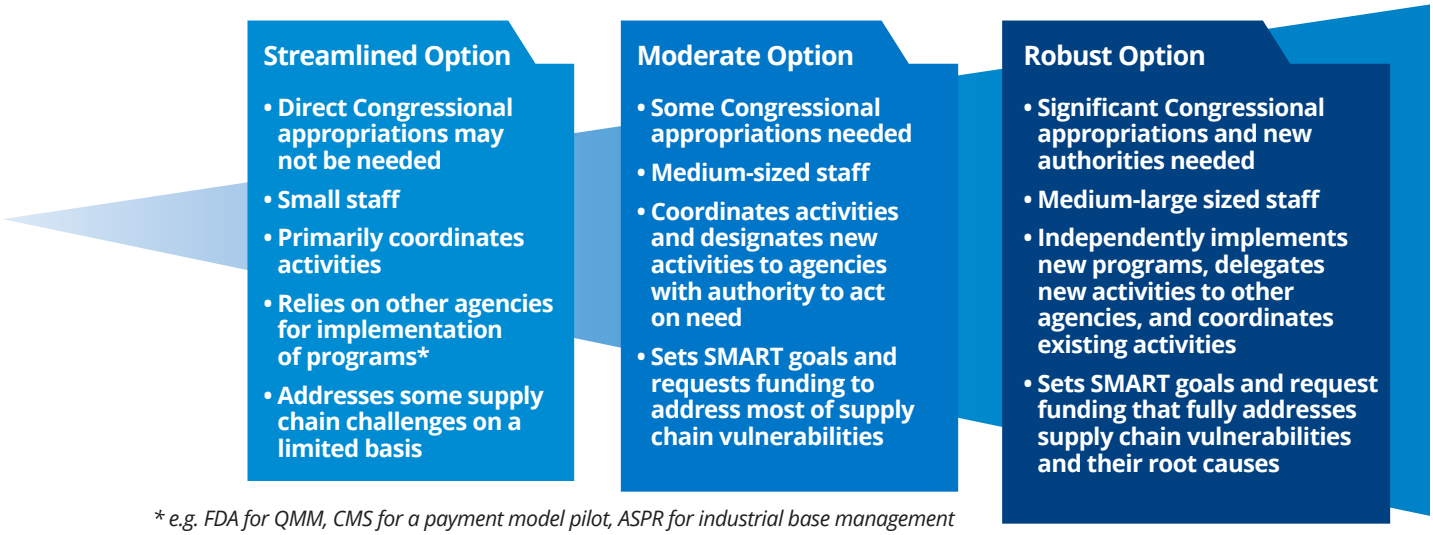
New Congressional appropriations could help advance the PDS Initiative. However, as shown in **Figures 2**, the scope and responsibilities of PDS Initiative are scalable and can begin immediately. As we and others have noted, effective and targeted implementation of this initiative and associated policies to support a more reliable supply of generic medications often in shortage would add only incrementally to the costs of those medications while avoiding the substantial costs associated with recurrent shortages of critical drugs. Carefully targeted investments in preventing drug shortages, if they achieve their intended impact, would be highly cost-effective, averting significant harm to patients and costs to the health care system as described in previous sections. The cost of other priorities of the PDS Initiative, such as expanding industrial base management activities and developing supply chain reliability measurement and tracking mechanisms, would likely add up to only a small fraction of the cost of a targeted payment program. A limited set of initiatives could be undertaken in advance of Congressional appropriations. However, this scaled down approach would likely not be able to fully address all of the Policy Priorities identified below to the full extent needed.

FIGURE 1: Example SMART Goals for drug supply chain reliability and key responsibilities of the PDS Initiative



Note: These SMART Goals are example goals. Ideally, the PDS Initiative will lead a substantial effort to build consensus on the most appropriate goals for this cross-cutting response. Assigning specific percentages to the SMART Goals is outside of the scope of this paper and should be addressed by the PDS Initiative.

FIGURE 2: The budget, authorities, and responsibilities of the PDS Initiative are scalable



** e.g. FDA for QMM, CMS for a payment model pilot, ASPR for industrial base management*

Tactical Gaps and Policy Priorities the PDS Initiative Can Solve

We identified the following four Tactical Gaps and Policy Priorities for the federal approach to improve drug supply chain reliability. The PDS Initiative should be responsible for addressing these gaps and pursuing these priorities but may delegate responsibility to other federal programs if appropriate and within the purview of that agency or department. The PDS Initiative, in collaboration with other agencies, also should conduct its own authority and gap analysis to determine appropriate areas for action.

TACTICAL GAP #1 Lack of tools and standards that measure supply chain reliability, including quality management maturity

PDS Initiative can solve this gap by:

- Advancing further development of FDA's Quality Management Maturity (QMM) program, potentially incorporating into a supply chain reliability program stood up through an independent third-party with significant FDA participation
- Developing other tools to form a robust toolkit of supply chain reliability measurement and tracking mechanisms
- Advancing best practices around use of these tools in committed contracting models, supply chain risk evaluations, and stress tests performed by drug purchasers and other stakeholders

• Policy Priority #1: The federal government, in collaboration with the private sector, should support development and implementation of tools that measure supply chain reliability, including quality management maturity, for drugs at high risk of shortages.

Recent and ongoing shortages have made clear that drug supply chain data is not integrated in a way that can generate actionable insights to prevent and mitigate shortages of critical drugs. Providers and finished dosage form (FDF) drug purchasers (as defined in **Appendix B**), as a result, currently have little ability to assess the relative reliability of their supplier options.

Consequently, when FDF drug purchasers choose suppliers, the purchasers generally have little reliable information available to them regarding the reliability, including quality management maturity, of the supply chains of the suppliers from whom they are choosing. Purchasers also have not invested enough on their own into developing resources needed to identify potential risks in their supply chains. Because low price is the primary quantifiable factor that influences purchasing

behavior and contracting decisions, competitive pricing pressure driven by concerns about high health care costs limits manufacturer return on investment in supply chain reliability, including quality management maturity, as described in the above "Root Causes of Drug Shortages" section. Keeping drug prices affordable is critical, but for older generic drugs that already have lower prices, cost pressures can make it difficult for manufacturers to remain in the market and limit their incentives to invest in needed upgrades to manufacturing equipment and processes.

Appropriately valuing manufacturer reliability, including quality management maturity, and creating incentives for needed investments in supply chains, starts with accurate and useful information on how reliable drug supply chains are today. FDA's QMM Program or a similar program should be fully funded and move from the pilot stage to implementation, either through FDA directly or an independent third party with significant FDA participation. Adjustments to the QMM program based on learnings from the recently-completed pilot program and other stakeholder feedback also still need to be implemented. For example, QMM should be carefully targeted towards essential generic medicines at risk of shortage and mechanisms to share useful information on supply reliability with the correct supply chain stakeholders, while appropriately protecting proprietary information, also need to be considered. The potential incorporation of QMM or a similar program into a supply chain reliability rating program should also be evaluated. Significant opportunities exist to equip relevant stakeholders with better information, such as on manufacturing capacity and flexibility, quality management maturity, company financial health, epidemiology, and other demand drivers, to prevent drug shortages or mitigate their impact.

In addition, a toolkit of measuring and tracking mechanisms is needed to accurately assess supply chain reliability, including but not limited to quality management maturity. Other promising options include U.S. Pharmacopeia's (USP) Medicines Supply Map, USP's General Chapter <1083> on Supplier Qualification, FDA's Risk Management Plans (RMPs) program, supply chain resilience rating systems, additional standardized insights into FDA site inspection observations and outcomes, TraceLink's Product Availability Intelligence tool, others that utilize drug serialization data generated through implementation of the Drug Supply Chain Security Act, and more. In addition to purchasers, other U.S. government entities and private sector stakeholders responsible for getting drugs to patients, including manufacturers, wholesalers, and health care institutions that need actionable insights to help anticipate supply chain vulnerabilities and their causes before shortages result, and inform rapid responses to mitigate shortages. The PDS Initiative should lead a cross-cutting government coordination effort to develop and implement an increasingly robust toolkit of supply chain reliability measures, including quality management maturity measures, which enable purchasers to appropriately value and use products with reliable supply chains. As more tools for measuring supply chain reliability are developed and implemented, the PDS Initiative could create a rating based on a weighted aggregate and curated robust toolkit of resources that together enable purchasers to accurately evaluate reliability.

The PDS Initiative should collaborate with purchasers and other stakeholders to design these tools in a way that supports sustainable purchasing behaviors and contracting methods that can enable more reliable drug supply. Best practices should consider how purchasers utilize contracting models that promote supply reliability. In addition, this effort also should consider how purchasers use supply chain measurement and tracking tools, perform supply chain risk evaluations and stress tests, and incorporate supply chain insights into purchasing decisions and contracting programs. The PDS Initiative should assess the degree to which purchasers adopt committed contracting models that focus on reliability and their impact on shortages, potentially through a public-private partnership or an independent third party.

New quality and reliability measures and supports for purchasing behaviors and contracts that encourage quality and reliability should target a fit-for-purpose list of essential generic medicines.

This contracting reform initiative should focus on purchasing arrangements between FDF drug manufacturers and purchasers and should incentivize purchasers to choose suppliers with higher ratings for supply chain reliability. Additional reliability measures and best practice supports may be needed further upstream in the supply chain (i.e., API supplier to FDF drug manufacturer), but in this white paper we focus on the relationship between FDF manufacturers and purchasers. Standards may need to be adapted for differences between these types of purchasers.

While a well-designed initiative to provide useful information on drug supply reliability will increase attention to reliability in drug purchasing arrangements, reforms to CMS payments and other policies are also needed. We describe these steps in the next section.

TACTICAL GAP #2 Lack of incentives and support for reliable supply chains for drugs at risk of shortage

PDS Initiative can solve this gap by:

- Developing innovative payment policies to support reliable supply chains
- Promoting increased use of committed contracting models
- Ensuring effective use of other industrial base management levers including federal grants, contracts, and loans

• Policy Priority #2 The federal government should provide well-targeted incentives and support purchasing approaches that increase supply chain reliability.

Proactive federal efforts to prevent drug shortages have primarily focused on "supply-side" incentives (up-front financial support, guidance, and other assistance directly to manufacturers intended to lower the cost of starting production and entering the market), such as tax credits, government grants, and contracts for domestic manufacturing, along with Def sense Production Act enforcement. However, progress made through supply-side incentives is likely unsustainable without adequate demand-side incentives (mechanisms intended to establish and maintain viable demand in the market) also in place to encourage purchasers to use products with reliable supply chains. Consequently, public and private sector partners should focus on a path to sustainability and reliability in the market.

The Buy American rule, which drives Federal procurements to domestically made products, will likely have a limited impact on supply chain reliability as direct government procurement accounts for less than 5 percent of all drug purchasing in the U.S. However, the U.S. government could provide a model for reliable purchasing by linking such procurement to high-reliability domestic suppliers. In addition, CMS can implement payment reforms and other steps that can encourage private purchasing behaviors and contracts with manufacturers with reliable supply chains.

Current Medicare payment rules have raised concerns about lack of alignment with more reliable--and somewhat costlier--manufacturing for generic drugs, especially more complex drugs such as sterile injectables. For example, Medicare Part A Diagnosis Related Group (DRG) payments to providers include a set rate for cases based on the patient's diagnosis, providing strong incentives for health care institutions to minimize costs for a hospital stay. One way that health care institutions can limit the cost of care is by choosing the cheapest generic supplier of a drug. The Medicare Part B Average Sales Price (ASP) payment model pays providers the ASP for a drug plus a certain percentage for overhead. As ASP is a blended rate across all generic suppliers for a particular drug, regardless of which generic supplier is chosen, it again encourages choosing the cheapest generic supplier of a drug.

Incentives to limit costs through bundled payments are widespread in health care financing, and hospitals must make a wide range of purchases within their DRG and drug payments, many of which involve products that are far more expensive than generic drugs that are often in shortage. Better information and transparency related to reliable drug supply should encourage the choice of drug suppliers that have made needed investments in manufacturing infrastructure and resiliency in their supply chains. But the relatively low adoption of generic drug purchasing arrangements that support reliability suggests that further steps may be needed.

The PDS Initiative should include CMS participation to develop further steps to encourage health care institutions to identify and contract with more reliable suppliers for drugs at high risk of shortage. Potential approaches could include:

- **Medicare quality and safety improvement initiatives** to help health care providers adopt more reliable purchasing practices, including committed contracting models
- **Hospital performance measures,** potentially including incentives or penalties, related to the reliability of their drug supply
- **Medicare and 340B conditions of participation** related to reliable drug supply
- **Reforms in Part B drug payments** for generic injectable drugs

In particular, financial incentives may be needed to help hospitals, especially smaller hospitals, safety-net hospitals, and others facing greater financial pressures, shift more quickly to drug purchasing models that efficiently support reliable manufacturing. Hospitals, and their GPOs and distributors, may face short-term costs in reforming their drug purchasing arrangements, and could see incrementally higher costs for many types of admissions and outpatient services as a result of paying for reliability. Similarly, relaxation of rebate requirements and other pricing penalties for critical generic drugs at high risk of shortage also could facilitate the transition to more reliable supply. As noted above, because these drugs are inexpensive, the cost of such programs would be relatively modest, and would have some offsetting cost savings for hospitals as a result of fewer disruptions in care and fewer patient complications.

Any such incentive is dependent on robust and accurate assessments of the relative reliability of manufacturers' supply chains, including relative levels of quality management maturity. The previous section of this white paper lays out initial steps toward better measuring and tracking reliability and quality management maturity in supply chains. The Duke-Margolis Drug Supply Chain Resilience and Advanced Manufacturing Consortium is developing more detailed recommendations on CMS-related and other demand-side policy reforms to support supply chain reliability.

TACTICAL GAP #3 Need for fit-for-purpose lists of critical drugs for use in policy decisions related to drug shortages

PDS Initiative can solve this gap by:

- Hosting drug lists on one website
- Describing the purpose of various drug lists
- Identifying gaps in currently existing drug lists and addressing gaps

• Policy Priority #3 The PDS Initiative should be the keeper of fit-for-purpose lists of medicines used to focus policy and private-sector efforts regarding manufacturing and supply chain reforms to prevent drug shortages.

Creating and maintaining fit-for-purpose lists of drugs that are critical for health care and at high risk of shortage is a relatively inexpensive element of a more proactive and comprehensive effort to prevent and mitigate drug shortages. Though shortages of almost any medication would have a negative impact on some patients' care, compiling, creating, and updating lists of the most essential medicines with the highest shortage risks (often generics) will help the PDS Initiative target its efforts for the greatest impact.

Many lists of essential medicines exist, with varying criteria for inclusion on each, largely based on assessments of patient impact, but too rarely accounting for supply chain vulnerability or shortage risks. FDA's list of essential medicines published in 2020 primarily focused on drugs, biologics, and devices used in "short-term treatment for severe injuries or illnesses, and urgent medical conditions," as well as medical countermeasures that could be needed to respond to "pandemics, epidemics, and chemical, biological, and radiological/nuclear threats." Notably, the list includes the APIs and other critical inputs needed to produce each medicine. The World Health Organization's (WHO) biannually updated list of essential medicines, based on "priority health care needs" with "regard to disease prevalence and public health relevance" is another prominent example. A list of Downselected Essential Medicines Needed for Acute Patient Care, developed by the Advanced Regenerative Manufacturing Institute with funding from ASPR, identified medicines "critical for minimum patient care in acute settings or important for acute care, with no comparable alternative available." Some gaps in existing lists include needs around identifying the most-used medicines for treating chronic conditions in the U.S., specific product categories for which shortages would

most severely impact patient health outcomes, medicines with most frequent shortages in recent years, and medicines with particularly vulnerable supply chains.

The PDS Initiative should be tasked with compiling useful existing drug lists and incorporating additional fit-for-purpose lists as needed, with a focus on identifying generic medicines that have a significant impact on patient care and are also at high risk of shortage. In the near term, this category of drugs should be the top priority for the PDS Initiative. In the longer term, and for other HHS agencies that coordinate with the PDS Initiative, lists with use cases related to various other factors may be valuable as well. A few examples include:

- Different etiologies of shortages (demand vs supply shocks),
- Different impacts on patients (medically necessary vs medically significant vs less patient impact),
- Different types of products (difficult to manufacture, pediatrics & essential populations, acute care vs chronic care, stockpile vs. consistent everyday use, generic vs branded, prescription vs. over-the-counter)

These fit-for-purpose lists should be designed with the intention of guiding policies, decisions, and private-sector engagement targeted toward reducing shortage risk for these specific sets of products. These lists can support several key activities, such as monitoring the frequency and severity of drug shortages, measuring success in terms of reduction of those shortages, informing patients and providers of potential or actual shortages, identifying priority products or market segments for policy action, and targeting incentives or penalties as needed.

The PDS Initiative should use these lists to target policy actions as described under **Tactical Gaps 1, 2, and 4** of this report.

TACTICAL GAP #4 Lack of proactive focus on preventing the most impactful drug shortages, regardless of the reason for the shortage

PDS Initiative can solve this gap by:

- Working with FDA, CMS, and ASPR to ensure that measurement tools and incentives are applied to:
  - The most essential medicines at risk of shortages when needed, not just medical countermeasures and pandemic-related products
  - The most impactful causes of shortages, including manufacturing quality issues causing chronic shortages of certain drugs, not just emergency events

• Policy Priority #4 The federal government should pursue a proactive, coordinated focus on preventing the most impactful drug shortages, regardless of the cause.

The authorities and expertise needed to carry out the policy actions described in the preceding three sections are distributed a scross a range of federal agencies, including FDA, ASPR, CMS, and others. Part of the challenge in achieving an effective federal effort to prevent drug shortages will be coordinating across different programs and activities that can help address drug shortages, but generally cannot do so alone, i.e., fitting the strategic pieces together. The PDS Initiative broadly and proactively should approach reducing supply chain risks for essential medicines, starting with the steps we have described for reducing the fragility of supply of many critical drugs, and extending to a more comprehensive approach that brings together the diverse range of federal initiatives that address different aspects and types of drug shortages.

A key feature of the PDS Initiative is its mission to take effective proactive steps to prevent shortages. Many federal drug shortage programs take a reactive approach to mitigating shortages after the shortage is already imminent. For example, FDA DSS acts after receiving notifications of a likely shortage from industry or other stakeholders. In some cases, FDA DSS is able to prevent patient impact, but in others, it is already too late. FDA DSS efforts to mitigate the worst impacts of shortages are critical, and this work should be supported and continued. However, preventing shortages from being close to occurring should be the primary focus of the

PDS Initiative, leading to the broader scope of reforms needed to prevent shortage risk. Prevention requires continuously assessing a wide range of supply chain vulnerabilities, and acting to strengthen risky supply chains and bolster manufacturing capabilities, before those risks manifest as shortages. Actions such as improving quality management, qualifying new locations of production, expanding production capacity or flexibility, and modernizing production facilities often require investments years in advance to proactively prevent a shortage. Since no entity is currently explicitly tasked with ensuring the reliable supply of prescription drugs, these proactive steps largely remain unaddressed.

ASPR does, in some instances, take a proactive approach to strengthen the medical product industrial base and reduce supply chain risks. However, ASPR's focus is on acute emergency disruptions--not the chronic quality issues that are the most common cause of drug shortages. Further, ASPR's focus is primarily on medical countermeasures and pandemic-related medicines, excluding other medical products, like oncology drugs, that can be essential to patient outcomes.

The PDS Initiative should coordinate efforts and amplify the impact of these programs and others—such as FDA's QMM program or a similar program stood up by an independent third party—advanced manufacturing technology programs, and development of new pull incentives for drug purchasers. The PDS Initiative also should take the lead on addressing gaps, including taking steps to prevent chronic, supply-driven shortages.

Implementation Options for Coordinated Leadership through the PDS Initiative

Since many federal agencies already work on drug supply chains in some capacity, several options exist for how and where to establish an PDS Initiative tasked with addressing the Strategic and Tactical Gaps described above. Several promising options, along with the potential advantages and disadvantages of each, are listed below. Regardless of which existing or new government entity is tasked with these responsibilities, it should be granted authorities and resources commensurate with the scale and scope of the challenge. Critically, the PDS Initiative also should include a clearly established avenue for soliciting input from experts and stakeholders outside of government—providers, patients, manufacturers, purchasers, and more—to ensure that its policies advance its mission effectively without creating adverse consequences.

The mission of the PDS Initiative—to coordinate a cross-cutting effort that reduces risks to patient health by ensuring a supply of essential medicines at high risk of drug shortages, including through improving economic incentives—requires reforms across multiple federal agencies.

- **Reporting Directly to HHS Secretary**

The PDS Initiative would be charged with leading a cross-cutting initiative that spans the purview of many federal agencies. The mission of the PDS Initiative—to coordinate a cross-cutting effort that reduces risks to patient health by ensuring a supply of essential medicines at high risk of drug shortages, including through improving economic incentives—requires reforms across multiple federal agencies. As a result, having the lead of the PDS Initiative report directly to the HHS Secretary may be the best option, and also would avoid the challenges that would be caused by attempting to fit the PDS Initiative within an existing federal agency. Under this approach, an initiative drawing on relevant expertise and ongoing activities across HHS could address near term administrative opportunities within FDA, CMS, and ASPR, as well as identify what new authorities it will need in-house to appropriately address more comprehensive, longer term policy solutions.

The HHS mission is to enhance the health and well-being of all Americans. The purpose of improving drug supply chain reliability and preventing drug shortages is perfectly aligned with this mission. Inclusion of the PDS Initiative within HHS would help ensure proper issue prioritization. HHS agencies also possess the health care, health system, pharmaceutical, and payment expertise that will be needed for success (albeit with additional dedicated, needed resources and support outside of HHS).

- **Administration for Strategic Preparedness and Response**

The PDS Initiative could be established within ASPR, building on existing ASPR initiatives, such as the IBMSC Office. In recent years, ASPR (in collaboration with FDA) has played an increasing role in preventing and mitigating drug shortages that affect the nation's ability to respond to public health emergencies. For example, during the COVID-19 public health emergency, ASPR increased and accelerated the supply of therapeutics and vaccines related to COVID-19 response. Through these efforts, ASPR has developed its expertise in medical supply chains, successfully coordinated with other relevant agencies, and, with the establishment of the IBMSC Office, has an interest in continuing its proactive work on shoring up supply chains for medical countermeasures (MCMs).

Historically, ASPR's purview has been limited to MCMs and other drugs and devices used for public health emergency response. The risks of shortage for these products are often driven by sudden spikes in demand, rather than supply-side challenges, so explicitly expanding ASPR's scope to a broader set of essential medicines may require new expertise and authorities. In principle, chronic drug shortages driven by supply-side issues could be considered a health security or public health hazard that could fall within ASPR's purview. But such steps have generally not been undertaken, outside of certain generic drugs at high risk of shortage that are likely to face increased demand in a public health emergency. Moreover, much of the necessary expertise on generic manufacturing and on health care provider purchasing of drugs outside emergencies lies outside of ASPR. Still, ASPR's bulk purchasing and other authorities have improved the supply of many drugs that are used in public health emergency responses, and could improve access to medicines that also are essential in routine patient care, especially acute care. In any case, ASPR's efforts could form critical contributions to the work of the PDS Initiative.

- **Food and Drug Administration**

FDA is another option to house the PDS Initiative given its expertise and the numerous existing FDA efforts in this space. However, critical legal and ethical concerns exist for FDA housing the PDS Initiative. Establishing private-sector drug purchasing standards is beyond FDA's legal authority and would hamper the agency's ability to fulfill its mission. As the regulatory body trusted to objectively assess the safety and efficacy of drug products, FDA does not have authority or program expertise in shaping payment incentives for products once they are on the market.

At the same time, as previously described, FDA has critical expertise in the effort to improve drug supply chain reliability. FDA's Drug Shortage Staff has extensive experience responding to and mitigating ongoing or anticipated drug shortages. FDA requires manufacturers to create risk management plans assessing vulnerabilities that could create disruptions to manufacturing and laying out plans to respond, if needed. FDA also has established efforts, such as the ETP and CATT, to encourage adoption of advanced manufacturing technologies and methods that can improve quality, flexibility, and reliability in drug manufacturing. FDA has created an essential medicines list, and the QMM program is intended to support more sustainable purchasing and contracting decisions by assessing and rating quality management systems.

If housed within FDA, the PDS Initiative could oversee and advance these initiatives while coordinating with other agencies on additional policy actions. The temporary 2018 FDA Drug Shortage Task Force could serve as a model for a more permanent effort. The Task Force was led by FDA and collaborated with other HHS departments, including CMS and ASPR, with an aim to advance long-term solutions to drug shortages.

- **White House**

If established within the White House, the PDS Initiative would be uniquely positioned to coordinate the multiple ongoing efforts under HHS and other federal agencies. This approach would avoid some of the downsides of placing the PDS Initiative within an existing agency and enable the PDS Initiative to draw on the agencies most well-suited for specific elements of the effort. For example, the PDS Initiative could work with FDA to use data on manufacturers to identify vulnerabilities and anticipate potential shortages or work with CMS on novel payment strategies to shape a more sustainable market for certain generic drugs. Clear and recent precedent exists of a similar White House-based lead position for a pressing national issue: the White House Office of Pandemic Preparedness and Response Policy, created by the Consolidated Appropriations Act of 2023, and tasked with coordinating federal preparedness and response across the many agencies that play a role in responding to public health emergencies.

While the PDS Initiative within the White House could be created by the Administration more promptly without Congressional legislation, it would be more removed from the operations of the HHS agencies particularly relevant to addressing drug shortages, could be more subject to

change or elimination as national priorities change, and also may not have as much requisite expertise readily available compared to other options.

- **Department of Commerce**

As the FDA Drug Shortages Task Force report detailed, many of the root causes of drug shortages are economic. Supply chain reliability, including quality management maturity, is not sufficiently valued in pharmaceutical contracting, purchasing, and reimbursement decisions for complex generic drugs, leading to limited enduring manufacturer participation in the market and underinvestment in manufacturing infrastructure, quality management maturity, and risk mitigation strategies.

Given these circumstances, the PDS Initiative could potentially be situated in an agency outside of HHS, such as the Department of Commerce, that has significant economic expertise and a strong economic toolkit. For example, the National Institute of Standards and Technology (NIST) at the Department of Commerce is administering the $50 billion CHIPS and Sciences Act program to revitalize the U.S. semiconductor industry, an effort to bolster manufacturing that in some ways parallels the work that should be done for the pharmaceutical supply chain.

The advantages of this approach are likely outweighed by other factors. Generic drug spending represents only about one percent of annual U.S. health care spending, and an even tinier fraction of the U.S. economy as a whole. Since the mission of the Department of Commerce is centered around economic growth and opportunity, reliability of the generic drug industry may not align intuitively with other Department of Commerce strategic initiatives. The Department of Commerce also likely does not have the requisite health care expertise to successfully accomplish the mission of the PDS Initiative.

Importance of Public-Private Collaboration for Effective Implementation

Wherever the PDS Initiative is housed within government, it will benefit greatly from robust non-governmental input, and should include a clearly established mechanism for two-way communication with non-governmental stakeholder organizations. Many of the policy priorities we describe will require significant industry support and adoption to be effective, and numerous private and non-profit organizations are already working to advance solutions in these areas, as we describe under the section "Overview of Ongoing Drug Supply Chain Resilience Programs and Initiatives." For example, drug purchasers, distributors, wholesalers, and manufacturers often have their own existing methods and metrics for assessing the reliability of their suppliers, paralleling the government efforts we recommend to increase transparency into supply chain reliability. Patient engagement and patient impact assessments are also critical. Collaborative organizations, like the EDSA, are already working to promote best practices for industry to prevent drug shortages, including through transparency measures. Whenever possible, the PDS Initiative should work with such non-governmental organizations to leverage their expertise and potentially use public-private partnerships to implement solutions for the Tactical Gaps we have described.

Administrative and Legislative Recommendations

We have identified a number of administrative actions that can and should be undertaken within current law to begin to address major causes of chronic drug shortages. In addition, future legislative action on drug shortages is needed. Legislation on drug shortages, which may move forward through Congressional committees, would likely be folded into other "must pass" legislative packages. This approach could include the Pandemic and All-Hazards Preparedness Act (PAHPA), given the opportunities to reduce drug shortage risk in and outside of public health emergencies. Furthermore, future legislation related to Medicare payment policy, quality, and safety can and should consider reforms that reduce the frequency and severity of drug shortages. We expect efforts to bolster critical U.S. manufacturing and supply chain

infrastructure—and in doing so, improve the quality and reliability of critical drug supply—will also remain an important legislative and administrative priority, which may afford further opportunities for policy action in this space. Finally, some of the gaps described here could be addressed in HHS agency appropriations bills. Altogether, a relatively modest amount of funding may be sufficient to implement some impactful steps to address chronic generic drug shortages, and that funding may lead to offsetting federal savings (e.g., in fewer costly Medicare complications, emergency expenditures to address critical drug shortages, and more robust manufacturing and supply chains for public health emergencies).

Congress should authorize and provide funding to staff and implement the proposed PDS Initiative, with an initial focus on reducing chronic drug shortages. The PDS Initiative would fill a pressing need for leadership of a permanent, cross-cutting coordination effort focused on improving drug supply chain reliability that brings together the requisite expertise from all relevant federal agencies, establishes SMART goals, identifies accountable parties for implementation, and continuously identifies gaps in approach. Limited coordination activities could be achieved without funding from Congress, which could later be scaled via funding provided through future legislation.

Congress should support ASPR coordination and other HHS actions to improve the reliable supply of drugs that are both needed in a public health emergency and also used outside of an emergency and provide appropriate funding for these actions. Because drugs that are often in chronic shortage also are critical for public health emergency response, including some critical analgesic and anesthesia drugs, immune modulators, and other products, PAHPA should support steps to address shortages of these medicines, which would likely be exacerbated in an emergency. As a starting point, ASPR and collaborating agencies could undertake further actions to increase reliable supply of the "Down-selected Essential Medicines Needed for Acute Patient Care" from the ARMI Essential Medicines Supply Chain and Manufacturing Resilience Assessment report created from Executive Order 14017. **These activities should progress in conjunction with continued support from ASPR for the availability of medical countermeasures and pandemic-related medicines.**

Congress should appropriate the funds requested by ASPR's IBMSC office in the President's FY24 budget. The IBMSC office represents an encouraging step toward a more proactive effort to ensuring reliable supply of select medical products. Sustained funding--beyond the COVID-19 emergency funding used to establish the office and fund its initial operations – will allow the effort to expand to a broader set of MCMs and could form a foundation for further work on improving the reliable supply of other essential medicines at higher risk of shortages.

Congress should appropriate additional funding to develop and implement FDA's QMM program or a similar program, stood up either through FDA directly or an independent third party with significant FDA participation. Such an initiative was not included in the President's FY24 budget, but as we have noted, HHS and the Administration could take initial administrative steps to improve coordination and start to address key drivers of recurrent drug shortages. Congress should work with the Administration to provide appropriate additional funding, which, as we have noted, could be relatively modest. Developing and implementing QMM or a similar program would be a first step toward introducing much-needed transparency into drug supply chains and form a basis for innovative changes to provider payment and contracting practices to support more resiliency and reliability.

The Administration and Congress should develop CMS policy reforms to support more reliable drug supply chains for essential medicines at high risk of shortages, and Congress should provide legislative support for relevant payment changes. For example, new Medicare and 340B conditions of participation, as well as new and innovative payment models for generic injectable drugs, should be considered to provide additional incentives for achieving supply chain reliability standards, including quality management maturity standards, and establishing committed contracts between purchasers and manufacturers. Temporary financial incentives could support a more rapid shift to efficient purchasing contracts for more reliable supply of critical generic medicines. The Duke-Margolis Drug Supply Chain Resilience and Advanced Manufacturing Consortium will publish more detailed recommendations in these areas in the near future.

CONCLUSION

The policy recommendations laid out above would be impactful, but would comprise only the first steps in a significant, sustained effort by the federal government, in partnership with private sector stakeholders, to make needed reforms that meaningfully reduce drug shortages. Drug shortages and supply chain vulnerabilities are severe, chronic issues that prevent American patients from getting the care they need. To meet these challenges in the long term, the Administration and Congress should utilize the authorities and resources available to them to support effective and innovative solutions, including establishing the PDS Initiative and acting on the other recommendations laid out in this paper. The focus of the Duke-Margolis Drug Supply Chain Resilience and Advanced Manufacturing Consortium in the coming months will turn to advancing these solutions via proposals on supply chain measurements, contracting, provider payment solutions, and advanced manufacturing technologies needed to address the core economic drivers that have led to the crisis. We will also continue to refine the authority, resource, and funding needs required to stand up and effectively run the PDS Initiative.

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APPENDIX A

Definitions, Current State, and Potential Next Steps for Product Quality, Quality Management Maturity, and Supply Chain Reliability

To illustrate the need for a more robust, coordinated, and sustained federal effort to prevent drug shortages and outline some recommended next steps, this white paper discusses the concepts of product quality, quality management maturity, and supply chain reliability. The purpose of this white paper is not to define these terms comprehensively or outline all the necessary next steps that should be taken; however, the working definitions of terms below are intended to provide context for the uses of these terms throughout the white paper. We also outline the current state and potential next steps that the PDS Initiative could help to coordinate.

	Product Quality
Working Definition	Quality prescription drugs meet quality standards which ensure that the products are safe and effective. FDA requires that manufacturers of pharmaceuticals marketed in the U.S. comply with Current Good Manufacturing Practice (CGMP) regulations, which are designed to ensure product quality and give patients and providers confidence in the safety and efficacy of the medicines they use. Simple adherence to CGMP quality standards does not indicate that a firm is investing in improvements or deploying statistical process control to prevent supply disruption – that is, it does not assure that CGMPs in supply chains and manufacturing processes will be implemented consistently over time, which in turn leads to the reliable supply of a safe and effective product over time.
Current State	Before a drug is approved or licensed by the FDA, a team of experts provides oversight to clinical trials and deems the drug to be safe, effective, and to meet quality standards. FDA facility evaluation and surveillance, including facility inspections, provide oversight around manufacturing site compliance with CGMP. Every time a manufacturer produces a batch of product and sells it to their customers, the manufacturer attests to the batch's compliance with CGMP. These standards and regulatory oversight help to ensure drug quality.
Potential Next Steps	FDA approval and adherence to CGMP quality standards is sufficient to determine the quality of a drug. Sometimes, manufacturers fail to fully comply with CGMP standards. Resulting impacts include rejecting batches before they are released to the market, Corrective and Preventive Actions (CAPA), negative FDA inspection outcomes, recalls, etc. The standard of quality used by current FDA regulatory initiatives is sufficient to determine the quality of a drug. However, more resources and flexibility in using existing oversight resources to support FDA's current regulatory oversight reform strategy (e.g., modernized data and analytics to prioritize oversight, more unannounced inspections and well-targeted quality testing) could further reduce the rate of noncompliant drugs reaching the US market.

	Quality Management Maturity
Working Definition	Quality Management Maturity (QMM) is the state attained by having consistent, reliable, and robust business processes to achieve quality objectives and promote continual improvement. Quality Management Maturity enables the sustained compliance and reliable production of quality drugs over time. Quality management maturity is one of the most important elements of supply chain reliability.
Current State	Too frequently, manufacturers display low levels of Quality Management Maturity. When a manufacturer produces a batch of drug product that does not meet CGMP standards, FDA regulations prohibit the substandard drug product from being released into the market. Manufacturers sometimes do not meet CGMP standards and are unable to release their drug product into the market, resulting in shortages. The "quality issues" cited throughout this white paper refer to such disruptions in supply. There is a need for greater investment in reliability in production – investments that are separate from CGMP but would be expected to reduce the likelihood of a finished product failing to meet CGMP standards.
Potential Next Steps	Continue development and begin implementation of QMM or a similar program. Continue to improve on the QMM framework based on learnings from the pilot program, standing up either through FDA directly or an independent third party with significant FDA participation Evaluate the incorporation of QMM or a similar program into a supply chain reliability rating program.

	Supply Chain Reliability
Working Definition	A reliable supply chain ensures that patients have safe and effective drugs, in adequate quantities, when they're needed. A reliable supply chain must have four key components in place (the 4 S's): Staff, Stuff, Space, and Systems. Product Quality and Quality Management Maturity (defined above) are necessary, but not sufficient alone, to achieve a reliable supply chain through the 4 S's. These elements are defined and described in our 2021 white paper, "Supporting Resilient Drug Supply Chains in the United States." Drug shortages result from breakdowns in supply chain reliability. In a reliable supply chain, manufacturers of drugs display a high level of quality management maturity and robustness that enable sustained production and delivery of quality products over time. When a manufacturing quality issue or another disruption occurs, a reliable supply chain avoids patient impact through practices such as redundant capacity in other facilities, inventory buffers, and risk management plans.
Current State	Too frequently, a lack of supply chain reliability causes patient impact to occur from drug shortages when demand shocks and supply shocks occur, or when adequate steps are not taken to prevent shocks from occurring.
Potential Next Steps	Implement a program to track the incorporation of QMM or a similar program into a supply chain reliability rating program. QMM or a similar program should be stood up either through FDA directly or an independent third party with significant FDA participation. Publish and update key validated metrics related to manufacturing reliability (or require manufacturers to provide such information consistently to purchasers) to inform purchaser decisions. Support the implementation of contracting and other purchasing practices by hospitals and other purchasers, and the group purchasing organizations and distributors that act on their behalf, to shift manufacturing norms with the goal of substantially reducing the likelihood that critical drugs result in shortages – potentially backed by CMS performance measures, hospital payment incentives, and conditions of participation to assure patient safety if needed.

APPENDIX B

Types of Purchasers of Finished Dosage Form (FDF) drugs

FDF drug purchasers are any customers of FDF drug manufacturers that play a key role in determining which drugs are used by providers. A purchaser usually contracts directly with the FDF drug manufacturer or utilizes a third-party contract such as through a GPO or PBM.

	Group Purchasing Organizations (GPO)	Pharmacy Benefit Managers (PBM)	Wholesalers/ Distributors	Health Care Institutions / Providers
Description	GPOs aggregate the purchasing power of health care providers to negotiate prices and contract terms with drug manufacturers.	PBMs negotiate drug prices and rebates with manufacturers and manage drug formularies on behalf of health insurance plans, employer groups, and others.	Wholesalers and distributors manage the distribution of product from manufacturers to health care providers. For some product types, wholesalers/distributors take on a role similar to GPOs in addition to their traditional storage and distribution role.	Procure product from the manufacturer, wholesaler, and/or distributor. Provide drug to patient.
Setting	Focus on provider-administered drugs in institutional settings, such as hospitals, health systems, outpatient clinics, etc.	Focus on retail drugs.	All drug types.	All drug types.
Role	Do not place orders or take possession of product.	Do not place orders or take possession of product.	Place orders and take possession of product.	Place orders and take possession of product, administer care to patients.

APPENDIX C Glossary of Selected Relevant Governmental Programs and Initiatives

FDA

Program	Description	Status
Quality Management Maturity (QMM) Program	The QMM Program aims to provide an objective third-party measure of quality management maturity practices at manufacturing sites. Ultimately, quality management maturity ratings may provide manufacturers, purchasers, and other stakeholders with a concrete metric on the risk of shortages due to quality issues. Grew out of Quality Metrics program; Federal Register notice in February 2013.	Advisory Committee voted unanimously to progress QMM in November 2022, Pilot programs completed in 2022, stakeholder meeting held in 2023. FDA has not received dedicated funding for a formal QMM program.
Risk Management Plans (RMP)	Manufacturers of certain drugs are required by FDA to create a risk management plan assessing vulnerabilities that could create disruptions to manufacturing and establishing planned response to such a disruption.	2020: CARES Act required certain manufacturers to develop RMPs as recommended by the Drug Shortages Task Force Draft of RMP guidance for manufacturers released May 2022.
CDER Emerging Technologies Program (ETP) and CBER Advanced Technologies Team (CATT)	These programs provide an avenue for drug manufacturers to meet with FDA to discuss the regulatory acceptability of innovative manufacturing approaches. These meetings can offer manufacturers greater clarity on FDA's expectations for a submission and offer FDA staff an opportunity to gain familiarity with new manufacturing technologies and approaches. ETP is responsible for products that would be regulated by CDER, and CATT those that would be regulated by CBER.	ETP graduated their first technology in 2021. ETP has approved 19 applications since 2015; CATT has had 28 meeting requests/ program inquiries in 2023 as of May 2023 (FDA Presentation June 2023). ETP was codified in Section 3203 of the 2022 Food and Drug Omnibus and Reform Act.
Framework for Regulatory Advanced Manufacturing Evaluation (FRAME)	FRAME is designed to support the development of regulatory frameworks for advanced manufacturing technologies likely to be included in submissions to FDA in the future, with a particular focus on end-to-end continuous manufacturing, distributed manufacturing, point-of-care manufacturing, and artificial intelligence. The initiative also aims to clarify regulatory expectations for manufacturers and support international harmonization on regulations around advanced manufacturing.	Released discussion papers on program's technology focuses in 2022 and 2023.
Drug Shortage Staff (DSS)	The DSS works to prevent, mitigate, and help resolve drug shortages by working with manufacturers of drugs in short supply as well as provider and patient groups that may be affected by shortages. DSS solicits manufacturer reports of supply disruptions, notifies other manufacturers of those products when a shortage is anticipated, and maintains a public database of ongoing and resolved shortages.	DSS has 25 full-time employees (FDA FAQ website).
National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing	The 2022 Food and Drug Omnibus Reform Act proposed a program to fund higher institutions to research advanced and continuous manufacturing technology and develop academic-industry-government partnerships to share expertise in advanced manufacturing.	Omnibus bill authorized $100 million for FY 2023-2027. No funds were appropriated to fund these activities directly in FY 2023.
Advanced Manufacturing Technologies Designation Program	Established in the 2022 Food and Drug Omnibus Reform Act, will create a new pathway for sponsors to receive the Advanced Manufacturing designation, which comes with certain incentives related to expedited review.	FDA must establish the program by Dec 2023 and issue a report evaluating the program by December 2025. June 2023: Duke-Margolis held a conference fulfilling PDUFA VII commitment of soliciting industry and public feedback on the Advanced Manufacturing Technologies Designation Program.
FDA Industry Guidance for Advance Notice of Discontinuance of Manufacturing	FDA draft guidance on the FDCA requirement that certain drug manufacturers notify FDA 6 months in advance, or as soon as practicable, of a permanent discontinuance of manufacturing or interruption in manufacturing of the drug that is likely to lead to a meaningful disruption in the manufacturer's ability to supply the US market. Similar notification requirements apply to discontinuations or interruptions in the API supply. Manufacturer report must include, among other things, the reason for discontinuation or interruption and, if API supply issues are a reason or risk factor, the source of the API and alternative sources known to the manufacturer.	Draft released in April 2023 that will, when final, replace the previous March 2020 guidance.

ASPR

Program	Description	Status
Industrial Base Management and Supply Chain Office (IBMSC)	The IBMSC Office works with manufacturers, wholesalers and distributors, and provider groups to ensure sufficient supply of therapeutics and vaccines for COVID-19. The office monitors demand for these medical products and partners with other government agencies to ensure projected supply is sufficient to meet projected demand. Though the IBMSC has thus far remained focused on products used to prevent and treat COVID-19, the formal mission of the office is to expand, secure, and build resilience across the entire public health and medical industrial base.	ASPR awarded $4.9 million to private sector to provide staffing support services for the office starting June 2023. $89,300,000 awarded to pharmaceutical companies to develop domestic production capability for critical APIs, including continuous manufacturing technology. HHS FY 2024 Budget provides $400 million in discretionary funding for ASPR to invest in securing the domestic supply chain.
HHS Coordination Operations and Response Element (H-CORE)	H-CORE provides logistical and operational support for research and development, production, and delivery of products needed for public health emergency response. To date, H-CORE has focused only on COVID-19 response but will remain in place for future health threats.	$604 million estimated spending for H-CORE from 2022-2026 for Public Health Emergency MCM development. $83 million provided in FY 2024 budget.
BARDA National Biopharmaceutical Manufacturing Partnership (BioMAP)	New program model replacing the Centers for Innovation in Advanced Development and Manufacturing (CIADM). Aims to expand manufacturing capabilities for medical countermeasures.	No sustainable funding source secured as of Feb 2023 (GAO).
BARDA DRIVe	Accelerates development of innovative technologies by funding and engaging with the private sector.	Established in 2018.
Supply Chain Control Tower (SCCT)	Established to monitor critical supply chains and inform decision making during a public health response. Receives voluntary data from pharmaceutical distributors, hospitals, and long-term care facilities.	Established in Fall 2022 through the implementation of the American Pandemic Preparedness Plan.
Strategic National Stockpile (SNS)	Stores certain essential medical countermeasures that could experience demand surges in an emergency and can release stockpiled MCMs to prevent a shortage in the short-term.	$6.81 billion estimated SNS department spending for FY 2022-2026. HHS FY 2024 Budget funding requests $995 million.
HHS FY 2024 Budget	Laid out spending for ASPR initiatives including BARDA and SNS.	HHS FY 2024 Budget provided $400 million in discretionary funding for ASPR to invest in securing the domestic supply chain
Division of Critical Infrastructure Protection	This division coordinates HHS's activities as the Sector Risk Management Agency for Healthcare and Public Health Critical Infrastructure. Manages public-private partnerships and information sharing between hospitals, sector stakeholders, and government.	Created in 2019, given expanded authority in 2021 by the National Defense Authorization Act.

NIH

Program	Description	Status
Advanced Research Project Agency for Health (ARPA-H)	Established in 2022 to advance high-risk, high-impact biomedical research, including a focus area on building resilient and integrated health care systems. ARPA-H was formally authorized by the PREVENT Pandemics Act in December 2022 with $500 million included for each FY2024 through FY2028.	$1.5 billion appropriated to ARPA-H in FY2023 budget available through September 2025. HHS FY2024 Budget requested $2.5 billion.

White House

Program	Description	Status
OSTP Bold Goals for US Biomanufacturing	Authored in collaboration by the Departments of Energy, Agriculture, Commerce, and Health and Human Services, as well as the National Science Foundation, this report set out a vision for public and private sector partners to advance biotechnology and biomanufacturing capabilities to build stronger supply chains (among other aims). The report laid out goals such as increasing manufacturing capacity for APIs and advancing capabilities around anticipating supply chain bottlenecks. OSTP will be responsible for implementing the plan.	Report released March 2023.
White House Steering Committee for Pandemic Innovation (SCPI)	Evaluated the implementation of the American Pandemic Preparedness Plan. Interagency committee to assess progress in developing U.S. pandemic preparedness and outlines future goals.	Established in June 2022, progress report released in September 2022.
Executive Order (14001) on a Sustainable Public Health Supply Chain	Invoked Defense Production Act and assessment of short-term availability and inventory of medical supplies and treatments.	Issued 1/21/21.
Executive Order (14017) on America's Supply Chains) on America's Supply Chains	Commissioned 100-day and 1-year reviews of Supply Chain Risks within critical sectors.	Issued 2/16/21. 2022 one-year report stated that HHS invested $105 million on developing advanced continuous synthesis of APIs with DARPA and USAF. Also reported the establishment of HHS Defense Production Act (DPA) Title III program with $60 million in funding to build public health industrial base capacity.
Executive Order (14081) on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy	Tasked Secretary of Commerce, Defense, and HHS to submit a report assessing how to use biotechnology and manufacturing to strengthen U.S. supply chains.	Issued 9/12/22.
National Security Memorandum 15 on Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security	Memorandum directing the implementation of the National Biodefense Strategy. Directed the Assistant to the President for National Security Affairs to oversee policy coordination and integration across federal agencies.	Issued October 2022.

Other Programs Outside of HHS

Program	Description	Status
Department of Commerce Critical Supply Chain Resilience Program (CSCRP)	Department of Commerce fund assists HHS with funding designated critical products.	Feb 2022: HHS identified the CSCRP as a sustainable funding source for HHS-industry contracts and support.
Department of Defense Acquisition Support for HHS	May 2021: Secretaries of DoD and HHS signed a Memorandum of Understanding establishing a framework for DoD to fund HHS acquisition efforts to strengthen domestic health and medical production capacity.	MOU expires September 2023.
Evaluation of the Department of Defense's Mitigation of Foreign Suppliers in the Pharmaceutical Supply Chain	Report made by Inspector General of the DoD that identified reliance on foreign suppliers for DoD and U.S. pharmaceutical supply chain. Proposed stricter pharmaceutical reporting requirements on origins of drug products.	Released September 2021. November 2021: Senators Rubio and Warren co-sponsored a bill to enact recommendations in the DoD report. Bill was referred to the Committee on Armed Services. January 2022: Rep Chrissy Houlahan (D-PA) introduced an identical bill in the House which was referred to House Committee on Armed Services.
National Institute of Standards and Technology (NIST) Hollings Manufacturing Extension Partnership	Manufacturing Extension Partnership (MEP) is based in the Department of Commerce's National Institute for Standards and Technology. MEP connects government agencies and companies with appropriate suppliers and has centers in each state to assist manufacturers with supply chain assessments, risk management, and adoption of new technologies.	June 2023: Biden Admin awarded in each state (about 400,000 per MEP center). Funds will be used to create a national Supply Chain Optimization and Intelligence Network to track supply chain capacities.

National Strategies/Reports

Program	Description	Status
Drug Shortages: Root Causes and Potential Solutions	This report, developed by the FDA's Drug Shortages Task Force, identified market incentives (or lack thereof) and logistical and regulatory challenges as the key drivers of drug shortages. The report recommended actions to reduce the frequency of drug shortages, including promoting sustainable private sector contracting practices and establishing a system for rating quality management maturity at manufacturing facilities.	Published in 2019, updated in 2020.
NASEM report – Building Resilience into the Nation's Medical Product Supply Chains	CARES Act mandated that HHS establish a committee with the National Academies of Sciences, Engineering, and Medicine (NASEM) to assess supply chain and provide recommendations for increasing resilience. The report recommended 7 improvements for supply chain shortage awareness, mitigation, preparedness, and response.	Released March 2022.
American Pandemic Preparedness Plan: Transforming Our Capabilities	Assistants to the President on National Security and Science and Technology identified goals and focus areas to improve bio preparedness. Goal #9 includes building supply chain resilience. The authors recommended creating a new program office to implement and coordinate these goals.	Issued September 2021. Annual progress report on implementation released in 2022 by the White House Steering Committee on Pandemic Innovation.
National Biodefense Strategy and Implementation Plan	White House plan included the goal of securing a critical supply chain to reduce the impacts of bioincidents. Used with National Security Memorandum 15 to establish greater coordination between federal agencies.	Issued October 2022. GAO report in March 2023 recommended that the Secretary of HHS direct federal agencies to clearly document guidance and methods for data analysis.
Short Supply: The Health and National Security Risks of Drug Shortages	Senate Homeland Security and Governmental Affairs Committee report on the current state and challenges of drug supply chain; provided recommendations for preventing drug shortages.	Chairman Gary Peters issued first report in 2019 and released updated report in March 2023.
Essential Medicines Supply Chain and Manufacturing Resilience Assessment	ASPR and the Advanced Regenerative Manufacturing Institute (ARMI) developed an action plan to address the pharmaceutical supply chain risks identified in the 100-Day Review under EO 14017. Produced list of 86 medicines most critical for typical acute patient care.	Issued May 2022
100-Day Review under Executive Order 14017 – Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth	Administration outlined steps to support domestic production of critical medicines. Directed HHS to use the Defense Production Act (DPA) to establish a public-private consortium for advanced manufacturing and domestic production.	Issued June 2021, HHS committed $60 million from DPA appropriations.
HHS' One Year Review under Executive Order 14017 – Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth	Reported the establishment of HHS DPA Title III program to provide sustainable funding source for building public health industrial base.	Issued February 2022.
National Health Security Strategy	ASPR's strategy included goals of building a sustainable and resilient public health industrial base and supply chain.	Released every four years, the current version applies to 2023 to 2026.
National Strategy for Advanced Manufacturing	Report by the subcommittee on advanced manufacturing of the National Science and Technology Council. Outlined goals and strategies to coordinate federal investments for developing advanced manufacturing technologies and enhancing supply chain resilience.	First plan for Advanced Manufacturing published October 2018, updated strategy released in October 2022.
House Committee on Energy and Commerce Legislative Hearing on Preparing for and Responding to Future Public Health Security Threats	The Health Subcommittee held a hearing on improving preparedness for public health emergencies with panelists from ASPR, CDC, FDA, GAO, and academic policy centers. In his presentation, Dr. Califf noted ways for the FDA and Congress to enhance supply chain visibility and expand FDA authority to prevent and mitigate drug shortages.	March 2023: The chair and two subcommittee chairs of the Committee on Energy and Commerce wrote a letter to FDA Commissioner Dr. Robert Califf requesting production and quantity information on critical APIs and drugs as mandated by CARES Act. Hearing was held in May 2023, and FDA's formal response was published.

Enacted Legislation

Program	Description	Status
Consolidated Appropriations Act – Omnibus (including PREVENT provisions)	Authorized $100 million to select and fund institutions of higher education as National Centers of Excellence in Advanced Manufacturing and required FDA to initiate Advanced Manufacturing Technologies Designation Program. Included PREVENT Pandemics Act, giving greater authority to BARDA to manage domestic manufacturing surge capacity; PREVENT also increased HHS authority over SNS and domestic manufacturing contracts. FDA ETP was codified in Section 3203.	Passed December 2022
American Rescue Plan	Allocated $10 billion for medical supply investments through the Defense Production Act (DPA) Title III program. The HHS DPA Title III program will be used to build the PHIB and fund acquisition of critical medical supplies and drugs.	Passed March 2021, December 2021: GAO reported that HHS has established offices to manage industrial base expansion efforts, however HHS has not specified how they will use DPA and funding to improve medical supply chain.
CARES Act	Directed NASEM to review the state of medical product supply chains and increased disclosure requirements for manufacturers to report to the FDA, including notification of a permanent discontinuance or interruption in production of a critical medical device. Expanded disclosure requirements and mandated risk management plans for manufacturers of certain drugs.	Passed March 2020

Potential Future Legislation

Program	Description	Status
Pharmaceutical Supply Chain Risk Assessment Act	Requires HHS to conduct a risk assessment on pharmaceutical supply chains with the Dept. of Defense, Dept. of Homeland Security, and the WH Office of Pandemic Preparedness and Response Policy. The assessment would focus on measuring foreign overreliance for critical medicines and national security impacts of drug shortages.	Introduced to the Senate by Gary Peters (D-MI) and Joni Ernst (R-IA) in June 2023 and referred to the HELP Committee.
Drug Origin Transparency Act	Requires drug manufacturers to report to the FDA the identities of their suppliers and details on APIs and materials sourced from each supplier. The bill also requires the inclusion of the drug and API manufacturer's name(s) and location(s) on public-facing labels.	Introduced to the House by Anna Eshoo (D-CA) in June 2023 and referred to Committee on Energy and Commerce. Two cosponsors added in July 2023: John Sarbanes (D-MD) and Angie Craig (D-MN).
MADE in America Act	Provides increased payment for domestically manufactured drugs and increased incentives for onshoring of APIs, drugs, and PPE to reduce supply chain reliance on foreign manufacturers.	Originally introduced in 2021, reintroduced in April 2023 and referred to House Ways and Means Committee. Sponsored by Buddy Carter (R-GA) and co-sponsored by 11 others including Matt Cartwright (D-PA), Darren Soto (D-FL), and Carol Miller (R-WV).
Drug Shortage Prevention Act of 2023	Amends the FD&C Act to require manufacturers to report increased demand for a critical essential medicine after 6 consecutive weeks of increased demand.	Introduced to House by Rep Sara Jacobs (D-CA) in April 2023 and referred to House Committee on Energy and Commerce. Has 30 co-sponsors.
Domestic Pharmaceutical Manufacturing Caucus	Advances legislation to promote domestic pharmaceutical manufacturing and improve critical medicine supply chain.	Launched March 2023: Co-chaired by Reps Buddy Carter (R-GA), Elissa Slotkin (D-MI), Chrissy Houlihan (D-PA), and Gus Bilirakis (R-FL).
House Cancer Caucus	Bipartisan caucus to promote legislation and funding for cancer research, testing, and prevention.	Co-chaired by Reps Mike Kelly (R-PA), Derek Kilmer (D-WA), Brian Higgins (D-NY), and Brian Fitzpatrick (R-PA). February 2023: Cancer Caucus re-launched in the 118th congress. June 2023: Cancer Caucus briefing on chemotherapy shortages held.
Essential Medicines Strategic Stockpile Act of 2023	Bill to amend the Public Health Service Act to ensure stockpiles of up to 50 essential generic medicines.	Sponsored in January 2023 by Rep Buddy Carter (R-GA) and cosponsor Lisa Rochester (D-DE). Referred to House Energy and Commerce Subcommittee on Health.
Drug Shortages Prevention and Quality Improvement Act	Directs FDA to establish a pilot program assessing manufacturing and supply chain management of essential sterile injectable drugs, penalize manufacturers that fail to provide FDA with data and make necessary changes to drug expiration information.	Introduced August 2021 by Senator Ben Cardin (D-MD) co-sponsored by Tina Smith (D-MN). Referred to Senate HELP Committee.
Mapping America's Pharmaceutical Supply (MAPS) Act	Directs HHS to collaborate with other relevant federal agencies to map the entire U.S. pharmaceutical supply chain, with a focus on identifying and monitoring for vulnerabilities in the supply chains of drugs needed for public health response or drugs for which a shortage would pose a significant threat to public health.	Introduced in July 2023 by Senator Gary Peters (D-MI), co-sponsored by Senators James Lankford (R-OK) and Mike Braun (R-IN). Referred to Senate HELP Committee.
Stop Drug Shortages Act	Provides exemptions from rebate requirements and pricing penalties for certain generic drugs and drugs in shortage. Directs the creation of studies around new payment programs to reduce drug shortages. Creates new reporting requirements for GPOs and other stakeholders. Increases enforcement of current FDA reporting requirements. Provides incentive for shelf-life extension studies.	Discussion draft released by Rep. Cathy McMorris Rodgers (R-WA) in July 2023.

Examples of State Efforts

Program	Description	Status
Missouri	Missouri Technology Corporation (MTC) awarded $9.45 million to APIIC (API Innovation Center) through the MTC Advanced Manufacturing Resiliency Grant Program. APIIC plans to build a pharmaceutical manufacturing base in MO to increase onshore API production and improve supply chain resiliency.	Grant awarded March 2023.
North Carolina	NC Biotechnology Center partners with biopharmaceutical manufacturers to build facilities and funds pharmaceutical innovation projects. NC Biotechnology Center also runs workforce and company training programs in NC.	Eli Lilly has spent almost $2 billion since 2020 to build a manufacturing facility in Research Triangle Park. Novo Nordisk started a 12-year biomanufacturing expansion project in Johnston County in 2022.
Virginia	Phlow Corporation partnered with Virginia Commonwealth University (VCU)'s Medicines for All Program and AMPAC Fine Chemicals to implement continuous manufacturing techniques for essential medicines.	February 2021: US Pharmacopeia announced creation of co-laboratory to develop methods and standards for continuous manufacturing. April 2023: Phlow fundraised $36 million to increase R&D capacity. February 2023: VCU and partners were awarded $15 million in state grants to support lab construction.
Indiana	Eli Lilly committed $3.7 billion to build new manufacturing facilities in Indiana to produce APIs. The Indiana Economic Development Corp provided incentives including tax rebates and tax credits through the LEAP initiative to bring manufacturers and technology business to Lebanon and Boone County, IN.	$2.1 billion committed in May 2023, $1.6 billion added in April 2023
California	In March 2023, California awarded $50 million to CivicaRx to produce insulin biosimilars for California residents through the CalRx Biosimilar Insulin Initiative.	An additional $50 million investment is planned to build an insulin manufacturing facility in CA to produce insulin biosimilars.