Duke | MARGOLIS CENTER for Health Policy

The Honorable Cathy McMorris Rogers
Chair
Committee on Energy and Commerce
United States House of Representatives

The Honorable Mike Crapo
Ranking Member
Committee on Finance
United States Senate

July 7, 2023

Dear Chair, Ranking Member, and Members:

The Robert J. Margolis, MD, Center for Health Policy at Duke University ("Duke-Margolis" or "the Center") appreciates this opportunity to provide comments and recommendations to address nationwide drug shortages. While recent drug shortages, particularly of oncology medications, have been particularly severe and require urgent response, chronic shortage issues have plagued the U.S. healthcare system for decades. The Center thanks the Chair and Ranking Member, and their respective committees, for their focus on the underlying root causes that contribute to repeated drug shortages, and that must be addressed to prevent future shortages.

The recommendations provided in this response are based on the Center's years of research and stakeholder engagements aimed at promoting drug supply chain resilience and preventing drug shortages. The Duke-Margolis Center for Health Policy earlier this year launched a new Drug Supply Chain Resilience and Advanced Manufacturing Consortium ("the Consortium"), which consists of a group of experts in supply chain, manufacturing, regulatory science, national security, and drug shortages from academia, private industry, and governmental agencies. The mission of the Consortium is to identify effective policy solutions that promote a resilient drug supply chain with advanced manufacturing capabilities and reduce the frequency and severity of drug shortages.

The recommendations herein do not necessarily represent the views of any Consortium Members or Observers, but are informed by the Center's work with the Consortium. In the coming weeks and months, Duke-Margolis and the Consortium will publish a series of research and recommendations related to supply chain resilience and drug shortages.

We have provided individual responses to the specific RFI questions below. To summarize these responses, our recommendations include:

1. The federal government should create and fund a **cross-cutting and sustained federal coordination initiative** to address drug shortages. This initiative should connect the pieces to the puzzle that sit in various federal agencies, and set specific goals with parties identified as accountable for implementation.
2. The federal government should support development and implementation of a **robust toolkit of resources**, most notably FDA's Quality Management Maturity (QMM) program, **that measure supply chain resilience and quality.**
3. The federal government should provide well-targeted financial incentives for supply chain resilience through **innovative reimbursement mechanisms** and other means.
4. The federal government should pursue a proactive, coordinated focus on preventing supply-driven drug shortages.

a. **Refocus ASPR's mission** and provide funding (especially for the new Industrial Base Management and Supply Chain office) to prioritize ensuring availability of the most essential medicines
    i. **Regardless of product type.** Current focus is solely on medical countermeasures and pandemic-related medicines.
    ii. **Regardless of the reason for lack of availability.** Current focus is solely on emergency events such as bioterrorism and pandemics.

Our team looks forward to working with you, your committees, and your staff to promote a more resilient U.S. drug supply chain and reduce the frequency and severity of drug shortages.

Sincerely,

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1. **How would you define the scope and impact of the recent and ongoing U.S. drug shortages?**
   a) **For drugs currently in shortage, what percentage of their market is reimbursed through public payers, such as Medicare and Medicaid?**

Public payers (Medicare and Medicaid combined) are the largest payment source for nearly all drug categories and care settings (inpatient[1], outpatient, and retail). This is very likely to be true for nearly all drugs currently in shortage, along with all other drugs.

Key takeaway: Changes to reimbursement policy are needed to incentivize more resilient drug supply chains. Such changes would be most effective if initiated by the largest payers - Medicare and Medicaid - but need not be costly or burdensome. Targeted reforms aimed at essential medicines with high risk of shortage would be impactful and cost-effective. Substantial reductions in future drug shortages can be achieved through cost-effective policy changes that would cost only a fraction of one percent of annual U.S. prescription drug spending.

   b) **What are the impacts of recent and recurring shortages of generics and other critical medicines on patient care?**

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 the U.S. Food and Drug Administration (FDA). The impact is broad and far-reaching. Pediatric cancer patients are forced to delay life-saving care. Providers are left to ration medications that have been the standard of care for years. Staff dedicate countless hours and dollars to finding treatment alternatives. Every health system, hospital, and patient may be at risk due to this chronic, systemic issue. While recent shortages of life-saving generic oncology are a particularly severe and tragic example, it is critical to note that drug shortages have long been prevalent in the United States and are only likely to recur until their root causes are addressed.

2. **What market and economic conditions undermine pharmaceutical supply chains or the availability of drugs? Please discuss any specific barriers in public payment programs.**

When drug purchasers (such as group purchasing organizations, pharmacy benefit managers, and wholesalers) choose suppliers on behalf of health care providers, the purchasers generally have little reliable information available to them regarding the resilience and quality of the supply chains of the suppliers between whom they are choosing. Purchasers also have not invested sufficiently in developing new resources that enable them to identify potential risks in their supply chains. As a result, the primary quantifiable factor that influences purchaser contracting decisions is price. This creates competitive pressure to keep prices low and eliminates incentives for manufacturers to reinvest in supply chain resilience and quality. Keeping drug prices affordable is critical, but for older generic drugs that already have very low prices, cost savings are minimal while cost pressures drive suppliers out of the market and prevent remaining suppliers from maintaining redundancies in the supply chain or investing in critical equipment modernization.

Incentive structures in CMS reimbursement also contribute to an unsustainable race to the bottom for generic drug prices. Regardless of reimbursement setting (inpatient, outpatient, retail), incentive

[1] While Medicare and Medicaid generally do not separately reimburse for drugs used in the inpatient setting, Medicare and Medicaid are still the largest payers for inpatient hospital services. These inpatient DRG-based payments are used by hospitals to procure drugs used in the inpatient setting.

structures in CMS reimbursement currently drive a race to the bottom when providers are choosing between various suppliers of a given generic drug. For example, Medicare Part A Diagnosis Related Group (DRG) payments reimburse providers a set rate for case based on the patient's diagnosis, and providers' profits are based on treating a patient for less than that rate. One key way providers can keep the cost of treatment low is by choosing the cheapest generic supplier for their drugs. Medicare Part B Average Sales Price (ASP) reimbursement 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, the provider again has an incentive to choose the cheapest generic supplier of the drug. While these incentives are designed to keep costs down, they can lead to providers choosing drug suppliers that may be maintaining low costs by cutting corners on needed investments in quality and resiliency in their supply chains – in other words, the products are less expensive, but the supply may also be less reliable and the risk of shortage may be elevated. See our response to Question 4 for steps public payers can take to improve these misaligned incentives.

3. **What are the regulatory challenges to manufacturing drugs in the United States, as compared to other countries? Please specify which agency issued and enforced such regulations.**

FDA can more easily conduct unannounced site inspections in the United States as opposed to foreign countries. To level the playing field, unannounced inspection pilot programs in China and India should be made permanent with funding appropriated. Capabilities for unannounced remote inspections should be implemented in all domestic and foreign facilities. FDA should identify additional countries in which to expand unannounced inspection programs. FDA could also be granted the authority to restrict products from importation into the United States if manufacturers and/or foreign governments do not comply with unannounced inspection programs. The Duke-Margolis Center laid out details around these proposal in comments on previous draft legislation. Some environmental regulations may be more stringent in the United States compared to some other countries, but ultimately the root causes of drug shortages are economic, resulting from current reimbursement structures.

4. **How can federal agencies, such as Centers of Medicare and Medicaid (CMS), better address the economic forces driving shortages? Are these agencies using their current authorities effectively?**

Reshaping targeted CMS reimbursements to encourage smarter drug purchasing decisions could have a significant impact. CMS reimbursements could be scaled according to certain measures of how well provider groups maintain a reliable supply of essential medicines for their patients. This will require careful development, design, and implementation of measures of manufacturer quality and reliability. One promising option is FDA's Quality Management Maturity (QMM) program. If that program were fully implemented, providers could potentially receive a small add-on payment from Medicare for buying from suppliers with a high QMM rating. Add-on payments could also be increased 1) when manufacturers meet certain standards for supply chain data reporting to purchasers and 2) when providers purchase through committed contracting models that meet certain contracting standards for promoting supply chain resilience. Another option to inform CMS add-on payments is to use existing FDA inspection authority to rate the effectiveness of product Risk Management Plans (RMPs) established through the CARES Act. FDA already publicly discloses facility site statuses after facility inspections and could take a similar approach for RMPs. Congress could take an important step of explicitly requiring and providing adequate resources to FDA to inspect RMPs periodically for essential medicines and to disclose RMP ratings. As more tools for measuring supply chain resilience are

developed and implemented, reimbursement could be adjusted based on a weighted aggregate of a robust toolkit of resources[2] that capture different aspects of resilience, together intended to accurately predict the likelihood of a shortage.

Certain minimum standards for promoting supply chain resilience could be enforced through CMS or 340B conditions of participation. Incentivizing excellence in preventing drug shortages may however be difficult through conditions of participation. CMS could consider adjusting these minimum standards using peer groups, so that disadvantaged health systems are not held to the same standards as leading health systems.

Such a program could be implemented through a CMMI pilot or a staged roll-out of a national program. By design, CMMI models are time-limited and often voluntary. We need systemic market change, and a time-limited proposal would not likely get the necessary commitment from participants, including manufacturers' support for QMM. To the extent CMS needs testing during roll-out, it can do so through a staged roll-out supported by continuous program evaluation.

Key Takeaway: CMS should develop an innovative targeted reimbursement model that incentivizes providers to identify, commit to, and buy from reliable suppliers of certain essential medicines. This could be implemented through a new add-on incentive payment program and/or CMS and 340B conditions of participation. As more tools for measuring supply chain resilience are developed and implemented, reimbursement could be adjusted based on a weighted aggregate of a robust toolkit of resources that capture different aspects of resilience, together intended to accurately predict the likelihood of a shortage. Importantly, any new incentives or reforms to reimbursement practices should be targeted toward a carefully selected set of essential medicines that have an elevated risk of shortage and/or would cause particularly severe patient impacts if in shortage.

5. **How does the current generic drug reimbursement structure in federal programs, including those programs' mandatory discounts and rebates, contribute to drug shortages, and what solutions exist?**

As described in our response to Question 2, Medicare reimbursement structures across settings encourage providers to choose the drug manufacturer offering the lowest price, without consideration for the reliability of their supply. For manufacturers of generic drugs, which in general already have relatively low prices, this intense competitive pressure on price and lack of recognition of the value of a resilient supply chain makes it difficult to reinvest in supply chain redundancies, quality management systems, and equipment upgrades. See more in our response to Question 9 as well.

As described in our response to Question 4, reforms to reimbursement that encourage smarter purchasing decisions – i.e. choosing suppliers based on projected reliability rather than just price – could be an effective solution, granted that reforms are based on a comprehensive assessment of reliability and resiliency and are applied to an appropriate set of essential medicines at high risk of shortage.

[2] Other potential tools include: USP's Medicines Supply Map Vulnerability Index, DSCSA serialization insights such as TraceLink's Product Availability Intelligence tool, FDA site inspection outcomes, ratings of robustness of manufacturer Risk Management Plans (RMPs), manufacturer compliance with USP standards such as General Chapter 1083 on Supplier Qualification, the RISC Rating System, Days of Inventory On-Hand at the manufacturer and wholesale chain, and more.

6. **Given that supply chain issues can trigger manufacturing delays and disruptions that result in shortages, are further incentives necessary to address manufacturing issues?**

Yes. Federal efforts to prevent drug shortages have primarily focused on supply-side incentives (up-front financial support 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 Defense Production Act enforcement. 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 domestically manufactured products and products with resilient supply chains. Once new manufacturing sites (often domestic) are established with the support of government incentives, public and private sector partners should focus on a path to long-term sustainability in the market.

See our response to Question 4 for potential further incentives to consider.

7. **What role, if any, has growth in the 340B program played in drug shortage trends?**

The Duke-Margolis Center plans to further evaluate the impact of 340B on drug shortages.

The 340B program reduces the incentives for manufacturers to produce some drugs.

Many of the most impactful drug shortages have occurred on generic injectable drugs primarily used in the inpatient setting. For many of these drugs, a relatively small proportion of purchasing goes through the 340B program.

8. **Would innovative CMS reimbursement models for drugs at risk of shortage status better allow manufacturers of these drugs to meet production and patient demand? What factors should be incorporated into any model seeking to address shortages?**

Well-designed innovative CMS reimbursement models have significant potential to reduce drug shortages. See our response to Question 4 regarding factors that should be considered for such models – particularly the need for a robust toolkit of measurement tools to ensure reimbursement factors in a comprehensive assessment of supply chain resilience. We also will provide more detailed recommendations on how to attach appropriate reimbursement incentives in future work products.

9. **How do existing inflation penalties in Medicaid and Medicare create additional barriers for generic manufacturers, leading to drug shortages? How does the discretion given to CMS to reduce or waive these penalties for drugs on the FDA's Drug Shortage list, as well as certain drugs facing severe supply chain disruptions, introduce additional uncertainty into drug development, and what can be done to remedy that uncertainty?**

Waiving inflation penalties for drugs on the FDA's Drug Shortage list may incentivize manufacturers to keep drugs on the FDA Drug Shortage list. Instead, CMS should consider waiving inflation penalties for a select set of essential generic medicines for which shortages should be avoided, regardless of whether these drugs are currently on the FDA Drug Shortage list.

Medicaid rebates and Medicare rebates reduce the incentives for manufacturers to produce some drugs. However, Medicare rebates implemented in the Inflation Reduction Act are unlikely to apply to most drugs in shortage. Medicaid rebates and Medicare rebates are not a major root cause of shortages

– many of the most severe shortages occur for generic injectable drugs used primarily in the inpatient setting where drugs are not individually reimbursed (and Medicaid and Medicare rebates are not paid).

10. **How might uncertainty in the drug coverage process, particularly as it relates to National Coverage Determinations (NCD) and coverage paradigms like Coverage with Evidence Development (CED), affect competition and, ultimately, the supply of drugs? What can be done to promote greater certainty in that process for FDA-approved drugs?**

The Duke-Margolis Center plans to further evaluate the impact of NCD and CED potential impact on drug shortages but does not have substantial input to share at this time.

11. **Are there any guardrails that Congress should to consider related demonstration projects, including via the CMS' Innovation Center, that would help protect against drug shortages? Are there any proactive demonstrations that would prevent drug shortages?**

See our answer to Question 4, including the included list of nascent resources that are being designed to measure supply chain resilience and quality. Most of these resources are in early stages of development and need to be scaled.

12. **How has consolidation among Group Purchasing Organizations and Prescription Drug Wholesalers led to less redundancy in the drug supply chain? Has this consolidation contributed to drug shortages, especially among generic drugs? Have business practices, such as just-in-time deliveries and limited-source contracts contributed to the drug shortage issue we are seeing?**

Consolidation has provided more purchasing power to Group Purchasing Organizations and Prescription Drug Wholesalers. This purchasing power enables GPOs and wholesalers to negotiate lower prices from suppliers, and lower prices have been shown to be a major driver of drug shortages. Consolidation may also reduce competition among manufacturers, as late-to-market generic entrants may have difficulty in finding committed customers. Late-to-market generic entrants may instead leave the market or contribute to the race to the bottom in pricing by offering unsustainably low short-term pricing.

Consolidation also provides GPOs and wholesalers with an opportunity to create advanced, consolidated systems for identifying supply chain risks. Consolidation also can enable GPOs and wholesalers to quickly enact systemic changes that move the market towards reliability.

Key Takeaway: Consolidation among purchasers has positives and negatives. The more important point is that providers need additional incentives, as described in our answer to Question 4, that cause them to direct their GPOs and wholesalers to value reliable supply instead of just lowest price.

13. **What factors would lead to a generic drug receiving approval but not coming to market?**

Insufficient likelihood of achieving profitability due to low prices and inadequate adoption of committed contracting models may discourage manufacturers from bringing a generic drug to market.

14. **Are there any other issues leading to drug shortages that we have not considered in this RFI?**

Please see our 4 key recommendations listed on page 1.