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

August 25, 2023

Dear Chair McMorris Rodgers,

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 regarding the discussion draft of the Stop Drug Shortages Act. Our comments herein follow on our response to the July 2023 Request for Information issued by the Chair on the same topic, and we again thank the Chair, the Committee, and Committee staff for their focus on preventing drug shortages.

Duke-Margolis has conducted years of research and stakeholder engagement aimed at promoting drug supply chain resilience and preventing drug shortages, most recently including the launch of the new Duke-Margolis Drug Supply Chain Resilience and Advanced Manufacturing Consortium. The recommendations herein do not necessarily represent the views of any Consortium Members and are not intended to limit the ability of Consortium members to provide their own comments on behalf of their independent organizations, but are informed by the Center's work with Consortium Members. In the coming weeks, Duke-Margolis will publish a white paper, also informed by our work with Consortium Members, with a broader set of recommendations for administrative and legislative action on drug shortages.

We provide recommendations on selected sections of the discussion draft below. The following summarizes our key recommendations and proposals for future legislation on drug shortages:

- **Exemptions from inflationary rebates under the Medicaid and Medicare programs, as well as exemptions from 340B pricing requirements, will likely improve the ability of manufacturers to invest in reliable drug supply chains. However, most comprehensive evaluations of the root causes of drug shortages indicate that these pricing programs may contribute to, but are not necessarily a major root cause of, drug shortages.**
    - Rather, the primary root causes of drug shortages include that providers face challenges in identifying and purchasing from manufacturers that are investing in supply chain reliability. This in turn means manufacturers must compete for buyers primarily by offering the lowest price and are not incentivized to make needed investments in reliable production. These issues are particularly challenging for generic manufacturers, which often operate on slim profit margins compared to branded manufacturers and have limited ability to invest in their supply chains.
    - In addition, many shortages impact drugs used primarily in the inpatient setting where drugs are not individually reimbursed (and Medicaid and Medicare rebates are not paid). This suggests that Medicaid and Medicare rebates are not a major root cause of drug shortages and that comprehensive legislation to address drug shortages should contemplate Part A payment reform.
- **Any exemptions from Medicaid inflationary rebates, Medicare inflationary rebates, or 340B pricing requirements should not be based on whether or not a particular drug is *currently* in**

shortage. Instead, these exemptions should apply to a set of generic drugs for which preventing shortages is most critical, regardless of whether these drugs are currently in shortage.

- Applying exemptions only during a shortage may create an adverse incentive in which a manufacturer scaling up production to end a shortage could actually reduce the manufacturer's profitability. In addition, manufacturers need the ability to continually improve their infrastructure on an ongoing basis, proactively investing in reliable manufacturing practices in order to prevent future shortages.

- **The Inflation Reduction Act exempted multisource generic drugs from the new Medicare rebate program, whereas previous legislation that created the Medicaid rebate program and 340B program did not. Title I and II of this proposed legislation would bring the Medicaid rebate program and 340B program methodology more in-line with the more recent Inflation Reduction Act methodology, thus providing further incentives for manufacturers to produce generic drugs at risk of shortage.** Importantly, the potential impact on rural and critical access hospitals should be quantified and carefully considered. Other financial incentives, perhaps from innovative payment programs, should be considered to help ensure rural and critical access hospitals are not negatively impacted by new exemptions.
- **We recommend that the Administration and Congress take urgent action to establish a new coordinating initiative to lead a cross-cutting effort to improve drug supply chain reliability,** bringing together relevant federal agencies and private-sector initiatives, establishing goals, and addressing policy priorities around preventing drug shortages. The Duke-Margolis Center will publish a white paper laying out the need and next steps for this coordinating initiative.
- **In the long term, incentives for manufacturing should be conditional on measurable improvements in manufacturing reliability.** Effective use of reporting requirements, along with voluntary programs such as a supply chain reliability rating program as discussed later in our comments, may provide the information that forms the basis for such conditions.

Title I. Medicaid.

Sec. 101. Exempting Certain Specified Drugs from Certain Increases in Rebates Under the Medicaid Program; Rebate Cap for Certain Drugs.

Current net prices after rebates for many generic sterile injectables are likely insufficient to sustain reliable manufacturing. As a result, providing exemptions from inflationary rebates could have a positive effect on drug supply chain reliability by allowing manufacturers greater ability to invest in manufacturing infrastructure and systems and encouraging more manufacturers to produce these drugs.

Sec. 101 indicates that inflationary rebates would be suspended for "specified generic drugs" and "specified injectable drugs."

- The "specified generic drugs" definition includes an inflationary rebate suspension for all generic drugs currently on the FDA Drug Shortage List. Suspending rebates during a time of shortage has a high likelihood of causing adverse incentives in which the occurrence of a shortage could improve manufacturer profitability. For example, when a manufacturer scales up production to end a shortage it could remove their rebate suspension and thus reduce the manufacturer's profitability. This provision could also compromise the accuracy of the FDA Drug Shortage List, as FDA relies on collaboration with and accurate information from manufacturers regarding line of sight to shortage resolution.
- Instead, these rebate suspensions should apply to a set of generic drugs for which preventing shortages is most critical, regardless of whether these drugs are currently in shortage. This list could be maintained by the Secretary, akin to the second provision (BB) in the "specified generic drug" definition. However, the Secretary likely should not only include drugs that have "severe supply chain disruptions" or "unique or unexpected events" impact their supply chains as currently listed in provision (BB). Instead, the list of "specified generic drugs" should apply to a set of generic drugs for which preventing shortages is most critical. Factors other than just "severe supply chain disruptions" such as low price, manufacturing complexity, and essential nature of the drug, could also indicate that certain drugs should be included in the "specified generic drug" list.
- The definition of "specified injectable drugs" appears appropriate.
- In the long term, policymakers should explore opportunities to tie these rebate exemptions to measurable improvements in reliability and manufacturing infrastructure investments.

Title II. 340B Drug Discount Program.

Sec. 201 Exempting Generic, Sterile Injectable Drugs from the 340B Drug Discount Program.

Removing 340B pricing requirements for multisource generic sterile injectable drugs would increase the incentive for manufacturers to enter the market for these critical drugs, and for those manufacturers in the market to invest in reliable manufacturing practices that prevent shortages. The potential impact on rural and critical access hospitals should be quantified and carefully considered. A healthy, competitive market with adequate pricing competition between manufacturers of multisource generic products should be able to provide affordable medications to all provider types. Other financial incentives, perhaps from innovative payment programs, should be considered to help ensure rural and critical access hospitals are not negatively impacted by new 340B pricing requirement exemptions.

Sec. 202. Study on Penny Pricing and Other Price Setting Policies.

Studying the rates of shortage for drugs with particularly low prices in the 340B program is a worthwhile next step, as the 2020 FDA report *Drug Shortages: Root Causes and Potential Solutions* notes that low and declining prices for a drug often precede a shortage of that drug. Such a study should also include analysis, for various sets of drugs, of the percentage of volume that goes through 340B contracts compared to the rest of the market, 340B prices compared to average manufacturer net prices, and other areas. The sets of drugs that should be evaluated could include generics vs brands, inpatient vs outpatient use, and others. A drug with an average manufacturer price of $1 or less is also likely very low-priced, so it is possible few manufacturers would choose to produce the drug even absent the 340B pricing requirements.

Sec. 203. Guidance on Preventing Diversion During Shortages

We have no substantial input on this section at this time, though we would note that the Committee should be aware of significant policies that impact this topic related to the Drug Supply Chain Security Act.

Title III. Medicare.

Sec. 301. Reducing Inflation Rebate Amounts for Certain Shortage Drugs Subject to Rebate Waivers under the Medicare Program.

As mentioned previously, any exemptions from Medicare rebates should not be based on whether or not a particular drug is *currently* in shortage. Instead, these exemptions should apply to a set of generic drugs for which preventing shortages is most critical, regardless of whether these drugs are currently in shortage. If this approach was taken, in addition to the prevention of adverse incentives potentially promoting the artificial elongation of shortages by manufacturers, there would be no need for the complicated methodology in Sec. 301 regarding a phase-out of rebate reductions after a shortage.

Regardless, the Medicare rebate program created by the Inflation Reduction Act will not apply to most drugs in shortage, which are mostly multisource generic drugs. The Medicare rebate program only applies to branded drugs and sole-source generics. As such, we do not see much impact from Sec. 301 related to preventing drug shortages.

Sec. 302. Study on Market-Based Pricing for Shortage Drugs Under Medicare Part B.

This would be a valuable study. This section could be more clear about what market-based pricing means. This section appears to possibly suggest that, in the study context, providers that buy from different manufacturers of the same generic drug would be reimbursed differently based on different manufacturer net prices. In theory, aligning Part B reimbursement to reflect actual net prices in this way could reduce some adverse incentives that occur in Part B. However, in the study, HHS should be careful to ensure that new proposed market-based reimbursement methodologies do not overly incentivize providers to prescribe more expensive options when choosing between various therapies. In this context, HHS could study several different potential methodologies for add-on payments, including positives and negatives of the ASP cost-plus model.

HHS should study the potential for add-on Medicare reimbursement payments that incentivize providers to choose more reliable suppliers of generic sterile injectable drugs and purchase generic sterile injectables through GPO committed contracting mechanisms. Such a study should explore what costs would be associated with add-on payments if targeted to drugs with the highest risk of shortage, whether add-on payments could meaningfully change choices of supplier, and how to enable reporting on choice of supplier while avoiding unnecessary provider burden.

Sec. 303. CMI Model on Alternative Payment for Generic Sterile Injectable Drugs.

See comments on Sec. 302 regarding potential net pricing reimbursement considerations.

Wholesale Acquisition Costs (WAC) are often significantly higher than actual net prices. For context, a drug with a net price of $10 may have a WAC of $100. Manufacturers may keep WAC significantly higher than actual net prices for a variety of reasons, and WAC is often nearly completely unrelated and divorced from actual net prices. We do not recommend setting drug reimbursement levels based on WAC.

Sec. 304. Study on Medicare Coding for Drugs in Shortage or in Danger of Shortage.

We encourage HHS to explore coding policies for generic sterile injectables and other Part B drugs in shortage or at risk of shortage. Payment policy changes have great potential to change provider purchasing behavior and ultimately reduce the risk of drug shortages, but such payments should be carefully targeted at lower-cost generic drugs at higher risk of shortage. A workable method of coding and billing those products separately without creating undue provider burden could enable some promising payment policy changes to be implemented effectively.

Importantly, this study should evaluate the Part A setting as well as Part B.

Sec. 305. Hospital Reporting of Group Purchasing Organization Remuneration under Medicare.

It is not clear how the reporting requirements proposed in this section relate to drug shortages.

Sec 306. Study on Flat Fee Payment.

If implemented effectively, this could reduce adverse incentives that exist in Part B that promote prescribing more expensive drugs. For example, when faced with a decision between prescribing two drugs with separate J-codes, providers currently have an incentive to prescribe the more expensive drug.

Sec. 307. Clarification of Medicare Average Sales Price Payment Methodology

It is not clear how the payment methodology changes proposed in this section relate to drug shortages.

<u>Title IV. Transparency.</u>

Sec. 401 Group Purchasing Organizations Reporting.

It is not clear how the reporting requirements proposed in this section relate to drug shortages.

<u>Title V: Food and Drug Administration.</u>

Effective use of reporting requirements would be productive measures to promote transparency and visibility into the drug supply chain. We provide specific recommendations on several sections below. In the long term, further legislation should focus on tying incentives like those described in Title I-III of this draft to measurable improvements in manufacturing practices or guarantees of reliability.

Sec. 501. Noncompliance Letters Relating to Volume Reporting.

Congress should ensure that timely and accurate information is provided to FDA pursuant to the volume reporting requirements under Section 510(j), as this information is critically important for FDA's work to prevent drug shortages. FDA's final guidance on volume reporting requirements, when issued, should be clear regarding what will occur if manufacturers do not comply with the requirement.

In the long-term, this volume reporting data could be one component of a robust toolkit of many supply chain reliability measures that can be used to inform sound decision-making. For example, Congress should also ensure that further work on designing and developing the FDA's Quality Management Maturity (QMM) program, or a similar drug supply chain reliability rating program through an independent third party with significant FDA participation, is completed to enable more readily available information on drug supply chain reliability for purchasers and other stakeholders. In addition, Congress should also consider how to ensure the most effective use of the Risk Management Plans authority provided to FDA through the CARES Act. For example, ratings regarding the strength of Risk Management Plans could be incorporated into the aforementioned drug supply chain reliability program.

Sec. 502. Incentive for Shelf-life Extension Studies.

Encouraging manufacturers to seek an extended expiration date is a likely underutilized tool that could better enable resilience efforts such as buffer inventory stocks. For example, the maximum buffer inventory stock level for the full supply chain for a drug with 18 months shelf life is likely less than 3 months (due to timing from manufacturing to quality control release and common business practices that involve quarantining product for destruction 6-12 months before expiration). After also accounting for variability in demand and supply, the supply chain is unlikely to be able to hold an adequate buffer inventory level to prevent shortages for many drugs, especially drugs with 18 months shelf life or less.

As we noted in our 2021 white paper, manufacturers currently may be disincentivized from seeking extended expiration dates as speed to market is critical in early product development and longer expirations dates may reduce demand for certain drug types. Awarding extended exclusivity could be an effective incentive for newer branded drugs; however, it is unclear whether an additional one month of exclusivity is the appropriate amount of value that should be provided to a manufacturer for conducting shelf life extension studies. In addition, extended exclusivity would not necessarily impact older generic drugs, which are the most likely to experience shortages.

To potentially improve shelf life for older generic drugs, Congress should direct FDA and DOD to create a report on their Shelf Life Extension Program (SLEP) that 1) reports on findings from the program and 2) assesses what it would cost to conduct long-term stability studies on every drug that is included in the Strategic National Stockpile and 3) assesses the feasibility of providing funds to support manufacturers running long-term stability studies for older generics drug. Stability testing should be designed to support labeling the drugs with the longest feasible expiration dating.

While in some cases extended expiration dating may reduce product demand and manufacturer profitability, this is often not the case. Extended expiration dating in many cases can increase manufacturer profitability by 1) reducing credit provided for expired product that is returned and 2) reducing manufacturing costs for replacement product. We anticipate that some manufacturers may seek extended expiration dating if they received funds to conduct the required long-term stability testing. Congress should also consider additional incentives that could encourage manufacturers of generic drugs at high risk of shortage to conduct long-term stability studies.

Sec. 503. Providing for a Lag Period for Outsourcing Facilities to Compound and Distribute Drugs in Shortage.

503B compounding facilities have in many cases served as a useful means to assist when drugs are in shortage, but we note that various practical, financial, and safety concerns exist which limit the ability of 503B compounding facilities to holistically solve for drug shortages. 503B compounded products are not subject to the same requirements as ANDA and NDA approved drug products and represent a higher risk.

Still, 503B compounding facilities can play a role as a stopgap in mitigating drug shortages. Sec. 503 would de-risk the investment required of 503B compounders to develop and produce during a shortage by providing more time for compounders to produce and sell their excess inventory after a drug shortage is resolved, minimizing wasted resources. Congress should consider whether a shorter timeframe for distribution and dispensing of a compounded drug after appearing on the drug shortage list, such as 90 or 120 days, would be appropriate while also minimizing unnecessary parallel distribution of compounded products. Other provisions in this draft legislation focused on the root causes on drug shortages are likely more impactful and should remain the primary focus of legislation in this space.

Sec. 504. Additional Information on Generic Drug Active Pharmaceutical Ingredients (API).

This is an important step that can increase FDA's visibility into the upstream supply chain. Policymakers should consider the potential value of adding reporting on the facility or location that is the source of the API, since a single API manufacturer may have multiple locations of production. We encourage Congress to consider how this information and information like it could be incorporated into a supply chain reliability rating program as we referenced earlier. In the coming months, Duke-Margolis plans to publish a white paper that will touch on this topic.

Sec. 505. Reporting on Use of New Authorities and Requirements with Respect to Drug Shortages.

This is an important step. The Risk Management Plans authority provided to FDA through the CARES Act has significant potential to prevent drug shortages but requires some changes to be made most impactful. For example, ratings regarding the strength of Risk Management Plans could be incorporated into the aforementioned drug supply chain reliability program. In the coming months, Duke-Margolis plans to publish a white paper that will touch on this topic.

Sec. 506. New Domestic Facility Inspection Pilot Program.

Conducting preapproval inspections earlier for new pharmaceutical manufacturing facilities can be an important aspect of increasing supply chain reliability and reducing the likelihood of drug shortages. This pilot program could be a productive step to streamline the regulatory process for establishing new domestic manufacturing facilities.