

**DRUG SHORTAGES: EXAMINING SUPPLY
CHALLENGES, IMPACTS, AND POLICY
SOLUTIONS FROM A FEDERAL
HEALTH PROGRAM PERSPECTIVE**

HEARING

BEFORE THE

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TUESDAY, DECEMBER 5, 2023

U.S. SENATE,
COMMITTEE ON FINANCE,
Washington, DC.

The hearing was convened, pursuant to notice, at 10:06 a.m., in Room SD-215, Dirksen Senate Office Building, Hon. Ron Wyden (chairman of the committee) presiding.

Present: Senators Stabenow, Cantwell, Menendez, Carper, Cardin, Brown, Bennet, Casey, Warner, Whitehouse, Hassan, Cortez Masto, Warren, Crapo, Cassidy, Young, Barrasso, Johnson, Tillis, and Blackburn.

Also present: Democratic staff: Shawn Bishop, Chief Health Advisor; Joshua Sheinkman, Staff Director; and Tiffany Smith, Deputy Staff Director and Chief Counsel. Republican staff: Kellie McConnell, Health Policy Advisor; Stuart Portman, Senior Health Policy Advisor; Gregg Richard, Staff Director; and Conor Sheehey, Senior Health Policy Advisor.

**OPENING STATEMENT OF HON. RON WYDEN, A U.S. SENATOR
FROM OREGON, CHAIRMAN, COMMITTEE ON FINANCE**

The CHAIRMAN. The committee will come to order. This morning the Finance Committee meets to discuss the drug shortages that are plaguing Americans in communities across the country.

In America today, if you receive a cancer diagnosis, chances are scientists and doctors have developed effective treatments to fight or beat this horrible disease. While most of the spotlight tends to fall on new, cutting-edge innovations, some of the most vital treatments for millions of Americans suffering from cancer and other chronic illnesses are lower-cost generic medicines that can really help and have been around for many years. These are the products where the shortages are felt the most, and it threatens the health and well-being of the country.

Earlier this year, the Finance Committee began to investigate what was causing a widespread shortage of ADHD medications in Oregon and across the country. What we found was shocking. The supply chains for these prescriptions that millions of Americans count on to work and learn were bogged down in what can only be called bureaucratic bedlam. Manufacturers, the DEA, and the Food and Drug Administration all offered conflicting explanations for

why the shortages for Adderall and its generics have persisted, and why patients have been in the dark without clear answers.

So, we are now pushing to resolve these shortages and add transparency and flexibility so it does not happen again. So today, the Finance Committee is going to examine the causes of these devastating drug shortages. In particular, the committee is going to look to use the power of Medicare and Medicaid, which covers millions of Americans and pays for hundreds of billions of dollars in health-care spending every year.

This is urgent business for this committee, and it is going to be key to find bipartisan solutions that are going to get at this persistent and tragic problem. The consequences of these drug shortages are not abstract. I have town hall meetings in all of my counties each year, and at all of these meetings I am hearing about the problems of shortages at pharmacies in Oregon, across the State—and this has hit rural communities and rural America like a wrecking ball.

There has been story after story of drug shortages resulting in rationing, inappropriately low doses, or alternative treatments that are not as safe and effective as the product that is experiencing the shortage. These shortages can be life or death for kids, especially when it comes to cancer drugs.

The evidence shows that the cause of the vast majority of drug shortages is, in effect, a set of market failures. Right now, they exist across the prescription drug supply chain from manufacturers to providers, as well as the middlemen that we of course know here: the PBMs and drug wholesalers.

The substantial portion of the market failures are driven by the consolidation of generic drug purchasing among a small group of very powerful health-care middlemen. There are many companies that manufacture generics, but they must compete for the attention of highly consolidated middlemen, such as the drug wholesalers and hospital group purchasing organizations, to gain access to markets.

In the case of drug wholesalers, three companies control 90 percent of the pharmaceutical market in the country, and all three of those companies are among the top 15 largest businesses in America by revenue. The generic manufacturers that are awarded contracts by these middlemen do so by offering penny-on-the-dollar prices that mean they cannot invest in the capacity or equipment that is the key to actually making reliable, high-quality medications.

So you have, in effect, a “race to the bottom” price war for generics that leads to quality control problems and factory shutdowns, which leads to a shortage of generic drug products that, of course, are in high demand.

So, we are in a position on the Finance Committee to correct this mess. Senator Crapo and I work often on these issues, particularly where we are dealing with issues that involve Medicare Part A and Part B; B in particular, paying for services in doctor’s offices, hospitals; Part A, including prescription drugs that are administered there like chemotherapy treatments and related injectable drugs.

Some of the injectables are facing the most serious shortages. In Part D, 90 percent of the medications dispensed are generics. As

the committee has found as we worked on the pharmacy benefit manager issue, even if manufacturers are selling generics at low prices, the middlemen have free rein to mark up prices along the way, and once again the circle comes back with seniors getting higher costs in America.

While middlemen get rich and consumers pay more than they ought to for generics, manufacturers may decide it is not worth the trouble to even produce the medicines and just get out of the market.

So those are some of the issues that we have to tackle. Suffice it to say not all of these issues relating to market failures will come up in coffee shops across America every morning, but we sure know that a lot of people are hurting, and they are talking about what is going to be done about this. We have a chance to work in a bipartisan way, as we have done on health-care issues so often.

I want to recognize my friend, Senator Crapo.

[The prepared statement of Chairman Wyden appears in the appendix.]

**OPENING STATEMENT OF HON. MIKE CRAPO,
A U.S. SENATOR FROM IDAHO**

Senator CRAPO. Thank you, Mr. Chairman. This year, the Finance Committee has taken unparalleled action on prescription drug access and affordability. Our bipartisan PBM reform legislation would cut patient costs at the pharmacy counter, strengthen provider choice for seniors across the country, and reverse warped incentives that currently favor higher-priced medications.

Our policies would accomplish all of this and more, while reducing the Federal deficit. Taxpayers, consumers, and community pharmacies deserve to see these bills passed by the full Congress and delivered to the President's desk as quickly as possible.

For patients with chronic conditions, as well as independent pharmacies at risk of potential closure, inaction is not an option. As our PBM process has shown, bipartisan, consensus-based, and market-driven policymaking can address a wide range of challenges facing seniors and working families.

In that same spirit of exploring effective legislative solutions, today we turn to another issue harming the health and finances of Americans in every State: the surge in drug shortages. For treatments targeting any number of conditions, from pediatric cancer to mental health ailments, our ability to prevent and resolve shortages can mean the difference between life and death. To develop meaningful policy improvements to reverse the current rise in drug shortages, however, we first need to understand and examine the economic drivers, with a focus on Federal programs within our committee's jurisdiction.

While high-priced medications have received outsized attention during prescription drug discussions in Congress, shortages disproportionately affect low-cost therapeutics, which operate in a largely different and increasingly challenging economic environment. In fact, 84 percent of shortages occur in generic drugs, and 56 percent of products in shortages have unit prices below a single dollar. Given that generics comprise roughly 9 in every 10 prescrip-

tions filled across the United States, these shortages can inflict drastic harm on massive populations of Americans.

The average shortage affects at least half a million consumers, forcing them to scramble for viable alternatives—or they will forgo treatment entirely. As experts and officials have broadly affirmed, the structure of the generic market incentivizes a proverbial race to the bottom on pricing.

Since 2016, generics have seen price erosion in excess of 50 percent. The razor-thin margins resulting from these dynamics trigger a host of dire consequences, from discouraging quality investments to spurring widespread outsourcing, including to China. Moreover, the generic drug maker exit rate currently exceeds the rate of entry, and upwards of 40 percent of generic medication markets are supplied by a single manufacturer.

Rather than reduce shortage risks, unfortunately a number of government policies make them even more pervasive. And worse, Medicaid's inflation-based rebates, for instance, can trigger massive uncapped losses on even low-cost generics, in addition to requiring literal penny pricing under 340B.

These and other price-control policies warrant serious scrutiny in the context of generic products, especially for sterile injectables, which carry high production costs and offer minimal return. More broadly, our reimbursement systems, including under Medicare, offer little opportunity or incentive for drug makers to compete on dimensions other than price, such as reliability and resiliency.

The House Energy and Commerce Committee's comprehensive work on this issue thus far is welcome. Enacting effective legislation will necessitate bipartisan and bicameral collaboration. The Finance Committee can build on our strong track record of solutions-oriented policymaking to address the rash of drug shortages afflicting families across the country.

Mr. Chairman, before I conclude, I would like to ask unanimous consent to enter a statement from the Community Oncology Alliance into the record.

The CHAIRMAN. Without objection, so ordered.

[The statement appears in the appendix beginning on p. 61.]

Senator CRAPO. This statement highlights the grave risks posed by shortages for those seeking cancer care. With that, thank you to our witnesses for being here today, and thank you, Mr. Chairman.

[The prepared statement of Senator Crapo appears in the appendix.]

The CHAIRMAN. I thank my colleague, and I think this is another issue, along with the work we have been doing on the PBMs and other matters, that is ripe for a bipartisan effort, and this would respond to both patients and taxpayers. I look forward to working with all my colleagues on it.

We have an excellent panel, sort of the NBA all-stars of the field, so to speak. Dr. Inma Hernandez is a pharmaceutical health services researcher and a professor at the University of California at San Diego. Her research focuses on improving medication uses, outcomes, and equity. We welcome you.

Next to you is Dr. Marta Wosińska, a senior fellow with the Schaeffer Initiative on Health Policy at the Brookings Institution.

She is a health economist who specializes in the question of markets—obviously the topic today—and has worked at the FDA, the Federal Trade Commission, and the Department of Health and Human Services.

Then we have Mr. Allan Coukell, vice president for public policy with Civica Rx, president of the Civica Foundation. He started his career as a clinical pharmacist in the field.

And then we have Jason Westin, professor of Medicine in the Department of Lymphoma-Myeloma at the University of Texas M.D. Anderson Cancer Center, and he is director of lymphoma clinical research there at the Center.

So we have an excellent panel. Let's begin with you, Dr. Hernandez, and I know everybody always feels sort of compelled to read every word in their statement. We will make your statements part of the hearing record in their entirety, and you can just take your 5 minutes or so and tell us what is important to you. Doctor?

STATEMENT OF INMACULADA HERNANDEZ, PharmD., Ph.D., PROFESSOR, DIVISION OF CLINICAL PHARMACY, SKAGGS SCHOOL OF PHARMACY AND PHARMACEUTICAL SCIENCES, UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CA

Dr. HERNANDEZ. Chairman Wyden, Ranking Member Crapo, and honorable members of the committee, thank you for the invitation to testify today. My name is Inmaculada Hernandez, and I am a pharmacist by training and a professor at the University of California in San Diego.

Mr. Chairman, I applaud you for holding this hearing. Drug shortages are a significant public health risk of the highest national priority. This year, doctors were forced to ration the use of cancer drugs due to a shortage. This shortage is only one of hundreds that threaten patient access to lifesaving medications.

In the U.S., drug shortages disproportionately affect low-cost generic products. There are many underlying factors contributing to shortages, but the primary drivers are economic and regulatory. My testimony will focus on economic drivers and offer potential solutions.

Generic drugs are equivalent versions of the same product manufactured by different companies. Generally, the pharmacy or the provider can choose any manufacturer's version. The reimbursement paid to the pharmacy or the provider is the same regardless of the generic version selected. As a result, pharmacies and providers are incentivized to purchase generic versions with the lowest acquisition cost. In other words, pharmacies and providers have no incentive to purchase drugs from manufacturers that have more resilient and dependable supply chains.

These reimbursement practices have been crucial to keep costs down in Medicare and Medicaid. However, they have eroded prices, and in some cases threatened market sustainability. Manufacturers lack incentives to invest in dependable supply chains. This is particularly the case for products with limited profitability, such as older but essential generic injectables. They are expensive to manufacture, and their prices have sunk after decades of competition.

Manufacturers respond to decreased profit margins by engaging in cost-containment strategies. These include reduced factory main-

tenance, for example, but also offshoring. Most generic drugs used in the United States are manufactured overseas, primarily in India and China.

Cost-containment strategies, including offshoring, increase the risk of quality issues. Manufacturers in India and China receive the most FDA warnings for violations of good manufacturing practices. Quality issues generate shortages because production must be halted until issues are resolved. In light of these changes, manufacturers may decide to discontinue the production of less-profitable drugs. This contributes to market concentration and limits the ability to respond to supply disruptions.

In summary, we have a drug supply chain that heavily relies on foreign manufacturing. This is a national public health risk. We also have a reimbursement system that fails to reward manufacturers to invest in dependable supply chains.

In some cases, profit margins are so low that manufacturers simply do not have incentives to produce the drug at all. Policy intervention is urgently needed to address these issues. Short-term, the Federal Government should consider funding the reshoring of generic manufacturing. Funding should be tied to supply guarantees and resilience of the supply chain.

In addition, we need to build incentives for pharmacies and providers to purchase drugs from manufacturers with dependable supply chains. This could be achieved through the incorporation of value-based payments, meaning that payments to pharmacies and providers could be higher when they select generics from more dependable supply chains.

Admittedly, these solutions will likely result in increased government spending. This spending is a necessary investment. Without intervention, drug shortages will continue to threaten patient access to lifesaving medications. Just as we invest in building roads and bridges and manufacturing semiconductors, we must invest in generic drugs. It is critical to further our country's health and to protect national security.

Thank you for your attention.

[The prepared statement of Dr. Hernandez appears in the appendix.]

The CHAIRMAN. Thank you very much, Dr. Hernandez. There was a little huddle here because we all think your testimony is so impressive, and we are trying to figure out the next steps. We thank you.

Dr. Wosińska, please, your testimony.

**STATEMENT OF MARTA E. WOSIŃSKA, Ph.D., SENIOR FELLOW,
SCHAEFFER INITIATIVE ON HEALTH POLICY, THE BROOKINGS
INSTITUTION, WASHINGTON, DC**

Dr. WOSIŃSKA. Chairman Wyden, Ranking Member Crapo, and members of the committee, thank you for inviting me here today. My name is Marta Wosińska, and I am an economist and a senior fellow in economic studies at the Brookings Institution. I have been studying drug shortages for over a decade. Much of my work deals with economic incentives that contribute to drug shortages.

In the follow-on conversation, I will be able to speak to drug shortages more broadly, but in my remarks, I would like to discuss

why low-cost generic, sterile injectable drugs are so vulnerable to shortages, and why this committee is well-positioned to address these shortages.

Generic sterile injectable drugs, or what I call GSI drugs, include drugs to treat cancer, crash cart drugs used to treat life-threatening emergencies, morphine, IV antibiotics and IV nutrition, and something as basic as saline and sterile water for injection.

GSI drugs are and have been for years the most common type of drugs to be in shortage. Typically, these drugs represent about half to two-thirds of all shortages. GSI shortages result primarily from manufacturing quality problems at facilities where the final product is made, often in the United States. The resulting shortages generally last months, and more increasingly, several years.

What is vexing about these shortages is that they are largely avoidable. Most of these shortages do not result from external shocks like pandemics or natural disasters, but instead from factors that drive how hospitals buy GSI drugs and the underinvestment in manufacturing operations that follows.

So what are the factors driving which GSI drugs hospitals buy? All payers, including CMS, reimburse hospitals in a way that gives them incentives to use the lowest-priced GSI drug available. These reimbursement mechanisms have a point. After all, two generic versions of the same drug are therapeutically equivalent, and therefore readily substitutable.

But therapeutic equivalence is not the same as reliability of supply. The price pressures put on manufacturers create a dynamic where there is little return on investing in manufacturing facilities, staffing, and oversight. These price pressures are particularly consequential for GSI drugs, because making those drugs requires specialized facilities where employees follow complex manufacturing processes and controls. There is simply less room for error in manufacturing because GSI drugs must be sterile and free of particulates.

As the largest single payer for hospital space and outpatient visits in the U.S., CMS is well-positioned to influence how hospitals buy. If we want to address the persistent GSI drug shortages, CMS will need to pay hospitals differently, incentivizing them to consider reliability of supply in their purchasing decisions.

This can and should be done by rewarding hospitals for buying reliably and for buffering before shortages happen. In my written testimony, I describe in detail how such a program could be stood up. Here, I will only mention that the proposed program builds on and boosts existing tools to assess reliability and efforts to reward supply chain reliability, such as the one that the next witness will discuss.

The program leverages the private sector's ingenuity in developing new tools and creating new contracting models, and the program goes beyond rewarding manufacturing quality. It also provides rewards to protect from other sorts of problems like natural disasters and geopolitical instability. The program also accounts for the differences in the economic environments that different hospitals face, which is really important.

And last but not least, the program can be stood up now, without having to wait for FDA to develop a set of quality metrics. But

CMS does not have the authority to set up such a program, especially one that is not budget-neutral. This committee, however, can grant that authority.

To conclude, I would like to say that this is not the first time we have had cancer drug shortages, and it will not be the last unless Congress steps in to support CMS's role in this space. Getting at the issue through CMS is critical because CMS is much better positioned than FDA to address economics.

For this reason, I would like to again thank Chairman Wyden and Ranking Member Crapo for holding a hearing on this issue. I hope you will consider the recommendations I provided in my testimony, and I look forward to answering your questions.

[The prepared statement of Dr. Wosińska appears in the appendix.]

The CHAIRMAN. Thank you very much.
Mr. Coukell?

**STATEMENT OF ALLAN COUKELL, SENIOR VICE PRESIDENT,
PUBLIC POLICY, CIVICA Rx, LEHI, UT**

Mr. COUKELL. Chairman Wyden, Ranking Member Crapo, and members of the committee, thank you for holding this important hearing on the pressing issue of drug shortages. My name is Allan Coukell. I am a pharmacist by training, and I lead public policy for Civica, also known as Civica Rx.

Civica is the only pharmaceutical company established specifically to address drug shortages. It was founded by a group of U.S. health systems and philanthropies who, after a decade of shortages, realized that the market is not self-correcting, and that a different approach is required.

They created Civica as a nonprofit with the mission to deliver a safe, stable, and affordable supply of essential medicines to U.S. patients. In our first 5 years of operation, our hospital membership has grown to 1,500 hospitals. We have 80 drugs now with nearly 150 million vials delivered. And with U.S. Government support, we have built a state-of-the-art injectable drug manufacturing facility in Petersburg, VA.

Civica drugs are not chosen for their return on investment; they are chosen by hospitals because they're in shortage or at risk of being in shortage. They tend to be old and low-cost, but absolutely essential and used in every hospital every day to treat patients. Because of our mission, Civica does some things differently from the traditional generic drug supply chain. For example, we enter long-term purchase and supply contracts that add stability to the market. We maintain a 6-month buffer inventory of every drug to ensure continuity of supply. We also emphasize U.S. sourcing whenever possible, with the EU and Canada as our next choice—and we do not source from China unless there is no other option.

To reduce the risk of a failure to supply, we perform an intensive quality audit of potential suppliers and ongoing quality reviews, and every drug is sold at the same price to any purchaser. The success of the approach has been proven. In fact, 20 of our top 25 products are currently in national shortage, and yet we are supplying a number of hospitals without interruption.

When a tornado hit a generic drug manufacturing plant in North Carolina a few months ago, we immediately let a number of hospitals know that of the 21 drugs we have that overlap with drugs from that facility, we would be able to supply double their committed volume. And a recent peer-reviewed study found that supply through Civica is not only more reliable than conventional sources, it also produced net cost savings. So, the resilience of this model points to steps that this committee could take to prevent future drug shortages.

And make no mistake; shortages are not a passing storm that will soon blow over. After a dozen years, they must now be understood as a built-in and permanent outcome of our current system. The U.S. system is designed so that purchasers of drugs are incentivized to choose the lowest price, saving pennies on already low-cost products instead of purchasing in a way that makes shortages less likely.

Civica's member hospitals have already taken steps to shift the equation, but many others have not, and without action, things will get worse. The immediate cause of most shortages is quality problems in the manufacture of the finished dosage form, but the root cause, as we have said, is low prices.

To put that in perspective, a vial of sterile injectable medicine typically costs less than this cup of coffee that I bought downstairs this morning. So this reduces the incentive of manufacturers to invest in quality or newer manufacturing facilities. Low prices push production offshore to low-wage markets where quality problems proliferate and the FDA presence is less consistent.

Finally, it takes time to ramp up pharmaceutical production. So, when one manufacturer leaves the market, we are facing a shortage, even if there are other manufacturers that already have FDA approval to make that drug.

So, policy responses to reduce shortages should include measures to incentivize or encourage providers to contract for adequate buffer inventory, purchase from manufacturers that are less likely to have quality failures, and enter long-term contracts that bring stability to the market.

We also encourage Congress to work directly with manufacturers to create an insurance policy. For the cost of about \$4 million a drug, Congress can ensure that we have backup domestic manufacturing capacity ready to go when a shortage starts. And how smart would we feel today if 5 years ago we had made this investment in cancer drugs, and we were prepared for the shortages we are experiencing now? A timely investment will provide a cost-effective insurance policy for the future.

Thank you again for your attention to this topic and for the opportunity to be here, and I look forward to your questions.

[The prepared statement of Mr. Coukell appears in the appendix.]

The CHAIRMAN. Thank you very much.
Dr. Westin?

**STATEMENT OF JASON R. WESTIN, M.D., MS, FACP, DIRECTOR,
LYMPHOMA CLINICAL RESEARCH PROGRAM AND SECTION
CHIEF, DEPARTMENT OF LYMPHOMA AND MYELOMA, M.D.
ANDERSON CANCER CENTER, HOUSTON, TX**

Dr. WESTIN. Chairman Wyden, Ranking Member Crapo, and members of the committee, it is my pleasure to appear before you to discuss the drug shortage crisis facing our patients. I am Dr. Jason Westin, professor of medicine, and director of lymphoma clinical research at M.D. Anderson Cancer Center in Houston, TX.

Today I am speaking on behalf of the Association for Clinical Oncology, or ASCO, the leading oncology professional organization, representing nearly 50,000 oncology professionals dedicated to improving cancer care. We deeply appreciate the committee's bipartisan dedication to addressing the root causes of drug shortages.

I am here to provide a firsthand account of the challenges faced by cancer patients and their health-care providers from oncology drug shortages. This crisis impacts whether patients receive life-saving and life-prolonging oncology drugs as intended, or are forced to receive suboptimal alternatives, reduced doses, delayed treatments—or worse, not receiving our best therapies.

Many of my colleagues have been forced to make impossible choices, including to choose which patients will be prioritized to receive potentially curative therapy. When physicians must use treatments that may not be standard of care, prior authorization, already an untenable burden, becomes even more intrusive. Patients and their families look to us as a trusted source, and we are left with no explanation.

In 2022, I encountered a shortage of a drug called fludarabine, a cheap and generic drug initially approved over 30 years ago. Fludarabine is not the most common drug anymore, but it is an essential component of CAR T-cell therapy, an almost science fiction-like technology that weaponizes a patient's own immune cells to fight their cancer and hopefully eliminate their cancer, which can sometimes cure patients of otherwise fatal cancers.

The effectiveness of CAR T-cell therapy, however, is dependent upon being given with fludarabine, and unfortunately there are no proven alternatives. My patients with rapidly progressing, relapsed aggressive blood cancers usually only get one shot at CAR T-cell treatment, because they may be too sick to try again. And with shortages, I do not know if CAR T-cell will work without fludarabine, and I cannot wait to try when fludarabine is back in stock.

In other words, the absence of a generic and cheap drug like fludarabine literally can be a difference between life and death. I recently treated a young mother of three with cancer that grew despite multiple lines of treatment. Contemplating hospice care, she received CAR T-cell therapy and now is in a long-term remission, offering her the potential for decades of life, and her children the security of having their mom alive and well.

Her story and countless others like it would not be possible without drugs impacted by these shortages. We know how to treat cancer, but shortages force impossible choices. We have drugs that are lifesaving and shortages that are life-threatening.

The U.S. needs a more robust drug supply chain to avert future shortages of key medications. Most oncology drugs in shortage are

older generic injectables that typically experience slim or sometimes negative profit margins. The leading cause of shortages is manufacturing quality issues, and correcting these can be expensive, leaving manufacturers shuttered for months or deciding to leave the market altogether.

Quality issues in one company can impact and have a domino effect on the entire supply chain. Current drug payment policies can compound quality issues, as purchasers have limited information, typically only price data, and do not have access to quality or supply information. This creates incentives for manufacturers to prioritize cost-cutting over quality improvements.

The current Medicare payment system bases drug reimbursement on average sales price plus 6 percent, which may result in artificially low reimbursement because of delays in updating ASP. This creates barriers for new manufacturers to enter, for production increases, and for correcting quality issues. Congress should consider alternative payment methodologies that would provide immediate relief from artificially low rates and encourage a more reliable supply of drugs.

CMS is constrained in how it pays for drugs, but it could use demonstration projects to set a reimbursement floor on shortage-prone critical drugs, could investigate tying increased reimbursement to guaranteed supply, or could leverage the FDA's pilot program, which promotes quality manufacturing and reliable drug supply.

There are existing examples of purchasers that were willing to pay increased prices for a return on guaranteed supply. Policymakers can incentivize drug suppliers that make changes by promoting advanced manufacturing technology and continuous manufacturing for critical drugs, by considering coupling enforcement mechanisms to existing risk management requirements, and by incentivizing purchases to favor manufacturing of reliable supply.

HHS could incentivize a private-sector reserve of essential medications, medical devices, and supplies. These proposals should be implemented in a manner that avoids hoarding or creates additional shortages or supply chain challenges, and includes consideration of the unique need of independent and private practices.

We recognize concerns around increased cost, but we will pay a greater long-term cost in the form of delayed or denied care if we do not address underlying economic forces driving shortages of generic drugs.

In conclusion, we at ASCO applaud the committee's effort to enhance the pharmaceutical and medical supply chain, to protect our Nation's most vulnerable patients. The shortage of critical cancer drugs is an urgent crisis, and we stand ready to collaborate with you to advance comprehensive solutions that ensure Americans with cancer receive lifesaving and life-prolonging treatments, to help end these life-threatening shortages. Providers should not have to make impossible choices about patient care.

Thank you. I look forward to your questions.

[The prepared statement of Dr. Westin appears in the appendix.]

The CHAIRMAN. Thank you very much, and all of you have been excellent.

I want to start with you, if I could, Mr. Coukell. I mean, you tell an incredibly important story. You talk about how, somehow you are able to get help to people even in this whole bedlam, as I described, of shortages, and yet your membership, your hospitals, you have been able to continue to meet their needs.

I think I would be interested in your thoughts if we were to—and we are going to work on this in a bipartisan way, so we are going to try and get as many ideas as we can out there. If we decided to direct Medicare to pay separately for sterile injectables, do you think that would give us a chance to get those twin objectives: not just price, but quality?

Mr. COUKELL. Thank you, Senator. I appreciate that question. I think potentially—and it would depend on how it was constructed—if the payment increased the provider reimbursement but did not change the incentive to buy below the reimbursement level, then you would have the effect of increasing the spread or the margin without really shifting the purchasing patterns that are driving shortages in the first place.

But if that reimbursement that you are talking about was tied to some of the shifts that many of the witnesses have talked about today, in terms of laying in extra inventory and selecting manufacturers that are less likely to have a shortage, you could see it having exactly the desired effect.

The CHAIRMAN. Good.

Dr. Hernandez, you basically, in a very impressive presentation—I gather you are coming out today with an analysis that will be in the *American Journal of Medicine*, is that correct? So we can talk about that and what you have shown about price gouging and the like.

But you believe—according to your testimony, you want to tie a lot of the reforms to value-based purchasing, which strikes me as an appealing idea. Can you give us a little bit more detail about how we might go about doing that? I know that time is short and we cannot get into lots and lots of information.

But I would just be interested in a little bit more information about your theory of tying this to value-based purchasing.

Dr. HERNANDEZ. So, I think the idea could be to tie the reimbursement to the provider on the quality and the resilience of the supply chain of the manufacturer selected; meaning, right now we are picking an average sales price. The average sales price is a weighted average of all generic and other versions for a product, right?

Providers are incentivized to buy at the lowest acquisition cost. But maybe you could still pay based on average sales price, but do something like average sales price plus 20 percent if you use the injectable drug manufactured from a manufacturer that has five out of five stars in resiliency of the supply chain.

That could need separate reimbursement, because most generic injectable drugs, which as we heard, are most prone to uncertainties, are reimbursed under Medicare Part A, and in some cases under Part B. But in Part A, they are not paid separately, meaning that the hospital gets a bundled payment for all of the services under the hospitalization.

If we want to pay more for drugs that get manufactured from resilient supply chains, we also need to apply that modifier to a drug claim level that I think would probably need separated reimbursements. So it is pretty much aligned with what Mr. Coukell said.

I think separate reimbursement would work, and we could attach to that a value-based modifier, meaning a percent increase based on how resilient the supply chain is of the generic version selected.

The CHAIRMAN. So, let me just use the rest of my time on this question of the price gouging and the middlemen markups on generics, and we will just throw this open to any panel member. *The Wall Street Journal* recently reported that PBMs mark up prices of generic medicines by hundreds, sometimes several thousand percent higher than the price paid to the pharmacy.

The markups jack up costs, leaving taxpayers to foot the bill, and do not do anything to help prevent drug shortages. I would be interested in what this panel thinks we ought to be doing as part of our efforts here to rein in this price gouging by middlemen, specifically on generics? I gather that Dr. Hernandez's study is going to come out today, be peer-reviewed, be more extensive.

So I think we know what the problem is. Why don't we get Dr. Wosińska—I know that you are an expert in this field and have background in government. Why don't we start with you? But I would be interested in what the four of you think, for my last question, we ought to be doing with respect to price gouging here. Doctor?

Dr. WOSIŃSKA. So, price gouging in the context of drug shortages happens more with the gray market, when the drug is in shortage and then hospitals are really desperate and trying to get product in hand. So I think this is how I could tie price gouging to shortages.

But perhaps I could speak to the role of PBMs in this sort of dynamic, and price pressure more broadly. So PBMs are vertically integrated with mail pharmacies and also with specialty pharmacies. And so, just like all pharmacies, they also, just like hospitals, try to buy the least expensive therapeutically equivalent product possible.

So in a sense, through the pharmacy channel, they are very much contributing to the downward price pressure. They don't really play in the generic sterile injectables space, but they very much contribute to the sort of price pressures in the oral dose products. And there again, there is no mechanism, there is no weight to put in place, really, on reliability of supply.

The CHAIRMAN. Let me just, because I am over my time—Dr. Hernandez, your thoughts on that. You know, what is going on here in the generic market? What can be done to rein in the middlemen?

Dr. HERNANDEZ. Let me just briefly summarize the findings of the paper, so that everyone is on the same page. So we just looked at the reimbursement rates paid by the six leading organizations in Medicare Part D for the top 50 generic drugs by Medicare spending.

We found 16 drugs reimbursed by at least one Part D organization at a markup of 1,000 percent or higher, okay? For instance,

I have here an example for you. Aripiprazole is an antipsychotic drug. The pharmacies paid an average of 17 cents per tablet.

Rite Aid—and when I say Rite Aid, I mean the PBM, not the pharmacy chain, because Rite Aid is also a PBM that offers Part D plans. So, Rite Aid paid pharmacies \$11.7 per tablet. Again, the price was less than 17 cents. So we are talking here about a 7,000-percent markup. CIGNA reimbursed pharmacies at \$4.6 per tablet, or a 2,700-percent markup. CVS Health had reimbursement rates that were very similar, so we are not just talking here about Rite Aid PBM.

These practices are concerning, because if patients, let's say, had a 30-percent cushion on the aripiprazole, they could pay 30 percent of the inflated amount. So they end up paying much more than actually the pharmacy paid for the drug, let alone what the manufacturer got for it.

So in summary, I think the way we pay for generics needs reform, because on the one hand, we are failing to incentivize manufacturers to invest in resilient supply chains. On the other hand, on the Part D side, we are allowing intermediaries—and by intermediaries, I mean PBMs—to inflate the cost of drugs without justification, which ends up in seniors paying more.

I truly appreciate the efforts, and I applaud the efforts of the committee to look at PBMs earlier this year, and I think the legislation that you put together has a major impact for making a difference.

The CHAIRMAN. We will be able to ask you more in the future, and you have been helpful. Thank you.

Senator Crapo?

Senator CRAPO. Thank you very much, Mr. Chairman. And again, thank you to all our witnesses for the expertise you bring to us today, and let me tell you the issue that I am focused on. Every one of you has made the point that one of the big problems here is that we do not compensate for quality of product. We compensate for price of product only.

And I get that. What I am trying to figure out, given the fact that we are talking about Federal Government-administrated payment systems, is who is going to decide—if we get a solution here, who decides which products are worth more compensation?

Dr. Hernandez, you said that maybe there should be a 20-percent markup compensated by us for those that got four stars. Who decides who gets four stars? Do we want to have a Federal Government agency evaluate every generic provider and decide? I personally have a little bit of trouble with that.

The hospital or the doctor who is providing or prescribing the medicine should be making that decision, but they are going to choose the one that they get the compensation for in a system where the government is paying the compensation. How do we incentivize the doctors or the hospitals to make the proper choice, and not create a Federal Quality of Generics Agency at the Federal level?

I hope you understand my question, and you raised your hand, Dr. Wosińska. Why don't you go ahead, and then Mr. Coukell and anybody can jump in?

Dr. WOSIŃSKA. Yes. I would love to speak to this. So there have been a number of proposals, and actually, if you look at the proposal that I put out earlier this year, I would like FDA to continue with the steps that they have been taking to develop metrics to ascertain whether a facility is following good manufacturing practices, and quality maturity.

But to really expect that FDA is going to be able to do it for all drugs would require incredible resources and many years. Even if we were to zero in on just generic sterile injectables, at this point we probably would be waiting several years, and we still do not know whether the program they would stand up and the metrics they would stand up would do exactly what we want them to do.

So the reason why my proposal is somewhat different is—I do think that those kinds of metrics could be built in, but I very much believe that a pay-for-performance program for hospitals, rather than an add-on or payment adjustment, is the way to go.

You can basically ask hospitals to look back at the end of the year. There are usually 30–40 shortages each year, and at the end of the year you basically ask them: how did you do in terms of preparing for these shortages? They do not know which shortages, but the idea is to sort of have them be thinking about which suppliers are more reliable, and be thinking, who did you buy from? Did you buy from Intas, which caused the shortage of cancer drugs, or did you buy from Fresenius Kabi?

And there is enough information out there already that hospitals—actually not hospitals. I actually should say, I do not expect hospitals to be doing the homework. Their GPOs are currently doing a lot of that homework, but they are not incentivized to use that because hospitals still want to buy the cheapest. So there are a lot of elements in place. Civica for example, Civica's program would do really well in this case.

And so, the idea is to look back and then score the hospitals. Did you pick right, where you buffered your inventory before there was any sign of shortage? It would really drive the development of tools, and then basically the idea is to have an add-on, compare hospitals, just like with a value-based payment program. Compare hospitals—so you look at Mayo Clinic and Intermountain. Who did much better here? And then there would be a payment adjustment at the end of the year, where CMS would basically reward the ones that are doing better. And you do not need FDA metrics to stand it up. We can stand it up now.

Senator CRAPO. All right.

Mr. Coukell?

Mr. COUKELL. Let me add a couple of points. One, we do not have to shift 100 percent of the market. We just need some big chunk of the market to shift toward more reliable supply, to give us that resiliency and redundancy that we need.

And number two, most purchasing is not done by individual small hospitals. It's done by big organizations on behalf of hundreds of hospitals. So these are sophisticated organizations that can do it. Civica's a small company, but we have a process for qualifying and validating our suppliers.

It would be useful if the FDA's quality metrics program were out and ready, but even absent that, if we create the market, create

the incentive for the private sector to choose quality, then I think various private-sector solutions will emerge to evaluate the quality of different manufacturers and make that choice.

Senator CRAPO. Thank you. I see my time is up. I would encourage both of the witnesses who did not get a chance to address that to please send us any written response to that, if you feel you have something to add. Thank you.

The CHAIRMAN. And thank you, Senator Crapo. This whole question of pay for performance, we can look forward, we can look backward, but we need more information on it. So I share Senator Crapo's views.

Senator Stabenow?

Senator STABENOW. Well, thank you, Mr. Chairman and Ranking Member, and thank you to all of you. And I appreciate what Civica is doing right now in looking at how we tackle this.

This is such a complicated issue. It is not just in what is happening in supply chains and so on, but price. And if you step back and look at the whole thing, it starts with taxpayers of this country giving hundreds of billions of dollars to drug companies for basic research.

We fund the basic research in our country for whatever is done in prescription drugs and so on, and then we allow write-offs for additional efforts in terms of putting together commercialization and so on. And then we have a situation where, in the interest of cheaper costs, those companies then go to India or China to be able to produce these drugs.

There is something wrong with this picture on multiple levels, as well as just, how do we incentivize? I mean, I think from a big picture perspective, there is a public interest, because this is medicine. It is about curing cancer. It is about making sure medicine is available.

So there is a public role, which means there is a role federally for us. And we did a piece of that last year in saying insulin—\$10 to produce, hundreds of dollars for someone to actually get it who is a diabetic—and we capped it for someone on Medicare at \$35 a month in the public interest, to help people get a lifesaving drug that frankly was over 100 years old.

And so we did that. We have looked at other pieces on the pricing side, but we know it is not enough if it is affordable. It has got to be available, and that is what today is about. Is it available? And so, I very much appreciate that first step the Biden administration is taking, looking at supply chains as it relates to drug shortages, taking action through the Defense Production Act.

That is one of the ways we have to be able to do that, which is important. In addition to that, essential medications, investing and including \$35 million to produce key materials for sterile injectable drugs, again I think in the public interest.

And we all know—we have been talking about it today—how important those medications are. And they are focused on a supply chain resiliency and shortage program with a coordinator and so on.

So all of this is very important to all of these pieces, and it is complicated. I mean, we certainly want to incentivize the right thing, and we're not interested in just giving more dollars to the

drug companies, who are already pricing folks out of their ability to get their medicine. But I do think within the system, we need to be trying incentives and so on.

Dr. Hernandez, I wanted just to ask you, back when we did the Affordable Care Act, there was language I put in there based on work done at the University of Michigan on value-based purchasing. Actually, it is in the ACA.

I do not know if you have looked at that or at any way to use that kind of language, even on what you are talking about, because value does matter. It is not just the cheapest medicine. Anybody getting health care will say, "Oh, just give me the cheapest, you know, give me cheap."

You want the best in terms of value and so on. But we did take some steps to try to signal that, and I do not know if you have looked at all at that language.

Dr. HERNANDEZ. I think we have done that in other sectors of health care, but not precisely on purchasing of generic drugs, which is where we have shortages.

Senator STABENOW. Yes.

Dr. HERNANDEZ. So I agree. I think we need to maybe apply that philosophy of paying for value, that I agree has been very well developed at the University of Michigan by a group of colleagues. So we need to apply that to the purchasing of generic drugs.

Senator STABENOW. Right. Thank you very much.

And let me ask, on supply chains and improving quality, Dr. Wosińska, let me ask—you talked about the shortages being caused by manufacturing quality problems. Can you talk a little bit more about what investments drug manufacturers could make to prevent frequent quality issues? Talk a little bit more about that.

Dr. WOSIŃSKA. So that is challenging. I mean, I can make a very long list of the things that they could do. They just do not have an incentive to do it. So that's where the struggle is. If you look at where drug shortages tend to happen, the reason why it's generics versus brands—so, I should say branded drugs do go into shortage sometimes too, but actually frequently it's because they have a really unexpected dynamic, such as all the GLP-1 inhibitors right now. Everybody wants Ozempic. They just cannot keep up with manufacturing, so this is a massive demand increase. And for generics, the margins are so small, there is no buffering. So a brand manufacturer will have dual suppliers. They will carry more inventory. They will take a lot of steps to buffer this.

There are a lot of things that I could list, but again, there just is not an incentive, and the incentive trickles down. If we were to put more requirements on these manufacturers, a lot of them would leave the market. So it really needs to come from thinking through the buyers, and sort of having these pooled strategies.

There are ways also to have the government support, but again, the market is not functioning in a way that we want it to. If we want resilience, we will have to pay for it one way or the other. That is the unfortunate truth on that.

Senator STABENOW. Thank you.

Thank you, Mr. Chairman.

The CHAIRMAN. I thank my colleague.
Senator Cassidy?

Senator CASSIDY. Yes. Now, Dr. Hernandez, thank you for including the references—and I want my colleagues to listen to what I am about to ask. In your reference No. 7, you speak about how PBMs are paying pharmacies much higher than their acquisition costs, a thousand times more, but then they are potentially clawed back.

What I have learned is that the Health Savings Account—from Obamacare—covers both the pharmaceutical benefit and the medical benefit. And so, the way this is structured, they are really using theoretically—the PBM—that HSA as a piggy bank to drain from the patient in order to claw back and put more money in their pocket. That is a reasonable scenario of what is happening, correct?

Dr. HERNANDEZ. So the problem is that the clawback data are confidential, so—

Senator CASSIDY. I understand that.

Dr. HERNANDEZ. Yes, yes, yes. So it does not have to be about the Health Savings Account. It can also be about the payments paid out of pocket in cash. So I think that the—

Senator CASSIDY. Either way, one fix of this is if we make the Health Savings Account only for the medical benefit. It would eliminate the incentive to charge a high markup fee relative to the acquisition cost. Whether that is occurring or not, it will eliminate that incentive, and that is something that this committee can do. So we can talk about that more, but—

The CHAIRMAN. I think Dr. Hernandez wants to respond again.

Dr. HERNANDEZ. I disagree with you, Senator. I do think we need to prevent these markups. I think they should be prevented through increased oversight of the PBMs, because the problem with excluding the pharmacy benefit from the Health Savings Account is that then patients may not be able to use it for things like expensive drugs for cancer, and I think that is concerning. Because if you think about it, the big, the more expensive drugs, are branded drugs, right, and then there are also generic drugs. So I think—

Senator CASSIDY. So the alternative would not be to make the patient pay for it out of pocket. The alternative would be to have it covered under the medical benefit.

Dr. HERNANDEZ. But the drugs that patients pick in the pharmacy are covered under Part D. There are like oral expensive drugs—

Senator CASSIDY. I get that. So, let's just talk about that, because it does seem as if the HSA—and this is not Part D; this would be commercial insurance. The HSA component of this—which I think our committee governs—HSA not health, needs to be examined, because I actually think that there is a negative incentive in order to use that as a piggy bank. But we can talk about that offline.

Dr. Wosińska, one thing: in Youngsville, LA, based on a grant from BARDA, they are making low-cost N95s and sterile gloves. But the cost of that is still not competitive relative to China.

Now I like your thing here, and again for my colleagues, I think I am going to highlight on page 7, your third paragraph, that we strengthen sections—and I will not go through that—of the Social Security Act, in order to actually increase the amount that CMS re-

imburses for this acquisition. Can you speak about that, because in your testimony you did not delve into that that much?

Dr. WOSIŃSKA. That's right. Thank you for the question. So CMS does have a tool where they are able to step in in some cases. It is not a particularly well—it is not at all a tool suited for rewarding reliability, because CMS would have to know who is reliable.

But it is a really good tool, for example, that was used with N95 masks, where CMS wanted to reimburse hospitals for purchasing domestic ones. So, this could be very much a national security-type scenario where the government decides we need to subsidize certain products.

But the problem is, the way the statute is structured, that CMS can only reimburse the IPPS or OPSS share. So, let's say that I am a hospital. I am going to buy—I have a choice of buying \$1 masks or \$2 masks—

Senator CASSIDY. Or a little bit more expensive generic, domestically produced mask versus one produced overseas with unknown reliability.

Dr. WOSIŃSKA. That's right. But if there is a price difference, I am only going to get reimbursed for half of it, or if I am doing—my IPPS is half. And that makes no sense as an economic agent. I am not going to do it. I will have to spend twice the amount of money that I am going to get reimbursed for. This committee could close that gap and think of certain situations where—

Senator CASSIDY. So, let me stop you, because I think you have made the point. But you do not want to continue to prop up an inflated price. In Youngsville, they are continually putting in efficiencies to lower their net cost. And so, how would you structure this so as to continue to incentivize lower costs for domestic production?

Dr. WOSIŃSKA. Yes, that is actually really important. This is, I think, where it should tie in with HHS's supply chain coordinator role. If we are going—CMS does not know which products would, for national security reasons, need to be propped up, right? They need to be told that. There needs to be an assessment of what is vulnerable to geopolitical risks and what is not.

And so, in a coordinator role like this, they can also be assuring that if there is only one domestic manufacturer, that they are not going to start charging \$1,000 per piece if the government is going to fully reimburse it. So, they could have contractual agreements on the front end, that if you are going to participate in this program, we are going to make sure you are not going to jack up the price.

Senator CASSIDY. Sounds great. And could I have the indulgence to have one more question of Dr. Westin?

The CHAIRMAN. Yes, yes, yes.

Senator CASSIDY. Dr. Westin, you talk about how do we reimburse more for certain drugs in order to—the same sort of thing. You have to have a pull-through. You may have a domestic manufacturer, but you have to have a pull-through. When I was in the House back in 2012, I introduced the Patient Access to Drugs in Shortage Act—and my bill was never adopted.

I changed the Medicare reimbursement rate for generic injectable products with three or fewer active manufacturers from ASP plus

six to wholesale acquisition cost. And we also exempted generic injectable products with three or fewer active manufacturers from Medicare rebates and 340B discounts.

One of you mentioned 340B discounts may give the purchaser the drug for pennies, and it is hard to believe that that is acquisition cost for an injectable. Any thoughts about my proposed legislation, knowing I have a pride of authorship—but nonetheless it seems still like a good way to go?

Dr. WESTIN. Senator Cassidy, thank you for the question. I would be happy to provide more answers to that in detail offline, because I know we are past time. But I think it makes sense in general, the idea of being able to look at these drugs in shortage, and being able to perhaps call out these drugs specifically to have a different reimbursement mechanism, such that they are not pennies on the dollar, as you said, and basically having a race to the bottom cost-wise.

So I think that your bill—I am not familiar with the specifics of it, but I am happy to look at it and get back to you.

Senator CASSIDY. And the question for the record that will be for you all, is to what degree, if we exempted these drugs from 340B and Medicaid rebates, how that would potentially benefit the overall industry. Is that enough of a market share—and I think it is—that it could actually increase the profit margin to continue production?

With that, I yield.

The CHAIRMAN. I thank my colleague, and I want to get more of an understanding, because my colleague knows I very much like working with him.

On this HSA point, it looked to me like what Dr. Hernandez was saying is, the patient is going to eat the cost one way or another. They are going to eat it out of pocket or they are going to eat it through the HSA. So let us just work together—

Senator CASSIDY. And that is assuming that it is subject to the deductible. If it is not subject to the deductible, then it would not be an issue.

The CHAIRMAN. We will follow up with you and talk about this.

Senator MENENDEZ?

Senator MENENDEZ. Thank you, Mr. Chairman.

Dr. Hernandez, in the market for generic drugs, sellers compete primarily on price, creating what I believe is a race to the bottom. Research has shown that the lowest-priced generic medications carry a substantially greater shortage risk.

In the face of narrow margins and declining profitability, some manufacturers exit the market for certain drugs or shut down entirely. Do you agree that the race to the bottom pricing is a driver of prescription drug shortages?

Dr. HERNANDEZ. I do. I think your summary was very complete. As I said, I think drug shortages have economic drivers behind them, where the race to the bottom is one of them. The race to the bottom has been key also to keeping costs down in Medicare and Medicaid, and enabling affordability of generic drugs.

But in some cases, it has to do with the market accessibility, as particularly is the case of generic injectables. So I very much agree with your statement.

Senator MENENDEZ. Yes. Now, wholesale distributors purchase drugs from manufacturers. They store them. They sell drugs to pharmacies and clinicians. These ventures collectively account for an estimated 90 percent of all domestic generic drug purchases, and they leverage their market power to serve as price-setters for generic products.

Do you agree that increased concentration among drug purchasers, such as wholesale distributors, is a factor in driving race-to-the-bottom pricing and making our supply chains more brittle?

Dr. HERNANDEZ. So, we have concentration in two entities on the purchasing side: wholesalers and group purchasing organizations. Both of them are highly consolidated, with only three or four accounting for the majority of the market.

Now on the wholesaler side, we have wholesalers buying generic drugs from manufacturers for basically like one-third of the country because of the consolidation. That means that only manufacturers that can produce a large enough volume are competitive to being what we call preferred list of wholesalers. So that also leads to concentration on the manufacturing side.

Now, on the group purchasing organization side, these entities—which are also very consolidated—aggregate purchasing power across pharmacies, hospitals, health systems, et cetera. They contribute to the race to the bottom because they are negotiating these contracts on behalf of a large number of members. But I just wanted to differentiate that there are the two types of entities.

Senator MENENDEZ. Okay; I appreciate that.

Dr. Wosińska, as we have heard, the generic drug market is one that largely encourages competition on price alone. This makes it challenging for generic manufacturers to invest in additional capacity, manufacturing upgrades, and quality control. As a result, manufacturers can experience quality issues that result in facilities going offline or drugs being discarded. Further, generic drug purchasers appear to have limited information about manufacturer and facility quality management.

Are there sufficient financial incentives for generic drug purchasers to prioritize quality and reliability in their purchasing decisions, and if not, what financial incentives should we be considering?

Dr. WOSIŃSKA. No, there definitely—the market does not reward reliability. I think it can be done on both sides. Definitely, it needs to be addressed through the buyers to change the weight that buyers place on reliability. That by far is the most important thing.

There have been a number of proposals, and in some of my work, I have also proposed that we do also direct investments and provide forgivable loans to help build up the infrastructure and to help manufacturers directly get up to par. But that will not change anything if there is still the race to the bottom.

So, until we actually address how the buyers buy and what they weigh, we are not going to make much progress. But if we start rewarding reliability, and manufacturers can maintain actually a higher price point because it is rewarded—that reliability—then there is going to be an incentive that will follow.

Senator MENENDEZ. All right.

Finally, for anyone on the panel: for many drugs, Medicare is the largest payer in the United States. Medicare Parts A and B typically reimburse providers for inexpensive generic drugs as part of a bundle of services and supplies, rather than on an individual drug basis.

By design, these bundled payments increase downward pressure on pricing, and these cost constraints impact contractual pricing arrangements across the supply chain. Are there payment and contracting reforms that can enhance predictability and stability with respect to generic drug pricing payments and volume commitments?

Dr. WOSIŃSKA. So, if I could actually speak—earlier there was discussion around unbundling payments and to what extent that would help. I just would like to emphasize that unbundling will help, again, if the price becomes a signal of quality. And you know, just unbundling is not going to solve this problem.

And the other witnesses spoke to that. So the question is, can we get reliable measures around what is reliable? And if you—I have more detail about it in my testimony, but I believe that if we wanted to wait, especially for generic sterile injectables, for FDA to develop this, it will take time.

But I think there are other ways for us do it through a pay-for-performance program, to engage hospitals in trying to do a better job of doing this homework, actually through the GPOs, because the GPOs are actually in a very good position. They already look at supply chains and the reliability of supply chains.

They are just not being rewarded for selecting the more reliable manufacturers on their contracts.

Senator MENENDEZ. Thank you.

Thank you, Mr. Chairman.

The CHAIRMAN. I thank my colleague.

Senator JOHNSON?

Senator JOHNSON. Thank you, Mr. Chairman. I think we need to focus a lot more on the root cause of this problem, and we are getting close to it. I think a number of the witnesses have said it is, you know, the low prices; it is the race to the bottom.

I think you have to find out what is causing that. Now, I have not heard the words monopsony purchasing power yet, where you've got basically the Federal Government, with the drug formulary, pretty well driving most of these prices. I would ask the witnesses, can you think of a common consumer product that is always in persistent shortages? Can anybody think of one?

You know, there may be some, but the reason there are not is you have millions, billions of consumers, and the marketplace takes care of all these problems. It demands higher quality. It demands better levels of customer service. It demands the best price.

But because we have the Federal Government being involved in the health-care marketplace, it has screwed everything up. Third-party payer systems through insurance are another kind of monopsony-type of purchasing power as well.

So, we need to focus on what we can do to bring consumers back into the process here. I am a manufacturer. I supplied the medical device industry for years. We actually were able to—and our cus-

tomers allowed us to charge—a higher price, to stabilize their pricing over a number of years, but also to ensure supply.

Mr. Coukell, that is basically your company's approach to this. You increase costs by having buffer stock, correct? So you are able to provide a service. You would probably be considered a middleman, and if your company makes any money off this, generally the members of this committee would be criticizing you for skimming off the top and driving up prices. But you actually provide a service, isn't that correct?

Mr. COUKELL. Thank you, Senator. We are a manufacturer, but part of what we do in contracting with hospitals is bypass the middlemen in the transaction. So we work directly with hospitals. We do not go through the GPO contracting process.

Senator JOHNSON. That is a marketplace solution; okay.

Mr. COUKELL. That is a marketplace solution.

Senator JOHNSON. Dr. Wosińska, when we were talking about PBM reform here—and by the way, I am the only one on this committee who voted against what the committee is trying to do here, because I do not understand how it is going to fix any problems.

One request I asked staff was, if this is going to lower prices for consumers, why is big pharma in favor of the PBM reform that they are proposing? Again, we are talking about, right now, shortages caused by a race to the bottom, too low prices.

Isn't it true that PBMs are negotiating lower prices for the organizations they are representing, and it's just not transparent in terms of how those prices benefit consumers, because it benefits them in lower insurance costs and that type of thing. Do you want to respond?

Dr. WOSIŃSKA. Yes. So PBMs really play a role in the oral dose market, not generic sterile injectables. They do not deal with hospitals, and really their role here is because they are a major pharmacy. This is the vertical integration. That is the piece, really not the contracting, but the fact that they own mail-order pharmacies and that they also have specialty pharmacies.

And just like any other specialty, they are incentivized to bring the lowest cost. What they mark up and how this shows up to the patient is the difference there.

Senator JOHNSON. They are bringing—they are putting downward pressure on drug prices, correct?

Dr. WOSIŃSKA. There is downward pressure on the—yes, there is absolutely downward pressure. And just to your previous question, and your previous point about sort of where things break down and why is it that the consumer suffers, I just would like to highlight this.

There are a lot of players in the chain, and each one of them is incentivized very differently, and they do not internalize the harm that results to patients. I will say it is including—you know, if you think about the cost on hospitals from shortages, \$360 million, that is \$60,000 per hospital.

Senator JOHNSON. In a free market, there would not be these shortages, certainly not with generic drugs. It just would not occur. But it is not a free market. Government has interfered and screwed it all up.

One point I want to make is, I think this is an enormous national security threat, the fact that we do not, by and large, produce precursor chemicals; we do not produce the active pharmaceutical ingredients.

I am not for general economic engineering. But in this case, I think we do need buy American provisions. Now again, as you have said, we are going to have to pay higher prices, but one of the reasons you have these huge markups from the middlemen is when you have a shortage.

So, if you did not have those shortages, you would not have those instances where people are responding to the marketplace, driving costs up 1,000 times. If you eliminated the root cause of the shortages—you know, bring back more consumerism, get rid of the monopsony-type of buying power—that would be a solution.

But we do need to address this, and we have not. We had this infrastructure bill. I do not think we spent a penny on trying to bring back the manufacture of precursor chemicals and API to America. That is an enormous national security threat, and we are just ignoring it. Anybody want to comment on that?

Dr. WOSINSKA. If I could speak to this briefly, I completely agree with you that we need to be thinking about sort of the geopolitical threats. Where we face a challenge is with the enormity of this problem. To onshore everything into the United States—I do not know—trillions of dollars?

What we need is to be really strategic about what are the essential medicines and which ones are really vulnerable.

Senator JOHNSON. It would not be trillions. It would not be trillions. Again, the marketplace would respond to it if we allowed the marketplace to do it. But we are not. We are trying to do this through government control, and again, government just screws things up.

Thank you, Mr. Chairman.

The CHAIRMAN. The time of the gentleman has expired.

Senator Carper is next.

Senator CARPER. Thank you, Mr. Chairman. Welcome one and all. Nice to see you.

A question regarding the Medical Supply Chain Resiliency Act. The COVID-19 pandemic taught us a bunch of different lessons, as you know, about the resilience of our Nation's supply chains, especially with respect to medical supply chains. Across America, certainly in my home State of Delaware, we have heard from patients, we have heard from caregivers, we have heard from providers, we have heard from manufacturers about the lack of access to medicine and to medical equipment that impacted their lives.

The aftermath of this once-in-a-generation health crisis emphasized that we as lawmakers, here and across Capitol Hill, need to take action to shore up our access to goods around the world. No one should have to worry about not being able to access a treatment that they need.

That is why I worked with one of our colleagues on this committee from North Carolina, Senator Thom Tillis, to introduce the Medical Supply Chain Resiliency Act. Our bill, as you may know, would give the President the authority to collaborate with other allies across the world to help diversify our supply chains, to increase

access to critical medical goods, and to mitigate the effects of the public health crisis.

Today, the medical supply chain backlog continues to affect access to lifesaving medications, with over 140 medications listed as active drug shortages—over 140 by the FDA. Improving the supply chain resiliency in the U.S. has never been more important.

A question, if I could, for Dr. Hernandez. Dr. Hernandez, in your testimony you emphasize the importance for drug manufacturers to build resilient supply chains. Can you just discuss with us for a couple of minutes how we, as lawmakers, can incentivize drug and medical product manufacturers that invest in secure supply chains?

Dr. HERNANDEZ. Thank you for the question, Senator. I think an idea would be to pay more to providers when they select drugs from resilient supply chains. And there is some discussion about how that could be achieved, in terms of how you could set up the payment system.

But the idea could be to not reimburse always the same regardless of the generic version selected, but rather reimburse more when hospitals, and potentially pharmacies, purchase drugs from manufacturers that have invested in redundancy; in upgrading factories; in upgrading equipment; in having some backup production lines, for instance, if the first one shuts down. So I think that could be the idea.

Senator CARPER. Thank you. Thanks very much, yes.

A second question, if I could, for Doctor Wosińska, a question on lessons learned and capacity building. We have heard discussions that in efforts to produce generic medications as inexpensively as possible, drug makers are limited in their ability to invest in building manufacturing capacity and ensuring quality.

We have seen several instances where demand for a drug is underestimated, and then we are caught unprepared and unable to adequately ramp up production. For example, last fall—and I think last winter—we saw a crisis of children battling an early severe flu season, alongside RSV and COVID-19 surges. Hospitals were at capacity while parents were facing empty shelves where children's over-the-counter fever and pain reducers should have been.

Even members of my staff have shared stories of the fear they experienced while caring for their own children when they became sick with fevers without access to medications as simple as Tylenol. The unexpected high demand for these common medications led to their shortage, and yet they are not included on the FDA's drug shortage list.

It is clear that we need to work together to find a long-term solution to build manufacturing capacity and oversight, and to ensure we have the capabilities to adjust and meet demands as they arise. Here is my question.

I often say that we need to find out what works, and do more of that. In that spirit, what did we learn from the shortcomings like this, and what actions should the Congress, and in particular this committee, consider, in order to ensure that we are prepared for a future crisis that faces such unexpected demand?

Dr. WOSIŃSKA. Thank you for this question. It is a really big question, so I will just highlight a couple of things. So, preparing for a dramatic demand increase, it can be done in two ways. One

is by having inventories of materials or finished dosage product. Another way is to have spare capacity and be able to turn it on quickly.

So those are sort of the two ways in which you can ramp up production, or have technology that is flexible enough that you can sort of switch the line to something else. So those are sort of the ways through which one can prepare for increases in demand.

And that is actually sort of the space where BARDA has been really active, because in a sense, that is what pandemic preparedness is or CBRN threats. Those are all about massive demand increases for products that can occur, which is somewhat different in terms of how we prepare for this than for manufacturing quality problems and the sort of economic drivers that we described.

Senator CARPER. All right. Thank you both; thank you both.

The CHAIRMAN. The time of my colleague has expired. We are going to try to just keep going and get all the way through this.

Senator Blackburn, you are next.

Senator BLACKBURN. Thank you, Mr. Chairman, and thank you all for being here, so that we can discuss this issue.

Vanderbilt is in Tennessee, which I represent. They have been dealing with 175 drug shortages for things that they are needing, and of course we know all across the State, we have different providers that are dealing with this. Now at Vanderbilt alone, more than 100 staff members are engaged in trying to manage and mitigate the disruptions that are caused by the shortages.

Recently, there was an incident that occurred with a vital chemotherapy that highlighted the severity, and the medical center faced the possibility of having to form an allocation committee. And they thought this was going to be a daunting task. Fortunately, a shipment arrived, and so they were able to avert the rationing. But this is something that is becoming all too common with our providers. So we appreciate that you all are here with us today.

Mr. Coukell, I want to come to you. Talk a little bit about how long-term purchasing contracts with hospitals and health systems play a role in prioritizing the production of generic drugs, and what type impact they can have on the drug supply chain.

Mr. COUKELL. Yes, thank you, Senator. If we treat generic drugs like commodities, then the market will function like a commodities market. So, if I want to buy a load of soybeans, I can buy a load of soybeans today and buy from somebody else tomorrow. But it does not create any long-term relationship or commitment between buyer and seller.

When the hospital or the purchaser enters a long-term agreement with a manufacturer, then that manufacturer is going to reserve line space, will know they have a market for that product for a period of 2 years or 5 years or whatever it is, and they will continue to be there to meet the needs of their customer.

Senator BLACKBURN. And then with the model of Civica Rx, talk with me about how that helps to stabilize a supply chain, and the impact that that has.

Mr. COUKELL. Yes, thank you, Senator. So, by having those long-term purchase commitments in place, we are both able to ensure that our manufacturers are there for the long haul, and that we vet them for quality so they are less likely to have a supply failure.

But we also then have predictable demand from the hospitals, because they have committed to a certain volume. And because we have predictable demand, we can then build up a buffer inventory of around 6 months' worth of drugs. We are always selling the older stock and continually replenishing it.

If something happens in the market, either with our own supplier or somebody else, we have a 6-month buffer inventory to continue to supply through that interruption.

Senator BLACKBURN. And to work through it.

Dr. Wosińska, I want to come to you. Do you think, as we are looking at this issue of the unpredictability in the supply chain, it should be mandatory that hospitals develop a plan, a contingency plan for potential shortages, and a management plan for their supply chain of pharmaceuticals?

Dr. WOSIŃSKA. That is an interesting question. I had not thought about a mandate like that. I have really been taking an approach of trying to change the hospital incentives really more through carrots. To have a hospital carry buffer inventory of all the products would be quite a tall order, and not all of them are nearly as vulnerable.

So here again, I think hospitals might be better positioned, and their GPOs, in figuring out what is more vulnerable than CMS coming in and saying "this is essential and this is vulnerable."

Senator BLACKBURN. Okay. So how do—you talk about those incentives. What would those incentives be? How would you encourage hospitals to commit to long-term purchasing contracts?

Dr. WOSIŃSKA. So, the proposal that we have put forward is not as specific as telling hospitals what to do. The proposal that we have is a pay-for-performance program that really looks at two metrics.

Let's say that there was a shortage of a drug. You look back to when the shortage was starting. Who were you buying from? Were you buying from the more reliable one? Oh, you picked wrong. Did you have buffer inventories of this product?

So, it does not really matter whether they had long-term contracts or not. It would encourage long-term contracts. That is how the hospital assures that for their high-risk products, they actually have committed product and they actually can get it from the more reliable manufacturer.

But with this, it is more of an outcome-based pay for performance, rather than, you know, take these behaviors. They have to be 2 years, 3 years. How do we know it is the right length, right?

Senator BLACKBURN. Yes.

Dr. WOSIŃSKA. And I am not sure that CMS is in a good position to sort of really judge all the little pieces of it.

The CHAIRMAN. The time of my colleague has expired.

Senator Tillis is next.

Senator TILLIS. Thank you, Mr. Chairman. I thank you all for being here.

Dr. Westin, not too long ago I voted for the CHIPS Act, and one of the reasons I voted for that is that we need to have supply chain resiliency in the semiconductor space. I think there is an analog here in terms of how we bring back manufacturing to the United

States by itself, particularly for the lower-margin drugs. We have so many obstacles that we have to overcome.

I am kind of curious if you could expand on that. I would see regulatory burdens being one of them. I can see just cost basis here, a lack of tax incentives, those sorts of things. And anyone else who wants to speak up: what should we be thinking about to make either the United States a better jurisdiction to address some of our supply chain vulnerabilities, or friendlier jurisdictions?

I have a particular interest in jurisdictions in this hemisphere; I think Mexico or Latin and South America. But can you give me some of your thoughts?

Dr. WESTIN. Thank you, Senator. I am a cancer doctor and not an economist, so I will defer to some of my panelists here to give some thoughts on that. However, what I would say is that this is an ongoing issue that really does need to be addressed in the way that you are talking about, to have additional resiliency.

So, we look at semiconductors or other national security issues. Not having access to generic drugs in some ways is a national security issue.

Senator TILLIS. Doctor Wosińska?

Dr. WOSIŃSKA. Yes, I would be happy to speak to this. The CHIPS Act is a great example of how something like this could be done. The big difference from semiconductors is that we are talking about 20,000 approved drug products. Each one of them has many phases and many facilities: 16,000 facilities, key starting materials.

So the framework is good, but I think what we need to layer on top of that is really an analytic approach on how we choose what is most important. And in my testimony, I have, with colleagues, put forward a framework for how the government should prioritize which supply chains are important.

I will give you an example. Cancer drugs are not on the essential medicines list, right? So one of the pieces that needs to be thought through again is, what is essential? Another piece is, what is really vulnerable? Going back to trade and so on, we need to be thinking about not just everything in the U.S.—that is not possible—but thinking about potentially friendshoring, nearshoring, and also thinking about full supply chains.

If the Federal Government were to move an API facility, active pharmaceutical ingredient facility, to the United States, but all of the upstream still comes from China and all of the key ingredients still come from China, then what problem did we solve? That is not a good use of taxpayers' money.

So we need to be really strategic in that approach and how we do it, and then we can take the steps that you have taken in the CHIPS Act.

Senator TILLIS. Mr. Coukell?

Mr. COUKELL. Thank you, Senator. I share your concern and desire to see a strong domestic, industrial base for pharmaceuticals. I do think it is helpful to think about what is the problem we are trying to solve. So, if we are trying to solve for long-term geopolitical risk, we absolutely have to think about that whole supply chain from end to end.

If we are trying to solve for the shortages problem that we are experiencing right now, most of the problem is with the finished

product. So there, we have to ensure we have a robust infrastructure to produce that finished product. Once you have a facility there, that can typically make many dozens of different drugs. But right now, at today's prices, few manufacturers can invest the capital required to build a brand-new manufacturing facility.

Senator TILLIS. Yes. Any suggestions on how to fix that?

Mr. COUKELL. Well, in my testimony I start with a very targeted proposal, which is just to say there are certain drugs that we can say with high confidence are going to go into shortage, mainly because they have been in shortage recently. Some of those sell at prices that are so low that no manufacturer in the U.S. could make them competitively and is going to invest in bringing them to market.

At a cost of about \$3 million to \$4 million per drug, we could make sure that there is a U.S. manufacturer that has that product, that has done all the analytics, sourced the API, got the commodity sitting there, has the FDA approval, and when that drug goes into shortage, you could turn that line on and produce that drug in the U.S. That is a pretty cost-effective insurance policy.

Senator TILLIS. Thank you all. Thank you, Mr. Chairman.

I just want to mention something else. Thank you all. We will also have some questions for the record for all of you. But, Mr. Chair, I just wanted to mention, I was very happy to be a part of the bipartisan PBM reform bill that came out of this committee recently.

I am hearing some rumblings that it may get paired with some not-so-popular provisions as it moves through the Senate chamber. I do not know if that is correct, but I just want to lodge my concern, because I really do hope that we can continue to work on getting that through, and getting it over to the House.

The CHAIRMAN. We are going to be focused on getting this passed, and what has put us in this position is working in a bipartisan way, and Senator Crapo and I were just talking about that this morning.

Senator TILLIS. Very good. Thank you. Thank you all for being here.

The CHAIRMAN. I look forward to talking with you.

Senator Brown is next.

Senator BROWN. Thank you, Mr. Chairman.

Dr. Wosińska, thank you for your comments. I want to take off on that, but my question is really to Mr. Coukell. I introduced, with Senators Blackburn and Peters, the RAPID Reserve Act. It would require DHS to award contracts to generic drug manufacturers in order to keep reserves—as you talked about, Dr. Wosińska—of active pharmaceutical ingredients and finished products that we can easily turn to during drug shortages.

We should not—you know this—we should not have to rely on foreign countries, and in many cases foreign competitors, for the drugs Americans rely on. A stronger domestic pharmaceutical supply chain will help to prevent those shortages and those delays; that goes without saying.

Mr. Coukell, you discuss in your testimony a proposal to invest in the domestic manufacturing of essential drugs at risk for a shortage; a similar concept—different but similar to the bill that

we have put forward. Elaborate, if you would, on the benefits of implementing these types of government contracts.

Mr. COUKELL. Thank you, Senator, and thank you for your work with the others that you mentioned on RAPID Reserve. We supported it when it was introduced and continue to support it. The concept there is to have a contract to produce API, to take that through to finished drugs, and as you say, that is quite similar to what I talked about.

The one difference is, what I talked about today, it creates an insurance policy so the manufacturer is ready to produce when the shortage starts, but does not assume that the production is ongoing. But otherwise, they are very similar concepts in terms of creating the readiness to manufacture in an economic environment where otherwise we would not have that.

Senator BROWN. Thank you.

Dr. Hernandez, a question for you, if I could. The U.S.-China Economic and Security Review Commission a couple of years ago recommended that Congress direct the FDA and other Federal agencies to identify alternative sources for APIs and other ingredients, including utilizing the Defense Production Act.

Last week, the administration announced plans to implement some of these recommendations. Congress has already provided some resources to the administration to use DPA authorities to ramp up production of medical supplies, including generic pharmaceuticals. I fought to include this in the CARES Act that Congress passed a couple of years ago. One domestic company, National Resilience, has already secured a DPA loan to expand domestic manufacturing capacity of essential medicines in a community called West Chester Township, north of Cincinnati.

Your testimony, Dr. Hernandez, highlights how drug shortages are a matter of national security. Can you speak to the importance of additional resources for authorities like the Defense Production Act. And also, as you answer that question, what are some additional authorities that the U.S. Government can use, including DPA, to bolster the domestic manufacturing of pharmaceuticals?

Dr. HERNANDEZ. Thank you for the question. I do not—I am not an expert in national security. It is just evident to me that this is a vulnerability, but I am not an expert. I will be happy to review this and get back to you with a written answer for the record.

Senator BROWN. Okay; thank you. DPA is something not especially well known around here in the country, but is something that a lot of these issues—whether it is smuggling fentanyl into the country, whether it is crypto's use internationally for various onerous uses—can come under and certainly are national security issues.

DPA may be a place to answer some of those; it may not. That is what we are trying to explore, and we will follow up with you. Thank you.

Mr. Chairman, thank you. I yield back 1 minute.

The CHAIRMAN. I thank my friend.

I am not going to be filibustering here. We are waiting for a couple of colleagues, and we have a vote coming up. I mean, it seems to me as we get close to the end here, we are talking about significant market failures.

It seems to me we are talking about a whole array of incentives that are out of whack, and some interest in how to use Medicare in a smarter and more creative way. Is that a fair summation? Would any of you like to speak for about 20 minutes or so? No?

We have a couple of colleagues on the way, and we will see if we can continue this discussion. I thank my friend from Civica from volunteering to spare me the filibuster.

Mr. COUKELL. I cannot promise you 20 minutes on any topic, Senator, but I will take the opportunity to bring up something that CMS actually recently proposed in their annual hospital payment rule, something that they did not ultimately decide to go forward with, and I think could use a little fixing, but the concept is sound. And what the agency said is, we propose to pay hospitals a little more if they keep a buffer inventory for essential drugs, or arrange for somebody to keep it on their behalf. I think having it held upstream from the hospital makes a lot of sense, for a number of reasons.

But they were proposing to use an existing Medicare payment authority to just say, we recognize that it may cost a little more to have that extra buffer inventory of essential drugs, but that would be a good thing to do, and we will pay a little more for it.

So, it is exactly along the lines that you are talking about, and I think it is an idea that this committee can come back to.

The CHAIRMAN. And what happened to said idea? Was it formally proposed? Is it on the table now?

Mr. COUKELL. It was formally proposed in the hospital prospective payment rule, but they decided not to move forward with it. But I think they got mixed feedback, and as I say, I do think it is a rule that, as it was proposed, could use a little adjustment. But they did propose it.

The CHAIRMAN. We will look at it.

Senator Bennet is always worth waiting for, and he is recognized for his questions.

Senator BENNET. That is never true, Mr. Chairman, but thank you very much for holding on to things. Ms. Wosińska, thank you for your testimony. Thank you, everybody, for your testimony today, for being here in this hearing.

Let me start here. I am hearing from many constituents that sometimes the brand-name ADHD medication Adderall is often available, but the generic version is not. And this is obviously more expensive for families. Many families cannot afford the entire out-of-pocket cost. I do not think parents should have to make these choices, and to be honest with you, I am hearing story after story after story of families that are dealing with this, not just this problem of generics versus not, but also just the availability of the medicine at all.

Could you explain what is going on here and what we need to do to fix it?

Dr. WOSIŃSKA. Thank you for the question, and thank you for the opportunity. I will have to start by saying that when a good friend of mine heard that I was going to testify, the first thing she said to me, she was like, "Can you talk about ADHD, because I cannot find the ADHD medication for my son"? So the ADHD—

Senator BENNET. Please give your friend my regards.

Dr. WOSIŃSKA. Yes, I will. This is actually a very different shortage. The shortage is driven to a large extent by an increase in demand for the product. And we are in a system where there are challenges in sort of expanding—there is another agency involved, the Drug Enforcement Administration, that has a cap on the amount of product that can be produced, and then they also assign basically market share to manufacturers to manufacture a quota.

And you know, we are the only jurisdiction that really has this kind of a system of dealing with potential misuse of controlled substances. And so what ends up happening is that, you know, you put a cap. There are more people who want it than can get it, and somehow, we are supposed to sort each other out, that the patients who really need it get it, and the ones who are taking it to study for exams and stay up all night do not get it.

There is no system for that. The cap does not do that. And then there are also challenges with how the manufacturer quotas are assigned, because they tend to be assigned based on historical purchases. That is why, in those markets and for controlled substances, the brand frequently gets the largest market share, and it is based on how the manufacturer quotas are assigned. So—

Senator BENNET. Why do they get the biggest market share? Say that again.

Dr. WOSIŃSKA. Because they have to give quota to manufacturers. The DEA has to manufacture supply for quota.

Senator BENNET. So the DEA—so there first, or maybe these are not in order. But there is a cap that they—

Dr. WOSIŃSKA. There is a cap.

Senator BENNET. And then, as a consequence, or in addition to that, they have to assign a quota to the brand-name part of it.

Dr. WOSIŃSKA. That's right, and they have to decide who gets it. And it tends to be—here is another example. One drug, Vyvanse, went generic this summer. There are 14 generic manufacturers that want to go up for it, and it is a big mystery to everybody how DEA is going to assign the market share to those 14, because they have no historical purchases of this, right? There were no generics prior to that.

So, this is not within the jurisdiction of this committee, but I do think this is a very worthwhile conversation to be had.

Senator BENNET. And do you think that—this probably is not within your jurisdiction as well, but the demand issues you are talking about, are you familiar with what is causing the increased demand for the drug?

Dr. WOSIŃSKA. So, it is not well documented. We know in which age groups this is happening. This is not happening in Medicare. This is happening with young adults and sort of 30-year-olds.

Senator BENNET. Yes. I mean, I think that you could probably draw a pretty straight line, or maybe a line around the COVID epidemic and the shortages that we are seeing.

That is when we started seeing this at the Target around the corner from our house, and families started to tell me that they were going to 20 pharmacies, 25 pharmacies, to try to find the medication for their children that had been prescribed. And I suppose this is an issue to raise with the DEA as well in terms of their cap.

Dr. WOSIŃSKA. On the supply side, definitely—and on the demand side, you know the FDA does have what is called REMS authority, where if certain patients should be getting this and it should be used in certain situations, there are ways to put in programs to try to sort of control the demand side of it. So there are other mechanisms to engage.

Senator BENNET. Well, thank you for your testimony. Thank you. Tell your friend I said, “hello.” And, Mr. Chairman, thank you for holding this hearing.

The CHAIRMAN. Senator Bennet, as usual you are raising a very important issue. We have been banging some heads at DEA and FDA, and particularly trying to force some disclosure with respect to whether these manufacturing quotas are being met. So we will have some more to talk about, absolutely.

Let’s see. Senator Whitehouse is next, and then our colleague, Catherine Cortez Masto.

Senator WHITEHOUSE. Thank you, Mr. Chairman. Thank you to the witnesses for being here with us.

I think many of us know that conditions like ADHD, and to some degree autism, are often treated with prescribed stimulants, and that patients experience considerable benefit from those.

And they also experience considerable difficulty getting access to the drugs. My office has been contacted by a mom in Riverside, RI who has an 11-year-old, and it has had to become really an almost daily project of the mother to try to call around to pharmacies, see where there might be some supply, and try to get there while there still is supply. There is a 20-year-old in Lincoln, RI who has had a similar experience; to be more specific, a prescription from August of this year they have not yet been able to fill.

So let me start with Dr. Westin. When you face patients who are having these problems, what does it do to your world and your workflow?

Dr. WESTIN. In the cancer world, it is certainly different than having to call around to pharmacies for your child to get prescriptions. That is a very big problem. But in our line of work, we are dealing with literally life-threatening conditions, and so not having access to medications for us—having to call different pharmacies would be a welcome alternative to dealing with potentially not being able to deliver lifesaving therapies.

Senator WHITEHOUSE. But the point is that this work backs up into physicians’ offices.

Dr. WESTIN. Absolutely. This has an impact on physicians as well; correct.

Senator WHITEHOUSE. Whether it is cancer or otherwise, it adds to the load and the burnout and the wear and tear on physicians.

Dr. WESTIN. Absolutely.

Senator WHITEHOUSE. The drugs I am talking about are controlled substances. They are regulated by DEA. One of the regulatory procedures that is used is an overall limit on supply, which seems like an unusually blunt instrument. I am getting a lot of head-nodding on that.

Tell me a little bit, maybe Dr. Wosińska, about the time lag between when somebody in DEA makes a determination that a particular supply limit should be imposed, and how long that persists

in time until it is implemented and ultimately amended. How long can the gap between the decision and the actuality of the limit be?

Dr. WOSIŃSKA. Thank you for this question. All I can really speak to is the fact that these lags exist. From what I understand, they can take months, and frequently a manufacturer might not obtain all of the quota that they asked for. So it's sort of this repeated process, and it is, from what I understand, really challenging figuring out what it would take to have DEA give you the quota that you want.

But this is probably a question much better directed at manufacturers, and I am sure that AAM would be able to speak to their experience of that, and I would recommend that.

Senator WHITEHOUSE. If there were a demand surge during that time period, the people who have the prescriptions that make up the demand surge are just stuck, right?

Dr. WOSIŃSKA. That's right. I mean, they are—that's right. So, one is the overall demand, and then also the process of assigning quota to individual manufacturers and trying to sort that out, and frequently the manufacturers are not given all of it at once. So it is—

Senator WHITEHOUSE. Would it make sense—you know, we have a strategic petroleum reserve. We hold certain reserves back in the event of an emergency need. Would it make sense for DEA to allow supply reserves that could be released in the face of a demand surge?

Dr. WOSIŃSKA. I will say, I do not understand why we think the quota system in the first place is a way to deal with misuse and abuse.

Senator WHITEHOUSE. It's a pretty blunt instrument at the end of the day.

Dr. WOSIŃSKA. It is a very blunt instrument that only is used in the United States. You know, it basically puts a cap, and then patients have to sort each other into like, well, I need it more than you. We do not have a mechanism to do it. So I do not even understand how the mechanism is supposed to help.

Senator WHITEHOUSE. For the record, my office interactions with DEA trying to get clarification for constituents have been unsatisfactory.

Last question, Mr. Coukell. We have talked about the role of regulatory limits with respect to controlled substances. Do you see a risk here where you have monopolies, single manufacturers for particular drugs, who can withhold supply to boost their pricing prospects and capabilities and put a supply demand in efficiency into the system to their benefit?

Mr. COUKELL. Thank you, Senator. I would say, when we are talking about drug shortages, in general what we are talking about is actually the opposite challenge, which is there are a number of manufacturers, and the consolidation among purchasers drives that price down to unsustainable levels.

The time then when the price can surge is when the drug goes into shortage, and there is only one manufacturer left that has product to sell. And then the cost of the product can go up 10- or 20-fold, and so it is that market instability really that we are trying to address when we talk about the problem of shortages.

Senator WHITEHOUSE. Thank you.

The CHAIRMAN. I thank my colleague from Rhode Island.

Senator Warner?

Senator WARNER. Thank you, Mr. Chairman. Thank you for holding this hearing. And I hate to say good things about my colleague from Rhode Island when he is actually physically here.

Senator WHITEHOUSE. I'll leave. [Laughter.]

Senator WARNER. But you know, the idea of a reserve supply—you know, frankly BARDA was part of that. And for this host of other drugs, I think it makes an enormous amount of sense, and I would love to work with you.

I know you have heard lots of stories. I was going to tell a story about a constituent in Virginia Beach who loves being in Virginia, but is experiencing a lack of access to chemotherapy drugs. But I want to take my time actually—and I hope, Mr. Coukell, that you have not gotten this kind of full attention from my other colleagues.

But part of the solution, I think, to what we are talking about today—we actually have a pretty cool idea happening in Virginia with Civica Rx, and Civica Rx is housed in Petersburg, VA, a community that had had Boehringer Ingelheim at one point, but is not necessarily historically known as a center of pharmaceutical manufacturing.

But over the last number of years, there has been a pharma manufacturing cluster created in Petersburg. This coalition was awarded \$53 million in the Build Back Better regional challenge grants, and it was recently named, as well, one of the 31 tech hubs, at least in terms of the preliminary piece, by the Department of Commerce.

So, we think this is an exciting, exciting idea. One of the stakeholders is Civica Rx, which was founded by a series of hospitals and philanthropists who said, “We are going to try a different model.” The notional idea is a nonprofit-based model that says, particularly around generics—because we know that for so many manufacturers, the pricing point has gotten down so low that they do not stay in the business.

I say this as somebody who is the father of a type 1 diabetic, and one of the drugs I know that you are looking at is insulin. So, a group of investors came together to see how you could get a predictable, reasonably priced supply of certain medicines, and you know, there was a series of drugs.

Civica Rx is going to be, as I mentioned, dealing with insulin, but other critical medications as well. So, Mr. Coukell, it is clear that you have maybe found, if not the full magic bullet, at least a part of the solution. If we could have that predictable yet affordable supply of generics, I think that is terribly important.

In the most recent Medicare hospital funding rule, CMS proposed but did not finalize an idea to provide financial incentives for hospitals to maintain that buffer of essential medicines. Do you think that what Medicare and CMS are proposing makes sense, and what else can Medicare do to make sure that very exciting solutions like you guys are working on can become a reality, not just in Virginia, but across the country?

Mr. COUKELL. I thank you, Senator. We are really pleased about the growth of the pharmaceutical cluster in Richmond and Petersburg, and proud to be part of the Commonwealth. Along with insulin, you mentioned we have about three dozen products in development for that facility with more to come, and we would love to have every hospital in the country as a member.

In terms of how we think about using CMS authorities to drive the purchasing toward more resilience, that rule that you mentioned, I think is the right kind of idea. And essentially what they said is, we recognize that it costs money to hold buffer stock, but we recognize the value of that. So, we will pay a little more so that hospitals can contract with somebody to hold that buffer stock, or do it themselves, which I think is probably not the way we want to do it.

But to say, yes, if you contract with somebody—you know, pick your essential drugs and contract with somebody that is going to hold that 6-month buffer stock for you—we will pay you a little more, and that way we will create a market for the entity that is holding on to that extra stock.

Senator WARNER. Well, I think it is a very exciting opportunity. I hope that, as we have talked about in the past, there are ways we can incent other hospital systems, even from the jawboning standpoint. But the whole idea of this coalition of hospitals, philanthropists, and others coming together to actually create a nonprofit approach is unusual, unique, and long overdue.

So I hope, Mr. Chairman, it can be part of our longer-term solution.

The CHAIRMAN. I thank my colleague.

I want to tell our witnesses what is going on, because they have seen Senators sprinting hither and yon. Our last two questioners will be Senator Hassan and Senator Warren. Thank you very much for wrapping up.

I just want to pose one matter to you, Dr. Wosińska, for the record. You know all year, we have been trying to bust heads with DEA and FDA with respect to this drug shortage issue, and the DEA finally, after we just pushed and pushed and pushed, has laid out some changes to how they set quotas for how much of these medications and other controlled substances each manufacturer can produce.

Obviously, there is a lot more to do, and the question I want to ask for the record, if you could get it say in a week or so, is whether these unique challenges around shortages for controlled substances are an area that we can tackle here in the Finance Committee. I suspect they are, and we are going to just ask you to do that in writing, okay?

Dr. WOSIŃSKA. I will follow up on that.

The CHAIRMAN. Great.

Senator Hassan, and then Senator Warren, and Senator Warren will close the hearing. I thank all our guests, and sorry for the sprint, but this is the way it is on Tuesday.

Senator HASSAN. Thank you very much, Mr. Chair, and thank you to the witnesses for being here and for your indulgence as we balance votes and the like. I am really grateful for the topic of to-

day's discussion, and I want to start, Mr. Coukell, with a question to you.

In your testimony, you point out that most drug shortages in the United States are really predictable—highly predictable. While manufacturers can fill gaps in the market by investing in medications that are at risk of shortages, companies have very little incentive to do so because the margins on generic medications can be so low.

It is clear that the Federal Government could do more to prepare for predictable shortages. If we already know what medications are at risk for shortage, what role should the U.S. Government play in preparing for inevitable shortages of essential drugs?

Mr. COUKELL. Thank you, Senator. Shortages *are* highly predictable, and we can look at a range of factors in terms of which manufacturers are making drugs and where are they getting their active ingredients. But the strongest predictor of a future shortage is a past shortage, and if we could just solve for the drugs that have been in shortage over the past 10 years, we would solve a huge amount of the shortage problem that we are dealing with.

But as you say, some of those drugs are selling at prices so low that no U.S. manufacturer can justify the investment to bring that drug to market, knowing that they are competing against somebody that is selling it at 50 cents a vial. So if the government were to say we know, based on history and based on today's market prices, that at some point somebody is going to step away from that drug and make something else, and we want somebody ready to step in and deliver that drug to patients when we need it, then the government could invest and have manufacturers in the U.S. ready to go, to bring that drug to market the second—or soon after—a shortage starts.

Senator HASSAN. Okay; thank you.

Dr. Wosińska, let me ask you a question. Hospitals in New Hampshire, including Dartmouth Health, are experiencing shortages of a range of medications, including antibiotics, steroids such as hydrocortisone, and lifesaving oncology medications.

We have really small hospitals in New Hampshire. A lot of our State is rural, and they are at the greatest disadvantage during shortages because they have less buying power and fewer staff available to navigate the shortages. Unfortunately, hospitals often have virtually no information on the supply chain used by a manufacturer, or the manufacturer's track record when they are purchasing medications.

This makes it really difficult for a hospital to reduce the risk of shortages by choosing to work with reliable manufacturers. So how can more transparency help hospitals avert and respond to medication shortages in the long run?

Dr. WOSINSKA. Thank you so much for this question. So, I would say that it depends what is their situation, because the information depends on the situation we are in. A hospital will need very different information during a shortage, right? They will want to know what is the allocation mechanism that the wholesaler is using; when might I get more product?

There are also questions like, how long will it last? That is a really hard question to answer. Having worked at the FDA closely

with the drug shortage staff, they frequently do not know how long it will take, because they do not know how long it will take the manufacturer to resolve it. The manufacturer might not know at the beginning.

So definitely, during the shortage it is different. Before a shortage, the questions are somewhat different. This is actually where I do think GPOs can be really helpful, because GPOs can help a hospital maneuver to what is more reliable. They can participate in programs where there are actually buffer inventories. Some of the GPOs have them. Civica definitely is open. So there are definitely ways.

I would like to take this opportunity—since you mentioned that you are speaking about small hospitals—I actually pushed back against the buffer inventory idea that was mentioned a couple of times that CMS put forward. And one big reason was that the mechanism—it would not be enough of an incentive for hospitals to use the program, because it would not pay enough, and also the small hospitals are the ones that usually get left behind in a shortage.

Senator HASSAN. Yes.

Dr. WOSIŃSKA. I will tell you, I have seen data that large hospital systems have gone from 3 weeks of drugs like cisplatin and carboplatin in their inventory to 6 months.

Senator HASSAN. Six months; okay.

Dr. WOSIŃSKA. They are in a much better position to do this. What we need to be doing is buffering those that usually get left behind. And you will see in my testimony, I actually propose that that rule that CMS used, that they are also able to potentially target who—not just which product—but who can get that subsidy, and then we could buffer them more.

Senator HASSAN. Okay. Thank you. And I am just going to move quickly.

Mr. Coukell, how does your organization's focus on U.S. manufacturers affect the reliability of your supply chains for products like vials and pharmaceutical agreements, as well as the cost of your medications, because we are talking about transparency here? How does the focus on U.S. manufacturers help in that regard?

Mr. COUKELL. Yes; thank you, Senator. We feel strongly that when the manufacturer is in the U.S., we can have the insight we need into their quality system and track record, and also that the FDA is there on a regular and consistent basis.

Which is not to say there are not good and bad manufacturers everywhere, but we have that insight. So we do prioritize U.S. sourcing, but we also think it is the right thing to do from a long-term national security point of view.

Senator HASSAN. Okay; thank you very much. Thank you.

Senator CARDIN [presiding]. Senator Warren?

Senator WARREN. Thank you. Thank you, acting Chair Cardin.

Senator CARDIN. Yes. I just all of a sudden moved up in seniority to chair the committee. [Laughter.]

Senator WARREN. There we go.

So, I am glad we are having this hearing today, because there are more than 300 drugs that are in shortage, meaning that companies do not produce enough to meet patient demand. That is

more than at any point in nearly a decade, and shortages can be devastating.

Shortages force patients to use less-effective alternatives, or to switch to drugs that may have more harmful side effects. Lots of factors can cause shortages that you all have been talking about today: spikes in demand, a manufacturing facility hit by a hurricane, or an inspection problem that needs to be addressed.

But a big shortage risk occurs when there are only a small number of companies that make the drug, and any one problem in one of those companies can take down a chunk of the market. Most drugs in shortage now are generics, meaning they are no longer protected by patents and can be made by any manufacturer. But even though generics can be made by anyone, most have very little competition. In the U.S., 40 percent of generic drugs are made by a single—one single company makes the drug.

So, Mr. Coukell, you represent the nonprofit drug manufacturer Civica Rx. So you understand the economics of the generic drug industry. Why is there so little competition for such a high number of generic drugs?

Mr. COUKELL. Thank you, Senator. Typically, when a drug goes off patent and companies can bring generics to market, a lot of companies compete to bring that product to market.

Senator WARREN. And that was the model we all thought would happen.

Mr. COUKELL. Right.

Senator WARREN. But?

Mr. COUKELL. Unfortunately, what happens is, when you have purchaser consolidation, contracting consolidation, it drives that price down, concentrates the market share, and so the price goes so low that other companies may not have market share and may not have much incentive to stay in the market.

Senator WARREN. Okay. So my understanding is, part of the problem here is that it is expensive to run a drug manufacturing facility. But as you are saying, the margin for many of these generic drugs is so low that domestic manufacturers just are not interested in making them. And as a result, we have become more reliant on foreign manufacturers to furnish some of our most basic and essential medicines. This obviously not only raises quality concerns, but it also poses a risk to our national security.

So, I was glad to see the Biden-Harris administration announce that it is expanding HHS's authority under the Defense Production Act to bolster domestic manufacturing of essential medicines, and that it will invest \$35 million in U.S. manufacturing of key starting materials for pharmaceutical products.

Now, Mr. Coukell, will investments in the manufacturing of key starting materials—that is a good thing—but will it be enough to alleviate drug shortages, or do we also need to think about investments in manufacturing finished drugs as well?

Mr. COUKELL. Yes; thank you, Senator. I agree that it is a good thing to invest in key starting materials. But if we are focused on shortages, the key starting materials, the precursors even upstream of API are way, way upstream and not usually the thing that is causing the shortage. Most of the shortages are caused at

the level of manufacturing the finished dosage for the vial or the syringe drug.

Senator WARREN. All right. That is a really important point, and I appreciate your making it.

To prevent drug shortages, the Biden administration, I think, should build on these commitments to also invest in the manufacture of finished drug products, and it is important that the administration ensures that taxpayers get something for these investments, for example, by negotiating contract terms that the drugs will be made available to government programs and patients at a fair price, if we are going to put taxpayer dollars into this. But I am concerned that even this will not be enough to fully address the market failures in the generic drug industry.

So one more question, Mr. Coukell. Are there generic drugs at high risk of shortage that are so unprofitable that Civica cannot produce them, but would be able to produce them if you had government assistance, a government contract to do it?

Mr. COUKELL. Senator, there are certain drugs that at today's prices, any manufacturer, even a nonprofit, would be selling at a negative margin. And as you can imagine, even as a nonprofit, you cannot sell very many drugs at a negative margin and continue to operate. So yes, the answer to your question is "yes."

Senator WARREN. All right.

So I think it is important to acknowledge that the market alone will not fix this problem. If there are drugs that are priced so low that even manufacturers that are dedicated to preventing shortages will not produce those drugs, then the government must step in.

And that is why I am reintroducing the Affordable Drug Manufacturing Act, to direct HHS to sign contracts to manufacture generic drugs in cases where the market has failed. Public manufacturing presents a powerful opportunity to resolve drug shortages, to secure the pharmaceutical supply chain, and to ensure generic drugs are both accessible and affordable for patients.

Thank you. Thank you, Mr. Chairman.

Senator CARDIN. Thank you.

Senator Cortez Masto?

Senator CORTEZ MASTO. Thank you, Mr. Chairman, and thank you to the panelists. Thank you for your written testimonies. I have listened to your testimonies today. Obviously, it is such an important topic.

Let me jump right in here. And, Dr. Hernandez, let me start with you, because I think we all were concerned reading *The Wall Street Journal* report that patients' insurance plans are paying thousands of dollars a month for certain specialty drugs, and that is because health insurers and PBMs are marking up the prices they set with pharmacies.

And you talked a little bit about that. I understand you have a report coming out, is that correct, on this very issue?

Dr. HERNANDEZ. Yes. We have a report published this morning that looks at the top 50 generic drugs by Medicare spending, and how much the main six Part D sponsors would pay for them. So we identified as many as 16 generic drugs that have markups of

over 1,000 percent. Imatinib, which is a cancer drug which is now available as a generic, is one example.

But another example, for instance, is aripiprazole, an antipsychotic drug where the pill actually costs the pharmacy less than 17 cents, but PBMs were reimbursing them as high as \$11 or \$5 per tablet. While I think this is not a contributor to shortages, and I think that is an important point to make, these drugs are—we are talking about drugs reimbursed by Part D, so, drugs used in the patient setting.

I think this is also another symptom of how the way we pay for generics does not work. Just as we fail to generate incentives for manufacturers to produce certain drugs, we are also somehow, on the Part D side, allowing intermediaries to unjustifiably increase the cost of certain generic drugs, which ends up in seniors paying more for their medications. So I just would like to make that point.

I think these are two different symptoms that show the current shortcomings of the way we pay for generics, and both of them need reform. But I do not think PBMs are at fault for shortages.

Senator CORTEZ MASTO. Right. And I think, from what I am hearing, there are several solutions. There are several things that we need to be doing. And, Dr. Wosińska, I thank you as well, because I was looking at your written testimony.

One of the things you highlighted in your testimony this morning that I want you to touch a little bit more on, is this idea that CMS pay for a performance program to shift hospitals' purchase decisions. You talk a little bit about this, and say under the proposed pay-for-performance program, hospitals would be scored on their behavior on two measures: do they buy from a reliable manufacturer, and do they buffer their inventory?

So, if you would, talk a little bit more about that. But I am also curious what you talked about—the buffering of the inventory for small hospitals—because we have a lot of small hospitals in rural Nevada, and you seem to indicate that we have to be careful when we are talking about that, when it comes to small hospitals. So, if you would, please elaborate.

Dr. WOSIŃSKA. Yes. So, one of the features of this pay-for-performance program is that it allows us to be grouping—the idea is to compare how you do to your peer. So I would not want Mayo Clinic to be compared to a small rural hospital.

And in a program like this, when CMS then assigns payments at the end of the year, they would be able to sort of assign a different amount of money to the different tiers of hospitals. So there would be opportunity to buffer certain types of hospitals more.

Now, going back to—you know, the pay-for-performance program would reward what hospitals do. I want to sort of highlight one more piece, that we want to be also thinking about what are the things that we are trying to prevent, versus what happens in a shortage.

A buffer really is, when there is a shortage, how it is related to the supply chain. And so it is really important that we just do not think about just buffering. The reason why we are looking at reliability and buying reliably is because that is what drives manufacturing quality.

If we do not solve that problem, we will continue to have disruptions, and the question is, are buffers enough? There is so much panic buying right now that goes on when there is a shortage. You would have to have really massive buffers for the market not to be reacting the way it is.

So we really have to get at the root cause of it, which is the manufacturing quality. And for things that we can't predict, such as natural disasters and whatnot, or geopolitical threats, that is where buffers really should be playing a role.

Senator CORTEZ MASTO. Fair enough; thank you.

I have a couple of other questions, but I know my time is almost up. I will submit those for the record. I thank you.

Senator CARDIN. Thank you.

So, let me just make an observation before we close the hearing, and that is that there is an inadequate supply of many essential drugs. They are not particularly expensive. The cost-benefit ratios are pretty dramatic, and it is affecting the proper medical protocols for treating certain illnesses and diseases.

In a Nation that spends the most for health care any way you want to judge it, where the profit margins are pretty high in the drug industry—and it is an area in which we see a continuous increase in the use of prescription drugs and the cost of prescription drugs, and yet those that are less expensive, we find in short supply.

So, Senator Warren is absolutely right. The market is not working in this regard. So we have to figure out how do we affect the market? So, there are a lot of different ways that we can take a look at that, but we must have the data. I am not yet impressed that we have the information necessary to make the type of judgments that we have to make. So I would just urge us to try to get as much information as possible.

One area that I have worked on is the expiration date on drugs, making sure that we have the maximum amount of time in order to use a current supply. But I would be interested in your observations as to the impact it has on traditionally underserved communities.

I find that if you know how to manipulate the system or use the system, et cetera, you can usually get your hands on whatever you need to. But if you come from communities that do not have that type of access or that type of supply chain, you are usually at the bottom of the ring.

So I see you are nodding your head. Tell me a little bit about the impact on underserved communities, and as we look at solutions for supply of drugs, how we protect the communities that have been traditionally left behind.

Dr. WOSIŃSKA. So, with retail drugs, the impact is going to depend very much on where the product is carried. I actually do not have—I have not seen the data, but I would not be surprised if certain chains were able to get the product more readily than others. To some extent, it is because the way DEA assigns quota, you have to come in with a contract to the DEA to say, I have a contract with this wholesaler, this distributor, or this pharmacy chain.

And so, if the DEA does not assign quota to that manufacturer, you are going to suddenly have, potentially, a gap. So that is sort

of part of this, sort of in which pharmacies this happens, and to what extent, for example, independent pharmacies are able to get access.

On the hospital side—I spoke very briefly about this—there is a lot of anecdotal evidence. I am actually doing a research study that we are hoping actually documents this. But there is a lot of anecdotal evidence, especially—there is an organization called Angels for Change, who try to actually help coordinate and find cancer products.

And if you talk to them, they will tell you of the incredible inequities that have resulted from this shortage, because it is the small, the independent clinics, the small rural hospitals that really just cannot get their hands on the product.

What happens is, if there is any signal of a shortage, those who have the means and have the buyers will basically try to procure as much product as they can. And then there is so much less on the shelves. And everybody is nervous, so everybody tries to buffer.

I sort of compare it to COVID and toilet paper, right? Initially, we were comfortable with maybe having four rolls of toilet paper before COVID, and then you are down to 12 and you have to go shopping, right? But when everybody does this, we pull so much more of the product out of the shelves. And then not everybody has the same ability to get to the product. So—

Senator CARDIN. So, let me try to get to solutions here. We recognize that we want to reduce or eliminate, as much as possible, the lack of supply of essential medicines, particularly those that are less expensive. But there will always be some shortages.

So how do we put in place a system—how can government put in place some protections and guard rails to avoid that inequity?

Dr. WOSIŃSKA. Yes. I will let Allan speak as well. But just really quickly, if the government is going to be creating any type of a stockpile—any type of a stockpile—there really needs to be an allocation mechanism in place. If you were to create a pediatric cancer drug stockpile—you know, they are in the 1 percent of patients among all cancer patients—that stockpile would be tiny.

Why would we possibly think that letting this stockpile be used in a shortage would go to pediatric patients? So we really need to be thinking about who can get it, who can't get it otherwise, and really have these kind of allocation mechanisms.

Even historical allocation mechanisms would go a long way, rather than let somebody buy, you know, 10 times what they normally buy and basically kind of buffer themselves, but leave others behind. So I think that would be my recommendation.

Senator CARDIN. Mr. Coukell?

Mr. COUKELL. Senator, we have some of the largest health systems in the country, our Civica members. But we also have small rural hospitals that have joined as onesies, and they pay exactly the same price for drugs from Civica.

When they commit to buy a certain volume of drug, we hold a physical reserve inventory sitting in a warehouse of about 6 months of that drug, and that hospital, regardless of the size, is going to get their committed volume. So I think that is the kind of approach we need to think about as we move forward.

Senator CARDIN. Well first, on behalf of the committee, we thank all four of you for your testimony here today, and for participating in this important debate, as we try to figure out the best way to deal with a problem I think we have all recognized.

For the information of the members and staff, questions for the record are due by 5 p.m. next Tuesday, December 12th.

There being no further business, the committee will stand adjourned, with our thanks.

[Whereupon, at 12:24 p.m., the hearing was concluded.]

APPENDIX

ADDITIONAL MATERIAL SUBMITTED FOR THE RECORD

PREPARED STATEMENT OF ALLAN COUKELL, SENIOR VICE PRESIDENT,
PUBLIC POLICY, CIVICA RX

Chairman Wyden, Ranking Member Crapo, and members of the committee, thank you for the opportunity to speak with you today on the pressing issue of drug shortages, and on policies to prevent and mitigate future shortages. My name is Allan Coukell. I am a pharmacist by training, and I lead public policy for Civica—also known as Civica Rx—which is a nonprofit generic drug company created specifically to prevent drug shortages.

THE PROBLEM OF DRUG SHORTAGES

Drug shortages have been a chronic and ongoing problem in the U.S. for well over a decade. At any given time, hundreds of drugs appear on the FDA drug shortages list. Currently, we are seeing an acute exacerbation of shortages as a number of manufacturers have experienced quality problems, causing them to permanently or temporarily leave the market. Cancer drugs and penicillin and cephalosporin antibiotics are among those products of highest current concern, but shortages cut across therapeutic categories of generic drugs. Sterile injectable drugs are predominantly affected, though not exclusively, due to the complexity of manufacturing and the low profit margins associated with these products.

Drug shortages disrupt patient care, causing procedures to be canceled or delayed. They require treatment regimens to be adjusted to alternate products, potentially increasing the risk of medication error or resulting in suboptimal care. They require commitment of enormous pharmacy and hospital staff time in attempting to source drugs that are in shortage. And, while the low cost of drugs is the ultimate driver of supply failures, once a shortage occurs, prices spike, adding to costs.

ABOUT CIVICA

Civica is the only pharmaceutical company established specifically to address generic sterile injectable drug shortages.

We were founded as a nonprofit, non-stock organization by a group of U.S. health systems and philanthropies who, after more than a decade of chronic shortages, recognized that the market was not self-correcting and that a different approach is required. They created Civica with the mission of delivering a safe, stable, and affordable supply of essential medicines to U.S. patients.

Civica marked its fifth anniversary in September. In that time, our hospital membership has grown to 55 health systems, accounting for one-third of licensed beds in the United States, and we have supplied more than 148 million containers of generic sterile injectable drugs—more than 80 different drug products.

With substantial support from the U.S. Government, we recently completed construction of our own state-of-the-art sterile injectable manufacturing facility in Petersburg, VA.

Civica's member health systems have taken steps to mitigate the risk of shortages by changing the way they purchase essential drugs. But many other hospitals have yet to develop or implement a systemic strategy for shortage prevention. Civica's unique model may offer a guide to what such a strategy should look like.

THE MODEL

The drugs that Civica delivers are those that are in shortage or at high risk of being in shortage. They are chosen by a committee of physicians and pharmacists from Civica member hospitals. They are typically old, low-cost, but essential medicines. They are not the products with the highest return on investment; they are the products required to deliver care every day in hospitals across the country.

Because our mission is to prevent shortages, several features of the “Civica model” are different from the traditional generic drug supply chain and may suggest potential improvements to the larger U.S. system. In particular:

- Civica enters long-term purchase and supply contracts that add stability to the market.
- We target a 6-month buffer inventory of every drug to ensure continuity of supply.
- We emphasize U.S. sourcing whenever possible, with the EU and Canada as a second choice. We don’t source finished drugs or API from China unless there is no other source.
- Civica performs an intensive quality audit of potential suppliers, supplemented by ongoing review of key metrics, to reduce the risk of a failure to supply.
- Every drug is sold on a cost-plus basis, with the same price available to any purchaser. Our prices remain stable even when the drug is in short supply.

Lastly, Civica has built a new, state-of-the-art sterile injectable manufacturing facility in Petersburg, VA, and is developing its own generic drug applications to further ensure supply of essential generic medications.

SUCCESS OF THE MODEL

The Civica model has demonstrated benefits. In fact, 20 of our top 25 drugs are currently in shortage nationally,¹ but we are able to supply without interruption.

When a tornado recently hit a generic drug manufacturing facility in Rocky Mount, NC, the Civica portfolio included 21 products that overlapped with products produced in that plant. We immediately let member hospitals know that we could supply double their committed volume for all 21 drugs.

And a recently published peer-reviewed study in the journal *NEJM Catalyst* showed that:

- (1) *Supply from Civica was more consistent* than from a traditional wholesaler model, and
- (2) Sourcing from Civica produced *net cost savings* to the health system.²

POLICY RESPONSES

When considering policy responses to drug shortages, it is important to recognize that chronic drug shortages have now become a built-in outcome of the current system. Market trends and the resumption of FDA inspections after COVID mean shortages are more likely to increase than to abate in the years ahead.

The immediate cause of most shortages of sterile injectable drugs is quality problems in the manufacture of the finished dosage form. But it is widely acknowledged that the root cause is the low cost of these products, which reduces the incentive or ability for manufacturers to invest in quality or in newer manufacturing facilities and pushes production offshore to low-wage markets where quality problems proliferate, and the FDA presence is less consistent.³

Therefore, policy responses should focus on changing the current system that causes shortages because it favors low prices over resiliency of supply. While Civica

¹ ASHP Drug Shortage list as of November 28, 2023.

² Dredge C, Scholtes S. “Vaccinating Health Care Supply Chains Against Market Failure: The Case of Civica Rx.” *NEJM Catal Innov Care Deliv* 2023;4(10). DOI: 10.1056/CAT.23.0167, <https://catalyst.nejm.org/doi/abs/10.1056/CAT.23.0167>.

³ For example, see FDA, “Drug Shortages: Root Causes and Potential Solutions,” 2019, <https://www.fda.gov/media/131130/download?attachment>; Brookings, “Federal Policies to Address Persistent Generic Drug Shortages,” 2023, https://www.brookings.edu/wp-content/uploads/2023/06/20230621_ES_THP_GSI_Report_Final.pdf; Duke Margolis, “Advancing Federal Coordination to Address Drug Shortages,” 2023, <https://healthpolicy.duke.edu/sites/default/files/2023-09/Advancing%20Federal%20Coordination%20to%20Address%20Drug%20Shortages.pdf>.

member hospitals have taken direct action to reduce their risk of shortages, many others have yet to take steps.

Using its authority over provider reimbursement and quality, we urge the committee to support providers in purchasing generic essential medicines, taking into account:

- Measures to ensure adequate buffer inventory;
- Measures to ensure that generic sterile injectable drugs are priced sustainably;
- Measures to create market demand from manufacturers that are less likely to have quality failures; and
- Support for domestic manufacturing.

Buffer Inventory

Production of injectable medicines is relatively inelastic. If a particular facility stops producing, others take many months to ramp up production (assuming other companies already have approval to produce the drug). Therefore, a system that operates on just-in-time inventory will always be at high risk of shortages.

However, the resources required to establish and maintain access to a buffer stock of essential medicines will generally be greater than the resources required to establish and maintain access to these medicines without such a buffer stock.

Congress should incentivize supply chain stakeholders to maintain buffer inventory. Civica's experience is that a 6-month reserve is the appropriate quantity to create added resiliency, as it allows suppliers to deliver additional batches in the event of a supply interruption.

The cost of a holding a buffer inventory can be calculated on a straightforward basis, by taking into account the weighted cost of capital for the inventory held, along with the cost of the storage facility itself.⁴

Congress could incentivize manufacturers, wholesalers, or providers to hold extra inventory. The most practical approach would be to provide incentives for hospitals, health systems and other providers to contract with manufacturers or wholesalers who actually hold the buffer stock. This maximizes the effectiveness of inventory allocation in a shortage situation and does not require providers to directly maintain or operate storage facilities, with the attendant cost, complexity, and risk of outdated inventory.

The Centers for Medicare and Medicaid Services, in its draft Inpatient Payment rule, recently proposed a very similar approach to providing supplemental payments to hospitals for this purpose. While CMS did not move the provision forward in the final rule, the committee should consider how, with minor improvements, it could be an effective approach.

Drug Shortage Prevention and Mitigation Strategies

Civica's hospital members have made investments and purchase commitments to reduce the impact of drug shortages, but all hospitals and health systems should have a drug shortage prevention strategy and review it on a regular basis. Elements of such a strategy could include:

- Identification of a priority list essential drugs that are at risk of shortages;
- Maintenance of buffer inventory to mitigate a supply disruption, including a contract for maintenance of inventory on behalf of the hospital; and
- Contracting procedures for those drugs that take into account:
 - Supplier quality,
 - Diversity of supply, and
 - Committed volume to bring stability to the market.

The committee should encourage and incentivize the development and implementation of such strategies, including through the use of Medicare payment policies.

"Insurance" Against Future Shortages

Drug shortages are relatively predictable and therefore targeted investments can create backup domestic manufacturing capacity as "insurance" against future shortages. This can be accomplished at modest cost.

⁴Weighted cost of capital is a measure of the cost companies pay to finance their operations.

Shortages occur across drugs in all therapeutic classes, but predominantly affect generic sterile injectable products. A variety of predictive factors can be considered, but the strongest risk factor for a future shortage is whether the drug has been in shortage previously. Therefore, it is possible to create a priority list of products that are essential medicines at high risk of shortages.

Current low market prices—often below \$4 for a vial—make it financially infeasible for U.S. manufacturers to develop many of these products and find commercial sales at today's prices. However, it takes a manufacturer roughly 2 years to develop a generic injectable product and obtain FDA approval. Therefore, starting that process after a shortage begins does not result in a timely response.

In contrast, if Congress were to create a targeted program to support domestic manufacturers to develop essential products that are at high risk of shortage (doing all the required studies and obtaining FDA approval of an ANDA), domestic manufacturers would then be ready to manufacture on short notice once a shortage starts. In this way, Congress could create an insurance policy against future shortages at the cost of a one-time investment of \$3 million to \$4 million per drug.

The committee has previously created grant programs to encourage the growth of other sectors and could use its authority to ensure that the United States has domestic manufacturers who are ready on short notice to produce essential drugs.

CONCLUSION

Thank you again for your attention to this important topic and for the opportunity to be with you today. I welcome your questions.

QUESTIONS SUBMITTED FOR THE RECORD TO ALLAN COUKELL

QUESTIONS SUBMITTED BY HON. RON WYDEN

Question. In your testimony, you recommend that Congress consider policy measures that would help ensure adequate buffer inventory of generic essential medicines. You also mention that Civica targets a 6-month buffer inventory for the products you supply.

Can you elaborate more on Civica's approach to building and holding buffer inventory for your health system members? For example, is this inventory typically held at the provider, manufacturer, or wholesaler level? How often do providers tap into buffer inventory for Civica products? What are the cost implications of producing and holding 6 months' worth of buffer inventory on generic sterile injectable medicines?

Answer. Hospitals contract with Civica to purchase specified minimum volumes of each drug (not every hospital purchases every drug, but those that decide to purchase commit to a specific annual volume). This predictable volume dictates the size of the buffer inventory that Civica establishes (equivalent to 6 months' worth of sales).

Through experience, we have found that a 6-month buffer is appropriate, in that it allows for continuity of supply for a disruption in the market by allowing our suppliers to produce additional batches.

Civica manages the buffer inventory in relation to a hospital's committed volume. Generally during a market shortage, the buffer inventory allows us to supply hospitals at double their committed volume (*e.g.*, if a hospital had previously committed to purchase 50 percent of their volume for that product from Civica, we could supply them with 100 percent of their needs; a hospital that opted in at 15 percent could receive up to 30 percent). In some circumstances, Civica will supply more than double the committed volume; other times, if supply is limited, we may use allocation to manage the inventory more tightly). This approach ensures equitable and efficient distribution.

Most of the buffer inventory is owned by Civica and is stored in a central warehouse, with some portion transferred to the wholesaler at forward distribution centers around the country. The cost to hold buffer inventory is essentially the cost of capital plus the cost of warehouse space.

The cost to a manufacturer (or any entity) to hold buffer stock is directly related to the cost of capital for the value of the inventory held. If the Finance Committee were to model a payment incentive, it could take into account that cost, plus a small

additional administrative fee for the cost of storage facilities. Such an approach would allow CMS to calculate a reimbursement premium that should exactly offset a hospital's slightly higher acquisition cost from a manufacturer (or wholesaler) who holds extra inventory on their behalf. By reimbursing separately for the cost of acquiring drug through a buffer stock program, CMS would effectively create a market for this service that values it at exactly what it costs to provide.

This effectively creates a level playing field without introducing perverse incentives. Take a hypothetical drug sold by a manufacturer at \$2/unit price through non-buffered supply. If the manufacturer builds in the cost of the inventory buffer and sells through a buffered inventory program at \$2.10, but the hospital receives an extra \$0.10 for purchasing buffered stock, the hospital no longer has an incentive to choose the non-buffered stock, but neither the hospital nor the manufacturer is "overpaid." The effect is to make a market for entities that hold buffer stock.

As noted above, incremental cost can be calculated based on the weighted average cost of capital for the inventory held, along with the cost of the storage facility itself, for each drug and hospital. However, companies may make different assumptions to calculate cost of capital; therefore, the Finance committee could direct CMS to standardize the payment premium by calculating cost of funds based on SOFR + a fixed percent, published quarterly. Moreover, the amount of the extra payment could be adjusted directly based on the amount of buffer stock actually held in the prior year/quarter (e.g., an average inventory of 6 months may dip to an average of 2 months when the drug is in shortage and the hospital is drawing on the buffer).

In any case, inventory should be held "upstream" of the individual provider by an entity that can allocate based on historical sales or committed volume. These removes the cost, risk and responsibility from the provider for managing a buffer inventory and allows the manufacturer (or wholesaler) to manage the inventory buffer in a way that prevents hoarding.

Question. Your testimony also recommends that Congress consider policy measures to ensure that generic sterile injectable drugs are priced sustainably.

How does Civica arrive at sustainable price points for the generic medicines you develop? Please elaborate upon the specific input costs and other factors Civica considers when pricing a product for your health system members.

Answer. Civica prices on a cost-plus basis to deliver the lowest sustainable price. The same price is available to all purchasers and remains stable even when a drug is in short supply. Like other generic manufacturers, we compete in a market in which price pressure on generic drugs is intense and can result in some products being priced with negative margins—a sure recipe for long-term shortages and unstable supply.

QUESTIONS SUBMITTED BY HON. CHUCK GRASSLEY

Question. I have heard from Iowans receiving cancer treatment about how cancer drugs in short supply have impacted their ability to access treatment. Some patients have even had to switch hospitals to maintain treatment, because another hospital was getting a more consistent supply.

Some hospitals seem to handle drug shortages better than others. Why do you think that is? Are there parts of the supply chain that weather shortages more effectively?

Answer. Because generic injectable drugs are chronically in shortage, nearly every hospital and health system devotes personnel and resources to sourcing of drugs when they are in shortage. It may be that some hospitals have more resources able to source during a shortage or procure in anticipation of a shortage, and also that varying relationships with wholesalers, group purchasing organizations and other supply chain entities result in some hospitals being able to acquire drug while others cannot. Procurement through Civica is an approach designed to be accessible and available to any hospital, yet currently only about one-third of U.S. hospital beds are in Civica member hospitals. This may suggest that many hospitals have not yet attempted to fully optimize shortage prevention strategies.

Question. Several testimonies described the need for increased communication and coordination across the pharmaceutical supply chain to prevent and manage drug shortages.

Given the persistence and scale of drug shortages, does there need to be more transparency within the supply chain? If so, by whom and how could this improve the situation? If not, who in the supply chain should do more with the information they have to address drug shortages?

Answer. The underlying cause of most shortages is a market that pursues the lowest cost at a cost to resilience of supply. Correcting this imbalance will require changes to incentives that support purchasing from manufacturers that are less likely to have supply failures. This could include incentives to purchase from entities that hold buffer inventory and incentives to choose manufacturers that are less likely to have a failure to supply. Providers and purchasing organizations looking to implement such an approach can already draw on a range of available information that is sufficient to both identify at-risk drugs and select manufacturers that are less likely to contribute to a supply failure. While this can be accomplished without additional supply chain transparency, we provide two examples of changes that would be beneficial.

1. Currently, health systems generally learn about a drug shortage once the product becomes unavailable, which may be weeks or months after the manufacturer supply disruption has become known to the FDA.

If health systems know about shortages sooner, they may be able to adjust utilization, such as by using drug only when necessary or switching to alternative products for suitable patients, for example, using an oral medication instead of an injectable. They can also implement waste reduction, for example, repackaging contents of vials to allow for use to treat multiple patients. However, for conservation measures to be most effective, earlier notice of a shortage risk is essential.

One risk of early notice of a shortage risk is that health systems will stockpile or “hoard” drug product during a time of scarcity, potentially precipitating a shortage. Therefore, we recommend that drug distributors, which are identified as “other stakeholders” in the FDA Risk Management Plan guidance, be required to have a risk management plan that involves immediately putting a drug on allocation when notified by FDA of a potential impending shortage.

Under an allocation strategy, no health system would be able to order significantly above its normal order volume for a drug on allocation without providing some justification. In this circumstance, allocation should apply not only to the specific NDA, ANDA or BLA product, but to therapeutically equivalent products and, in some cases, therapeutic alternative products. This would help prevent shortages of alternative drugs needed to treat the same condition(s).

To prevent over-ordering in a potential shortage situation, allocation should also be part of risk management plans for manufacturers of equivalent products and, in some cases, for therapeutic alternatives.

Allocation of inventory is not a new measure, but currently often happens after hoarding of product has depleted existing inventory in the supply chain.

To take a recent example, hospitals were not given any advance notice of the manufacturing disruptions for intravenous contrast media. This lack of notification limited the ability and impacts of health systems to implement repackaging programs that would allow the existing supply to treat more patients.

When FDA notifies drug distributors to implement an allocation strategy for specific products, the agency can also notify health systems at large to adopt conservation strategies, potentially blunting the impact of a shortage.

2. FDA’s inspection reports—Form 483s or 483s—are a source of existing information that, if it were more readily available, could be used in multiple salutary ways, including:

- Knowledge that a 483 would quickly become publicly available with little or no redaction would spur manufacturers to proactively improve quality rather than face increased public scrutiny associated with adverse findings.
- Timely access to 483s would provide a near-real-time quality signal that could help the market anticipate or mitigate potential shortages. For example, knowledge of quality problems at a facility could allow Civica to increase orders with alternate manufacturers and could allow health systems to reduce use of a drug by using an alternate product, where possible.
- Improved access to 483 information would provide purchasers of drugs, such as health systems and group purchasing organizations, with a quality signal that could inform procurement decisions and vendor selection.

Unfortunately, not all 483s for drugs are posted on FDA's website, and those that are posted often take up to a year to appear. Moreover, in many of the documents posted, FDA redacts information that is critical to predicting drug shortages, including the name of the drug(s) that are the subject of adverse findings, even though disclosure of that information is not restricted by law.

FDA's current policy is to generally post 483s that have been the subject of multiple FOIA requests or that FDA expects to be subject to multiple requests. All others can be requested under the Freedom of Information Act (FOIA), but that route is unpredictable and at best generally takes at least 4 months, and sometimes years.

There is precedent for automatically posting a specific category of 483s where the use of FDA resources is justified by important public health concerns. After a serious incident related to compounding pharmacies, FDA started to post all 483s issued to compounding pharmacies.

FDA needs to adopt a similar approach with respect to 483s that are issued to drug/biologics manufacturers, and to post all drug-related 483s within 30 days of issuance. This could be accomplished by dedicating a single employee to the task. Even in a year with a high number of drug-related 483s there were 500. A single employee dedicated to this effort would only have to redact and post on average two 483s per day. Another advantage to having a dedicated person on this task is greater uniformity of redactions and that the employee would gain expertise in the issues that arise in connection with 483s, which could lead to fewer redactions.

In some instances, FDA has redacted information where there is no apparent legal justification, including the name of the currently marketed drug(s) at issue and other information, including about manufacturing, that is critical for predicting shortages and is neither trade secret nor proprietary. Eliminating or reducing the extent of redactions would allow more detailed information about quality risks into the public domain. Less redaction would presumably also facilitate speedier release of information.

However, as noted above, much relevant information on the drug supply chain and quality already exists, but is underutilized. We urge the Senate Finance Committee to incentivize hospitals to take active steps, using existing information and mechanisms, to take supply resiliency into account when procuring generic drugs.

QUESTIONS SUBMITTED BY HON. MARIA CANTWELL

Question. Washington State has been hit hard by nationwide drug shortages. A pediatric oncologist at Seattle Children's Hospital told me that 75 percent of the 20 most essential pediatric drugs have been in shortage over the last 5 years. This doctor is currently treating a 14-year-old girl with bone cancer who needs three essential medications. However, two of those three drugs are already in shortage and the third is running on low supply. Pediatricians and pharmacists now have to spend hours calling around to try to find emergency supplies of medications, while trying to avoid the unthinkable situation of rationing drugs.

For example, the Swedish Cancer Institute in Seattle already said this summer that it has been forced to "conserve and prioritize supply" because it is running so low on cancer medications. MultiCare, which runs 12 hospitals in Washington, has decided to prioritize curable patients when distributing medications.

Your company, Civica, was created to help make generic medicines accessible at an affordable price for everyone. Civica operates an innovative model that prioritizes the long-term predictability of supply and partners with health systems to identify potential gaps in supply. That goal is critical and it's something that everyone in the industry should be striving for.

We need manufacturers, providers, and everyone else in the drug distribution system to work together to prevent drug shortages so that patients like the 14-year-old at Seattle Children's Hospital can access lifesaving medications.

Can you describe in detail how Civica's model differs from others and helps reduce drug shortages?

Answer. Because our mission is to prevent shortages, several features of the "Civica model" are different from the traditional generic drug supply chain and may suggest potential improvements to the larger U.S. system. In particular:

- Civica enters long-term purchase and supply contracts that add stability to the market. This ensures that manufacturers have predictable demand over a period of years and therefore commit to, and invest in, continuing to supply that product.
- We target a 6-month buffer inventory of every drug to ensure continuity of supply. While there is a cost to holding additional inventory, having extra stock allows for continued supply through a supply disruption, such as a quality problem at another manufacturer making the same drug. A 6-month inventory is generally sufficient to allow for delivery of replacement batches before the buffer is exhausted.
- We emphasize U.S. sourcing whenever possible, with the EU and Canada as a second choice. We don't source finished drugs or API from China unless there is no other source. Too often, the market pursues the lowest cost drug without considering its source.
- Civica performs an intensive quality audit of potential suppliers, supplemented by ongoing review of key metrics, to reduce the risk of a failure to supply.
- Every drug is sold on a cost-plus basis, with the same price available to any purchaser. Our prices remain stable even when the drug is in short supply.

Question. Two Washington State hospitals, Providence and Common Spirit, are already members of the Civica network. How can the Finance Committee encourage other health systems to take similar steps?

Answer. This committee has a broad range of tools at its disposal, through oversight of Medicare and other public programs, payment policy, quality programs, and conditions of participation.

These tools can be used to encourage and incentivize health systems to put shortage mitigation strategies in place, such as participating in Civica or taking similar steps toward more resilient supply.

For example, CMS recently proposed a small bonus payment to hospitals who held, or contracted for, a buffer inventory of essential drugs. CMS did not move forward with this proposal, but with a few minor improvements that approach has the potential to really mitigate shortages. The immediate cause of most shortages of sterile injectable drugs is quality problems in the manufacture of the finished dosage form, but the root cause is a system that pursues low prices at the expense of supply resiliency.

Civica's approach to preventing shortages has been shown in a peer-reviewed analysis to be both more reliable than the conventional wholesaler channel and to produce *net cost savings* over time (Dredge C, Scholtes S. *NEJM Catal Innov Care Deliv* 2023; 4(10)). The savings result because when a drug is in shortage, hospitals can no longer acquire at the GPO contract price and may have to pay many times more than the pre-shortage price. However, because Civica may not be the lowest cost when a drug is not in shortage, many hospitals have yet to adopt this, or similar, strategies for shortage mitigation.

The Finance Committee should use its authority over provider reimbursement and quality to support providers in purchasing generic essential medicines, taking into account:

- Measures to ensure adequate buffer inventory,
- Measures to ensure that generic sterile injectable drugs are priced sustainably,
- Measures to create market demand from manufacturers that are less likely to have quality failures; and
- Support for domestic manufacturing.

Buffer Inventory

Production of injectable medicines is relatively inelastic. If a particular facility stops producing, others take many months to ramp up production (assuming other companies already have approval to produce the drug). Therefore, a system that operates on just-in-time inventory will always be at high risk of shortages.

However, the resources required to establish and maintain access to a buffer stock of essential medicines will generally be greater than the resources required to establish and maintain access to these medicines without such a buffer stock.

Congress should incentivize supply chain stakeholders to maintain buffer inventory. Civica's experience is that a 6-month reserve is the appropriate quantity to cre-

ate added resiliency, as it allows suppliers to deliver additional batches in the event of a supply interruption.

Congress could incentivize manufacturers, wholesalers, or providers to hold extra inventory. The most practical approach would be to provide incentives for hospitals, health systems and other providers to contract with manufacturers or wholesalers who actually hold the buffer stock. This maximizes the effectiveness of inventory allocation in a shortage situation and does not require providers to directly maintain or operate storage facilities, with the attendant cost, complexity, and risk of outdated inventory.

The Centers for Medicare and Medicaid Services, in its draft Inpatient Payment rule, recently proposed a very similar approach to providing supplemental payments to hospitals for this purpose. While CMS did not move the provision forward in the final rule, the committee should consider how, with minor improvements, it could be an effective approach.

Drug Shortage Prevention and Mitigation Strategies

Civica's hospital members have made investments and purchase commitments to reduce the impact of drug shortages, but all hospitals and health systems should have a drug shortage prevention strategy and review it on a regular basis. Elements of such a strategy could include:

- Identification of a priority list essential drugs that are at risk of shortages;
- Maintenance of buffer inventory to mitigate a supply disruption, including a contract for maintenance of inventory on behalf of the hospital; and
- Contracting procedures for those drugs that take into account:
 - Supplier quality,
 - Diversity of supply, and
 - Committed volume to bring stability to the market.

The committee should encourage and incentivize the development and implementation of such strategies, including through the use of Medicare payment policies.

QUESTION SUBMITTED BY HON. JOHN THUNE

Question. One of our health systems in South Dakota is a member of Civica and has told me the value they've experienced from the model Civica has developed. It has helped them maintain a stable supply of drugs for patients, especially those that are commonly in shortage.

In your testimony you mention that Civica takes quality into account when considering suppliers for drugs.

Can you tell us more about how considering quality has improved the reliability of your drug supply? How can Medicare policies better link payment for drugs to quality?

Answer. Civica performs an intensive quality audit of potential suppliers, including a physical inspection, supplemented by ongoing review of key metrics and quarterly quality reviews with each supplier, to reduce the risk of a failure to supply. In addition, we have a preference for U.S. sourcing, followed by other countries with mature regulatory systems (such as in the EU). We also exclude companies that have problematic quality histories. This approach selects for suppliers that are less likely to be responsible for recalls or otherwise have a failure to supply.

QUESTIONS SUBMITTED BY HON. TIM SCOTT

Question. Although America remains the world's top innovator in life sciences, it dramatically lags behind countries such as China and India in the manufacture of antibiotics and active pharmaceutical ingredients (APIs) formulated into tablets, capsules and medicines, and vitamin C. While States like mine reap extraordinary benefits from foreign investment by international manufacturers, returning the manufacturing and sourcing of life sciences products to our country is not only a powerful economic driver—it's a path to national and global stability. My Manufacturing API, Drugs, and Excipients (MADE) in America Act would help bring pharmaceutical manufacturing back to the United States by incentivizing pharmaceutical manufacturing in designated "Opportunity Zones," using tax credits to encourage production of vital products and ingredients in America.

Do you believe it to be critical to our national security to unwind from nefarious actors like China and prioritize manufacturing of APIs, generics/biosimilars, and essential medicines in the United States?

Answer. While we benefit in many ways from being part of a global economy, there are risks associated with dependence for essential medicines from China and other low-cost economies. These include both the immediate and ongoing risk of drug shortages and supply disruptions associated with quality problems (including, in some cases, intentional adulteration of drugs)¹ as well as the national security risk associated with our inability to produce essential drugs during a global public health crisis in which every country, understandably, will put the needs of its own population first. In addition, we must consider the risk to the United States if a trading partner were to use the drug supply as an economic lever in a future trade dispute or other conflict. It would be wise to make targeted investments and policy decisions to improve the resilience of the drug supply and insure it against future interruptions.

Question. Your proposal to incentivize redundant production plans for critical drugs on the shortage list is intriguing. Could you elaborate on how these contingency plans would function, and what role they would play in preventing shortages?

Answer. The current drug shortage crisis represents a continued failure of the U.S. and global pharmaceutical supply chain. At any given time, dozens or hundreds of essential medicines are on the FDA Drug Shortages list. These are generally old, off-patent, low-cost drugs, which are nevertheless essential to the operation of the U.S. health-care system.

Drug shortages are relatively predictable. A variety of risk factors can be considered, but the strongest prediction of a future shortage is whether the drug has been in shortage previously.

Shortages occur across therapeutic classes, but predominantly affect sterile injectable drugs. The immediate cause of shortages is generally a quality problem associated with the manufacture of the finished drug product (*e.g.*, vial). The root cause is economic: generic drug prices have been driven so low that many or most domestic producers have stopped producing the medication and the manufacturing is being done offshore in low-wage countries that are more likely to have quality problems and where FDA presence is less consistent.

Drug supply is relatively inelastic, so when a shortage occurs, there is generally not a facility with the capacity or approved process to rapidly increase production. In addition, there are no new entrants due to the inability to recover the cost of development and approval. Since it takes about 2 years to develop an ANDA submission and obtain FDA approval to market the drug, the market is slow to respond to any shortage.

Abbreviated New Drug Applications (ANDAs) are the process through which manufacturers apply to the FDA to produce generic drugs. Developing an ANDA for a generic injectable drug and obtaining FDA approval costs a manufacturer roughly \$3 million for development of analytical methods, formulation development, API qualification, manufacture of engineering and stability batches (required prior to FDA submission), stability studies and FDA Generic Drug User Fees. For some generic drugs, which sell for under less than \$4 per vial (sometimes less than \$1), the products simply can't be produced competitively in the U.S. at today's prices. Therefore, manufacturers are unlikely to maintain manufacturing capacity to produce drug in the event of a shortage.

With U.S. Government support, U.S. manufacturers could develop targeted ANDA products (those that are essential drugs at high risk of shortage) and maintain a stockpile of active pharmaceutical ingredient specifically for the purpose of increasing U.S. manufacturing capacity and mitigating future drug shortages. At modest cost, a one-time investment for each drug would create an insurance policy ensuring backup U.S. manufacturing capacity for essential drugs to rapidly respond to future shortages or other national security needs.

Question. Although generic medications save money for the health-care system, they are often not profitable enough for drug manufacturers, leaving little incentive to invest in their manufacturing. Additionally, because of a fragile supply chain, dis-

¹For a discussion of intentional adulteration of drugs from China, see Pew, "After Heparin," <https://www.pewtrusts.org/-/media/legacy/uploadedfiles/wwwpewtrustsorg/reports/health/pewheparinfinalhrpdf.pdf>.

ruption of a single manufacturing facility can turn into a widespread shortage. Civica Rx was launched by a group of hospital systems in 2018 with the goal of reducing prescription drug shortages and prices and has grown to represent 55 health systems. Civica focuses its efforts on essential medicines that are at elevated risk of shortage.

What role can nonprofits play in bringing low-cost generic and biosimilar medications to market and how can this model be supported?

Answer. Nonprofit pharmaceutical companies have potential to address patient needs that aren't adequately addressed by traditional pharma models. This includes opportunities to increase the resilience of the supply, develop new therapeutics that might not be attractive for traditional investors, and to develop generic and biosimilar products in order to deliver cost savings to consumers. For example, Civica is developing the three insulin analogs that account for most U.S. insulin use (insulin glargine, lispro, and aspart, which correspond to Lantus, Humalog, and Novalog, respectively). We are funding the development of these products through philanthropic contributions and public-private partnerships so that the development costs won't have to build into the price of the product. Civica intends to make these insulins available at transformative low prices, without engaging in rebating or other pricing strategies that distort the market and harm consumers.

As a nonprofit, our focus on supply chain resiliency includes steps (such as holding 6 months of inventory) that our dictated by our mission and not by the need for quarterly profits or shareholder returns (Civica is a nonprofit and does not have shareholders). Congress could take a number of steps to support the emergence and growth of nonprofit pharma models, including through tax code changes that would make it easier to establish new 501(c)(3) or analogous pharmaceutical companies, and through grants, cooperative agreements or other funding mechanisms that would ensure that non-profits (which can't seek traditional venture capital funding) are able to develop new products that are in the public interest.

Directly related to mitigating shortages, we would like to see more hospitals participate in Civica (or similar models) to bring stability to the drug supply and focus on more resilient models of purchasing and supply. In addition, the concept of funding ANDA development, discussed above, would support the ability of Civica or another nonprofit to develop drugs in anticipation of future shortages.

Question. Hospitals typically make their purchases on a just-in-time instead of a just-in-case basis. Earlier this year, the Centers for Medicare and Medicaid Services (CMS) proposed reimbursing hospitals for creating a 3-month stockpile of essential medicines; however industry has voiced multiple concerns. One such concern is that reimbursement would, in reality, likely only support well-financed hospitals that could afford a 3-month stockpile—otherwise, it will be a significant expense for hospitals with limited liquidity and (in worst case) exacerbate existing access disparities.

Can you discuss incentivizing the private sector to establish and maintain reserves, and what safeguards should be in place to prevent unintended consequences like hoarding?

Answer. The purpose of buffer stock is to allow for continuity of supply in the event of a supply interruption by any supplier in the market. Drug manufacturing is a relatively inelastic supply, meaning that even if multiple manufacturers have approval to make generic versions of the same product, it typically takes many months for production to increase.

The Civica model makes use of buffer stock, and its success is demonstrated by the fact that we have been able to consistently supply Civica member hospitals, often at double their committed volume, even when the product is in a national drug shortage. The availability of buffer inventory enables this resiliency. A recent peer-reviewed study found that the Civica supply model was both more reliable than the traditional wholesaler supply and, over time, produced net cost savings by providing stable pricing when a drug is in short supply and no longer available at the GPO contract price (Dredge C, Scholtes S. "Vaccinating Health Care Supply Chains Against Market Failure: The Case of Civica Rx." *NEJM Catal Innov Care Deliv* 2023;4(10), <https://catalyst.nejm.org/doi/abs/10.1056/CAT.23.0167>).

The cost to a manufacturer (or any entity) to hold buffer stock is directly related to the cost of capital for the value of the inventory held. Therefore, by taking into account that cost, plus a small additional administrative fee for the cost of storage facilities, it is possible to calculate a reimbursement premium that should exactly

offset a hospitals slightly higher acquisition cost from a manufacturer (or wholesaler) who holds extra inventory on their behalf.

By reimbursing for the cost of acquiring drug through a buffer stock program, CMS effectively creates a market for this service that values it at exactly what it costs to provide. This effectively creates a level playing field without introducing perverse incentives. Take a hypothetical drug sold by a manufacturer at the same \$2/unit price through non-buffered supply. If the manufacturer builds in the cost of the inventory buffer and sells through a buffered inventory at \$2.10, but the hospital receives an extra \$0.10 for purchasing buffered stock, the hospital no longer has an incentive to choose the non-buffered stock, but neither the hospital nor the manufacturer is “overpaid.”

If properly constructed, there is neither a practical barrier nor a cost penalty to less-resourced hospitals for participating in a buffer stock program. For example, Civica has both large, for-profit health system members and individual rural non-profit hospitals participating on the same basis. Civica offers the same price to both types of institutions and builds a buffer stock directly proportionate to their individual order volume.

In addition, it is important to understand that additional buffer stock anywhere in the system benefits the entire system (even non-participating hospitals) by mitigating the shortage and increasing total inventory available.

To prevent hoarding, buffer stock should be held “upstream” of the provider, rather than at the individual hospital level. Holding the inventory at the individual hospital level would not be the most efficient approach to inventory management. In general, hospitals rely on suppliers to make frequent (often daily) deliveries of medication and do not routinely maintain physical facilities to allow for storage and management of large amounts of additional pharmaceutical inventory. Nor do hospitals have the system to manage inventory or want the financial risk of expired inventory.

In contrast, manufacturers and wholesalers already operate GMP warehouses with inventory management systems suited to this quantity of products. In addition, there would be substantial efficiencies in inventory allocation by storing the buffer stock “upstream” where it could be shipped as needed and hospitals would not face the risk and potential cost of expired inventory that they do not use in a timely manner. The upstream approach guards against “hoarding” at the individual provider level, because the manufacturer or wholesaler can allocate limited stock equitably by shipping product based on historical purchase volumes.

QUESTIONS SUBMITTED BY HON. BENJAMIN L. CARDIN

Question. In a 2019 report from the FDA on drug shortages, the agency notes that FDA heard from stakeholders that some contracts currently include “low-price clauses” that allow group purchasing organizations to unilaterally walk away from a contract if a competing manufacturer is willing to supply the same product or bundle of products for a lower price.

How do practices like “low-price clauses” impact drug shortages?

Answer. Civica does not participate in GPO contracts and is therefore not subject to such clauses. However, we note that the market for generic sterile injectables is fragile. Manufacturers that do not have market share, or who are at high risk of losing sales even when under a contract, have limited ability and incentive to invest in quality or to make capital upgrades in newer facilities that may be less likely to have quality failures and thus contribute to shortages. If a manufacturer enters a contract at a fixed price, but is obligated to immediately lower that price if another supplier undercuts it, it creates a “race to the bottom” on price that is a well-documented driver of shortages.

Question. Now we hear that some PBMs have chosen to start group purchasing organizations even as PBMs use group purchasing organization services.

How might these relationships impact drug shortages, particularly patients’ ability to access low-cost drugs that typically do not provide much profit to manufacturers?

Answer. In general terms, it is natural and beneficial in a market when purchasers have sufficient buying power to keep prices low. However, when purchasing power is sufficiently consolidated, purchasers can push prices down in a “race to the

bottom,” at which point suppliers may exit the market or make decisions (such as offshoring) that result in instability of supply. This happens when the market considers price instead of considering price alongside other important factors such as quality and supply resiliency.

QUESTION SUBMITTED BY HON. SHERROD BROWN

Question. In its 2022 report, the United States-China Economic and Security Review Commission, or USCC, recommended that Congress direct the FDA and other Federal agencies to identify alternative sources for APIs and other ingredients, including utilizing Defense Production Act Authorities.

Recently, the administration announced its plans to implement some of these recommendations. Congress has already provided some resources to the administration to use Defense Production Act, or DPA, authorities to ramp up production of medical supplies—including generic pharmaceuticals. I fought to include this funding in the CARES Act.

One domestic company, National Resilience, has already secured a DPA loan to expand domestic manufacturing capacity of essential medicines in West Chester Township, OH.

What are additional authorities that the U.S. Government can use, similar to how the Defense Production Act is being used, to bolster the domestic manufacturing of pharmaceuticals?

Answer. To bolster the domestic pharmaceutical sector (as governments in other countries have), the U.S. Government can consider procurement policy, trade policy and, in some cases, targeted direct investments to address risks that can't be addressed as a purely commercial proposition in the current market. One opportunity is to use DPA or ASPR funding, or a similar mechanism, to invest directly in ensuring backup U.S. manufacturing capacity for essential drugs at high risk of future shortages.

Drug shortages are relatively predictable. A variety of risk factors can be considered, but the strongest prediction of a future shortage is whether the drug has been in shortage previously.

Shortages occur across therapeutic classes, but predominantly affect sterile injectable drugs. The immediate cause of shortages is generally a quality problem associated with the manufacture of the finished drug product (*e.g.*, vial). The root cause is economic: generic drug prices have been driven so low that many or most domestic producers have stopped producing the medication and the manufacturing is being done offshore in low-wage countries that are more likely to have quality problems and where FDA presence is less consistent.

Drug supply is relatively inelastic, so when a shortage occurs, there is generally not a facility with the capacity or approved process to rapidly increase production. In addition, there are no new entrants due to the inability to recover the cost of development and approval. Since it takes about 2 years to develop an ANDA submission and obtain FDA approval to market the drug, the market is slow to respond to any shortage.

Abbreviated New Drug Applications (ANDAs) are the process through which manufacturers apply to the FDA to produce generic drugs. Developing an ANDA for a generic injectable drug and obtaining FDA approval costs a manufacturer roughly \$3 million for development of analytical methods, formulation development, API qualification, manufacture of engineering and stability batches (required prior to FDA submission), stability studies and FDA Generic Drug User Fees. For some generic drugs, which sell for under less than \$4 (sometimes less than \$1), the products simply can't be produced competitively in the U.S. at today's prices. Therefore, manufacturers are unlikely to maintain manufacturing capacity to produce drug in the event of a shortage.

With U.S. Government support, U.S. manufacturers could develop targeted ANDA products (those that are essential drugs at high risk of shortage) and maintain a stockpile of active pharmaceutical ingredient specifically for the purpose of increasing U.S. manufacturing capacity and mitigating future drug shortages. At modest cost, this one-time investment for each drug would create an insurance policy ensuring backup U.S. manufacturing capacity for essential drugs to rapidly respond to future shortages or other national security needs.

For some categories of drugs, creating a U.S. manufacturing source will require the establishment of new, dedicated facilities. For example, penicillin antibiotics and cytotoxic cancer drugs cannot be manufactured in facilities shared with other drugs. For some of these products, a major capital investment cannot be justified at today's prices (when a company is competing against products from old facilities in low-cost economies that may have been directly subsidized by foreign governments). Therefore, for certain priority drug classes, the U.S. Government may need to support capital investment directly.

QUESTIONS SUBMITTED BY HON. JAMES LANKFORD

Question. My bill, the Ensuring Access to Lower-Cost Medicines for Seniors Act (S. 2129), aims to mitigate disincentives for favorable generic and biosimilar coverage. Currently, large Part D plans routinely exclude or disadvantage lower-cost biosimilars and complex generics and steer patients towards more expensive branded biologics and specialty drugs, exacerbating inflationary pressures currently facing seniors. These distorted dynamics also threaten the sustainability and long-term viability of competitive markets, as manufacturers confront the prospect of eroding returns, particularly for biosimilars—increasing consumer costs in the short term, as well as driving up health system spending in the long run.

How do current Part D plan and PBM benefit designs and coverage strategies impact uptake and access for low-cost alternatives to branded products, such as highly discounted biosimilars?

What impact might these types of coverage policies and formulary designs have on the viability of competitive markets with multiple entrants in the longer term?

Without a shift in these PBM and insurer practices, to what extent might current uptake challenges—such as those facing biosimilars and certain generics—signal or create shortage risks over time?

Answer. Historically, both Medicare D plans and many commercial insurance plans have favored brand drugs with high list prices and large rebates over competing biosimilar drugs with lower list prices and smaller rebates. Recent changes to Medicare D design in the Inflation Reduction Act may shift this calculation, as health plans now have less financial incentive to see beneficiaries advance into the catastrophic phase of coverage. However, the incentive remains in commercial insurance, and it remains to be seen whether biosimilar uptake will increase. As biosimilars should be a key strategy for reducing the prices of new medicines (as generics are for small-molecule drugs), it is important to have a market that takes advantage of biosimilar competition when it is available. If it does not, it will be difficult for the sector to continue to make continued investments, resulting in less long-term competition and higher prices.

Question. Within my role serving on the Senate Homeland Security and Governmental Affairs Committee, Chairman Peters and I have introduced the Mapping America's Pharmaceutical Supply (MAPS) Act (S. 2364). The MAPS Act would require that the Department of Health and Human Services work with other Federal agencies and relevant stakeholders to map the U.S. pharmaceutical supply chain. This policy would establish a database of critical active pharmaceutical ingredients (APIs) and drugs to prioritize for mapping and would use data analytics to assess threats and vulnerabilities so that we can more proactively prevent upcoming shortages.

We largely know what the root causes are of shortages, such as improper coverage and pricing schemes, inventory mismanagement, and lack of supply chain transparency, but how can we best pinpoint the most critically vulnerable supply chains? And how can we continually monitor supply chains to prevent future shortages?

Answer. The root cause of most drug shortages is a system that pursues low prices for sterile injectable generic drugs at the expense of supply resiliency. This results in market instability and reliance on manufacturers that are likely to have quality problems that result in shortages.

To manage long-term geopolitical risks, it is important to consider the manufacturing supply chain holistically from key starting materials to active ingredient to finished drug. But in terms of drug shortage, it is the finished drug manufacturing that is most likely to cause the shortage.

Fortunately, drug shortages are relatively predictable. The strongest predictor of a future shortage is a previous shortage. Therefore, the overall problem of drug shortages can be substantially addressed by tackling products that have been in shortage in the past 5 years. In addition, there are predictive models, such as a tool developed by the United States Pharmacopeia, that take additional risk factors into account. By focusing on drugs on the essential drugs list that have been in shortage recently and making targeted investments (at a one-time cost of about \$4 million per drug), the United States could create reserve manufacturing capacity for the highest-risk products in the supply chain.

Question. How can additional public-private partnerships be helpful here?

Answer. With U.S. Government support, U.S. manufacturers could develop targeted ANDA products (those that are essential drugs at high risk of shortage) and maintain a stockpile of active pharmaceutical ingredient specifically for the purpose of increasing U.S. manufacturing capacity and mitigating future drug shortages. At modest cost, this one-time investment for each drug would create an insurance policy ensuring backup U.S. manufacturing capacity for essential drugs to rapidly respond to future shortages or other national security needs.

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QUESTION SUBMITTED BY HON. ROBERT P. CASEY, JR.

Question. My colleagues and I have long called on the FDA to address drug shortages. In 2018, before the pandemic, several Senators and I sent a letter to the FDA to address the ongoing and worsening drug shortage. Now, we're seeing shortages at the highest they've been in almost a decade. I'm concerned that our current system to address drug shortages is too reactionary, leaving patients and their families worried about when the next drug might become unavailable.

What are some of the challenges of manufacturing drugs that are often in shortage and your thoughts on how we can build a more robust and resilient system to ensure drugs are always available when needed?

Answer. While FDA personnel work diligently to manage and prevent shortages, it must now be clear that chronic drug shortages have now become a built-in outcome of the current system of drug production and procurement. Market trends and the resumption of FDA inspections after COVID mean shortages are more likely to *increase* than to abate in the years ahead.

The immediate cause of most shortages of sterile injectable drugs is quality problems in the manufacture of the finished dosage form. But it is widely acknowledged that the root cause is the low cost of these products, which reduces the incentive or ability for manufacturers to invest in quality or in newer manufacturing facilities and pushes production offshore to low-wage markets where quality problems proliferate, and the FDA presence is less consistent.

Therefore, policy responses should focus on changing the current system that causes shortages because it favors low prices over resiliency of supply. Using its authority over provider reimbursement and quality, Congress should support providers in purchasing generic essential medicines, taking into account:

- Measures to ensure adequate buffer inventory;
- Measures to ensure that generic sterile injectable drugs are priced sustainably;
- Measures to create market demand from manufacturers that are less likely to have quality failures; and
- Support for domestic manufacturing.

PREPARED STATEMENT OF HON. MIKE CRAPO,
A U.S. SENATOR FROM IDAHO

This year, the Finance Committee has taken unparalleled action on prescription drug access and affordability. Our bipartisan PBM reform legislation would cut patient costs at the pharmacy counter, strengthen provider choice for seniors across the country, and reverse warped incentives that currently favor higher-priced medications. Our proposed policies would accomplish all of this—and more—while reducing the Federal deficit. Taxpayers, consumers, and community pharmacies deserve to see these bills passed by the full Congress, and delivered to the President's desk, as quickly as possible.

For patients with chronic conditions, as well as independent pharmacies at risk of potential closure, inaction is not an option. As our PBM process has shown, bipartisan, consensus-based, and market-driven policymaking can address a wide range of challenges facing seniors and working families.

In that same spirit of exploring effective legislative solutions, today we turn to another issue harming the health and finances of Americans in every State: the surge in drug shortages. For treatments targeting any number of conditions, from pediatric cancer to mental health ailments, our ability to prevent and resolve shortages can mean the difference between life and death.

To develop meaningful policy improvements to reverse the current rise in drug shortages, however, we first need to understand and examine the economic drivers, with a focus on the Federal programs within our committee's jurisdiction.

While high-priced medications have received outsized attention during prescription drug discussions in Congress, shortages disproportionately affect low-cost therapeutics, which operate in a largely different—and increasingly challenging—economic environment. In fact, 84 percent of shortages occur in generic drugs, and 56 percent of products in shortages have unit prices below a single dollar. Given that generics comprise roughly 9 in every 10 prescriptions filled across the United States, these shortages can inflict drastic harm on massive populations of Americans. The average shortage affects at least half a million consumers, forcing them to scramble for viable alternatives or else forgo treatment entirely.

As experts and officials have broadly affirmed, the structure of the generic drug market incentivizes a proverbial “race to the bottom” on pricing. Since 2016, generics have seen price erosion in excess of 50 percent. The razor-thin margins resulting from these dynamics trigger a host of dire consequences, from discouraging quality investments to spurring widespread outsourcing—including to China. Moreover, the generic drugmaker exit rate currently exceeds the rate of entry, and upwards of 40 percent of generic medication markets are supplied by a single manufacturer.

Rather than reduce shortage risks, unfortunately, a number of government policies likely make them more pervasive—and worse. Medicaid's inflation-based rebates, for instance, can trigger massive, uncapped losses on even low-cost generics, in addition to requiring literal “penny pricing” under 340B. These and other price-control policies warrant serious scrutiny in the context of generic products, especially for sterile injectables, which carry high production costs and offer minimal returns.

More broadly, our reimbursement systems, including under Medicare, offer little opportunity or incentive for drugmakers to compete on dimensions other than price—such as reliability and resiliency.

The House Energy and Commerce Committee's comprehensive work on this issue thus far is welcome. Enacting effective legislation will necessitate bipartisan, bicameral collaboration.

The Finance Committee can build on our strong track record of solutions-oriented policymaking to address the rash of drug shortages afflicting families across the country.

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One Page Summary of Submitted Comments for the Record on “Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective”

- There is a shortage of critical cancer drugs that is a growing crisis. These drugs, notably carboplatin, cisplatin, and fluorouracil, although decades old, are mainstay treatments for many different types of cancers, including curable cancers. As a result of these drug shortages, Americans with cancer are facing treatment delays, potentially receiving inferior treatments, and even having their treatments stopped.
- This is not a new crisis. I testified to Congress nearly 12 years ago and then again this year on shortages of injectable generic drugs used to treat cancer. This crisis is more severe and is due to denial and inaction about the root cause: financial. It is increasingly unprofitable to manufacture these sterile injectable drugs, which are not like making simple pills and tablets.
- Solutions proposed to deal with the crisis of drug shortages include early warnings and regulations from generic drug manufacturers, which may well backfire because the market is already over-regulated.
- The fundamental financial problems for generic drug manufacturers are that the Medicare Part B drug reimbursement system based on average sales price, also used by commercial payers, caps drug prices; mandatory 340B drug pricing discounts and Medicare rebates erode drug prices; and Inflation Reduction Act (IRA) drug price inflation caps further put downward pressure on injectable generic drug prices. These products at best are so unprofitable that there is little to no margin to invest in manufacturing upgrades. At worst, there is little manufacturing redundancy as manufacturers leave the market.
- Price caps, discounts, rebates, and regulation need to be stripped from the market or shortages will worsen. Congress needs to stop band-aiding the problem and fix the fundamental financial problem, as well as bring manufacturing back to the United States.
- Just recently, FDA Commissioner Robert M. Califf, M.D. spoke of drug shortages¹ and made the following point:

“One of the many reasons for drug shortages today involves manufacturers of older generic drugs and particularly injectables. These manufacturers face intense price competition, uncertain revenue streams, and investment requirements to maintain quality conditions. ***If the basic economics and contracting practices of the generic drug market are not fixed, more patients will be impacted by these shortages and we will miss this amazing global public health opportunity.***” (emphasis added)

Detailed Remarks for the Record

I appreciate the opportunity to submit these comments for the record on the Senate Finance hearing on “Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective.”

I am the executive director of the Community Oncology Alliance (COA), an organization dedicated to advocating for the complex care and access needs of patients with cancer and the community oncology practices that serve them. COA is the only non-profit organization in the United States dedicated solely to independent community oncology practices, which serve the majority of Americans receiving treatment for cancer. Since its grassroots founding 20 years ago, COA’s mission has been to en-

¹ Remarks by Commissioner Robert Califf to the Healthcare Distribution Alliance Board of Directors meeting, November 15, 2023

sure that patients with cancer receive quality, affordable, and accessible cancer care in their own communities where they live and work, regardless of their racial, ethnic, demographic, or socioeconomic status.

My wife Susan practiced as a certified oncology nurse for 10 years, administering cancer therapies to patients with solid tumors. Like many Americans, we have had family and friends with cancer, living with it and dying from the disease. **I want to make it very clear that my overriding goal is to ensure that every American with cancer has access to the highest quality, most affordable cancer care close to home.**

Through my time leading COA, including interactions with physicians, researchers, manufacturers, and health policy experts, as well as extensive previous experience founding and running health care delivery companies, I have gained a firsthand understanding of the underlying economics of our cancer care delivery system. I am submitting these comments to share this knowledge to help the Senate Finance Committee better understand and fix what is a true public health emergency that needs to be urgently addressed.

Background

The focus of my comments is on describing the problem of and providing legislative solutions to the current public health threat; namely, the shortage of critical cancer drugs that we are now facing. This is a growing crisis for cancer patients. As I am sure you have heard, given all the extensive national and local news coverage of this crisis, there is a severe shortage of low-cost generic drugs used to treat cancer. These drugs, notably carboplatin, cisplatin, and fluorouracil, although decades old, are mainstay treatments for many different types of cancers, including curable cancers. As a result of these drug shortages, Americans with cancer are facing treatment delays, potentially receiving inferior treatments, and even having their treatments stopped. What is especially heartbreaking, and simply unimaginable in this country, are our fellow Americans with potentially curable cancers who may miss the treatment and the cure because of shortages. Our inaction in fundamentally solving the cancer drug shortage problem, which has existed for years but is now the most severe that we have ever faced, has already likely signed a death sentence for some Americans.

If I sound angry in these comments, I am angry. Frustration and outright anger do not begin to describe how I feel in reading heartbreaking story after heartbreaking story of patients with cancer not being able to receive treatment due to shortages of decades old, low-cost generic drugs. My anger and frustration is exacerbated by the fact that nearly 12 years ago I testified to Congress on the then current cancer drug shortage crisis.² Also testifying was Scott Gottlieb, MD, who went on to become the FDA Commissioner.³ Although we did not know each other before testifying, independently we arrived at the same conclusion: *The fundamental root cause of cancer drug shortages is financial*. And, as I relate in these comments, the fundamental root cause of the current cancer drug shortages remains financial, just more pronounced than 12 years ago.

Unfortunately, solutions advanced in pronouncements from organizations, congressional letters to the FDA, and recent legislation introduced all deal with symptoms of the problem but none address the financial root cause at the heart of cancer drug shortages. Imagine being very diligent about staying out of the sun and getting regular skin checkups. If you had a suspicious looking mole, had it biopsied, and found out that you had melanoma, you would not be in denial and simply put a band-aid on the mole. You would have the underlying cancer treated. The problem is with many of the “solutions” being advanced is that they involve tracking early warning signs of shortages and placing even more regulations on generic drug manufacturers, which can actually have unintended consequences of exacerbating the problem. At best, these are mere band-aids. Congress is simply in denial of the financial prob-

²“Testimony on: Drug Shortages Crisis” to the United States House of Representatives Committee on Oversight and Government Reform Subcommittee on Health Care, District of Columbia, Census, and the National Archives,” Ted Okon, Community Oncology Alliance, November 27, 2011, https://oversight.house.gov/wp-content/uploads/2012/01/11-30-11_HealthCare_Okon_Testimony_FINAL.pdf.

³“The Causes of Drug Shortages and Proposals for Repairing these Markets,” Testimony to the United States House of Representatives Committee on Oversight and Government Reform Subcommittee on Health Care, District of Columbia, Census, and the National Archives,” Scott Gottlieb, M.D., American Enterprise Institute, November 27, 2011, https://oversight.house.gov/wp-content/uploads/2012/01/11-30-11_HealthCare_Gottlieb_Testimony.pdf.

lems that are at the root cause of these drug shortages. That denial is now costing Americans hope and even their lives.

Before describing aspects of the underlying financial problem and proposing specific solutions, I want to note that following my testimony on cancer drug shortages nearly 12 years ago, a concerned then Representative Bill Cassidy, M.D. introduced the Patient Access to Drugs in Shortage Act (H.R. 6611) in the 112th Congress. So, there has been legislation to address some of the root financial causes of cancer drug shortages introduced over 11 years ago. However, neither this legislation nor any other similar to it have been acted upon. Like an untreated cancer, the problem of cancer drug shortages is much worse and unnecessarily now costing lives.

The Fundamental Financial Problem

This is very simple and does not require a Ph.D. in economics: if a generic drug manufacturer cannot make a profit on a drug they will simply stop making the drug. If a manufacturer makes a very small margin on the drug it will cut costs, however possible. That includes running the manufacturing facility 24/7, cutting corners on quality, and not investing in new equipment and facilities. Cost cutting makes drug manufacturing facilities more prone to equipment failures and/or the kinds of problems that result in FDA inspections shutting down plants. Unfortunately, given many of the drugs in short supply are money losers, we have seen more and more manufacturers leave the market. Today, not only is there no manufacturing redundancy at the manufacturer level but there is little to no redundancy in the market as a whole.

Let me also explain that we are dealing with shortages of sterile injectable drugs, which are physician-administered intravenously or by other injectable means (referred to herein as “injectable” drugs). These are not pills or tablets. The manufacturing involved in producing sterile injectable drugs is far more involved and exacting, as well as capital intensive, than making pills or tablets. That is why, except for specific and short-lived supply or demand issues, shortages have not hit the pill or tablet market to the same degree as the sterile injectable market.

Before discussing the specific financial causes, let me address the belief by some that the current shortages were caused by the pandemic and resultant supply chain disruptions. Certainly, the “perfect storm” of the pandemic, supply chain disruptions, and resulting record high inflation may have been the fuse that lit the current generic drug manufacturing problem *but the root cause remains financial*. That is proven by the fact that cancer drug shortages have been around for well over a decade, before COVID, supply chain problems, and high inflation. These drug shortages are just now more pronounced due to the current environment and worsening financial picture, which I will describe.

I also want to be crystal clear that these comments and solutions I propose do not let pharmaceutical brand manufacturers off the hook for the high costs of drugs. They play a role in our health-care system, and we cannot deny that. However, Congress must understand that we are facing drug shortages for low cost, often money-losing, injectable generic drugs, not headline-making new and expensive brands. Injectable generics are a different part of our drug supply system that is adversely impacted by the bad economics of generic drug manufacturing, which desperately needs special consideration and immediate action.

Until we cure the fundamental financial cause of these drug shortages many Americans with cancer will be unable to access the treatments and cures that they deserve. That is simply unacceptable in this country!

The Reimbursement Problem

As background, the Medicare Modernization Act of 2003 (MMA) changed Medicare Part B drug reimbursement from average wholesale price (AWP) set by the manufacturer to average sales price (ASP), a market-based price. Oncology facilities administering chemotherapy are reimbursed by Medicare at ASP plus 4.3 percent, which is intended to cover drug cost, overhead, staff, and materials. In actuality, reimbursement is lower than ASP plus 4.3 percent due to manufacturer-to-distributor prompt payment discounts included in the ASP calculation. It is also important to understand there is a perpetual lag of 6 months in updating ASPs each quarter, which results in providers subsidizing Medicare for drug price increases.

The old AWP-based reimbursement system allowed generic drug manufacturers to compete on the margins they established by setting a drug’s AWP and then selling the drug at a discounted price. The ASP-based system changed generic drug manufacturers’ means of competing to solely on actual sales price. That and the 6-month

lag in updating Medicare reimbursement rates have resulted in a system that is effectively price capped. There has been steady downward pricing pressure on most generics since 2005, the year ASP was first implemented.

It is important to understand that ASP-based reimbursement is also used by commercial payers, in addition to Medicare. Additionally, ASP masks the true decline in net prices for manufacturers because they do not reflect other discounts and rebates exempt from the calculation of ASP.

Part of the motivation for replacing the AWP reimbursement system was to stop drug “arbitrage”—setting the AWP higher and selling at a discounted price. Ironically, the old AWP system actually allowed generic drug manufacturers pricing profitability. They could compete by adjusting their margins. The ASP-based system essentially price caps generic drugs. Then, when subject to mandatory government discounts and rebates, they have products that are barely profitable or even priced at a loss. And, just as ironically, the ASP-based system of reimbursement was the fuse that led to the explosive growth in what was once a little obscure government discount program—the 340B Drug Pricing Program—that has further eroded generic drug margins.

340B Drug Discount and Medicaid Rebate Problems

Generic manufacturers have felt additional pricing pressure from an increasing volume of 340B discounts, which they are required to extend to 340B-eligible hospitals and other entities who qualify for the program. Over the last 2 decades, as more independent community oncology practices facing lower reimbursements and financial pressures have been acquired by 340B hospitals, the scope and magnitude of these discounts have increased. Furthermore, Medicaid best price rebates exert further downward pricing pressure on true net prices realized by generic drug manufacturers.

History has clearly documented that repeated and misguided cancer care payment cuts have forced independent cancer care providers to close or merge with expensive hospital systems.⁴ When independent practices close, medical care almost always shifts to much more expensive hospitals, which typically are 340B hospitals. This has caused the 340B program to grow by over 1,600 percent from 2005—the first year of implementation of the ASP-based reimbursement system—through 2021. Thus, mandatory 340B discounts, coupled with Medicaid rebates, severely push down low-cost generic drugs to pennies, if that, making them increasingly not financially viable.

I understand that there are many in Congress who do not want to touch the 340B program. However, 340B is simply out of control *in the hospital market*. Investigative reports by *The New York Times*⁵ and *The Wall Street Journal*⁶ demonstrate how 340B funds intended to help patients and communities in need are simply not helping the disadvantaged. Rather, 340B has become a veritable printing press for hospitals. Additionally, 340B discounts incentivize the use of more expensive drugs, which is resulting in hospitals shunning biosimilars,⁷ which have the potential to bring down the high price of biologics. **I want to state for the record that COA supports the 340B program as it is intended to be used; that is, support patients and communities in need.** However, although the Federal grantees—community health, hemophilia, and HIV centers, et cetera—are using the program to support those in need, more hospitals are simply not.

Although some may be in denial, the reality is that mandatory 340B discounts and Medicaid rebates are major contributors to making the manufacturing of injectable generic drugs a losing proposition. And I will add that Congress expanding Medicaid rebates to generics exceeding the inflation rate was a terrible move that further compounded this problem.

IRA Inflation Price Cap Problem

While COA has acknowledged that one of the positives in the IRA is the inflation cap where brand drug manufacturers rebate any price increases above the current

⁴“2020 Community Oncology Alliance Practice Impact Report,” Community Oncology Alliance, April 24, 2020.

⁵“How a Hospital Chain Used a Poor Neighborhood to Turn Huge Profits,” *New York Times*, September 24, 2022.

⁶“Many Hospitals Get Big Drug Discounts. That Doesn’t Mean Markdowns for Patients,” *Wall Street Journal*, December 20, 2022.

⁷“The Role of Financial Incentives in Biosimilar Uptake in Medicare: Evidence From the 340B Program,” *Health Affairs*, May, 2023.

inflation rate, the unintended consequence of this portion of the law is that it puts further downward pressure on the price caps that generic drug manufacturers already face with the ASP-based reimbursement system. This inflation cap makes it virtually impossible for a generic drug manufacturer to increase the price of their products above the inflation rate to pay for manufacturing plant or machine upgrades and investments that are critical to avoiding drug shortages. This cap further contributes to the financial unattractiveness and instability in the injectable generic drug market.

Unfortunately, the IRA provision extending Medicare rebates to generic drugs exceeding the inflation rate doubles down on the Medicaid inflation cap rebate. These misguided policy moves are contributing to systematically destroying the injectable generic drug market.

Legislative Solutions

In order to fundamentally fix the chronic problem of drug shortages, I propose the following solutions.

Changes to the Reimbursement System

The Energy and Commerce Committee needs to include similar provisions as in H.R. 6611 (1112th Congress) in a legislative package to fundamentally fix the drug shortages problem. This legislative solution provides market incentives for injectable generic drugs with three or fewer active manufacturers. For a single source drug, Medicare reimbursement would be based on wholesale acquisition cost (WAC) rather than ASP. WAC will provide stable market-based pricing. It is the manufacturer's list price and is a real price, unlike AWP. WAC is used by the Centers for Medicare and Medicaid Services (CMS) to reimburse for new drugs that do not yet have an ASP at market launch.

Exemption from 340B Discounts and Medicaid Rebates

As in H.R. 6611, exempting low-cost injectable generic drugs from 340B discounts and Medicaid rebates is essential to achieving pricing stability and financial viability. These are low-cost generics, so the overall impact on 340B and Medicaid is very small. Additionally, these discounts and rebates are meaningless when a drug is in short supply and cannot be procured. Pricing changes and exemptions only occur when there are three or fewer manufacturers of these low-cost drugs. If the market is functioning correctly, there are no changes.

Exemption from the IRA Inflation Price Cap

In order to give generic drug manufacturers more pricing flexibility as incentive to invest in manufacturing facilities and to stay in the market, they should be exempted from the IRA inflation price cap.

Make Each Generic Drug a Unique Product

Another issue is that injectable generic drugs have been totally commoditized by CMS because all similar generics products are placed in the same reimbursement category. As with pill and tablet generic drugs, they are treated as interchangeable commodities. The result is that manufacturers have virtually no pricing latitude to increase prices to pay for plant and product manufacturing upgrades. Each injectable generic drug needs to have its own product code and treated as a unique product. Not only will this allow generic drug manufacturers more latitude in pricing flexibility but this is a necessary requirement to implementing the next solution.

Move Generic Manufacturing Facilities Back to the United States Via Value-Based Incentives

Drug manufacturers need to be incentivized to manufacture injectable generic drugs in the United States. We simply should not be relying on countries outside the United States for our supply of critical generic drugs used to treat cancer.

One obvious incentive is to use tax breaks. However, another way is to create "value" incentives for manufacturing plants that run according to "quality" standards to be rewarded with value-based payments. Manufacturers should be rewarded for investing in plant upgrades and hitting pre-agreed quality metrics. This is a creative approach to rewarding manufacturing excellence and follows the trend in health care of moving to value-based payments.

The scope of these comments is such that these are just outlines of legislative solutions. COA welcomes the opportunity to work with the Energy and Commerce Committee in greater detail to turn these conceptual solutions into comprehensive legislation.

Conclusion

If Congress does not address the basic fundamental financial root cause of generic drug shortages, the crisis will only worsen. We simply cannot regulate our way out of this mess, which some are suggesting we do with band-aids and more regulation. Let me be very clear that the current market is already too regulated, which is part of the problem. If we place any additional regulation and reporting onus on generic drug manufacturers we risk toppling what is already a house of cards. Band-aids will not solve the underlying financial problem. Not only are we in denial if we try to band-aid an ailing system but regulation will likely have negative unintended consequences and do nothing to solve the underlying financial issues behind drug shortages. Congress has to understand that Americans are paying a high cost for artificially low prices for drugs that are not even available right now to treat cancer.

Just so the urgency of this crisis is not lost on any member of Congress, as well as the administration, please consider the following very real stories provided by oncologists of their patients struggling with this current crisis.

Male patient, 72 years old, with stage III Merkel cell high-grade cancer requires pre-op carboplatin and etoposide due to the size and location of the cancer. With no carboplatin available, treatment cannot be switched to the second option because he has a liver transplant. So, he received the third treatment option of attenuated intensity chemotherapy. Chemotherapy treatment has been delayed and has resulted in an increase in the tumor size.

Female patient, 46 years old, with stage IIa poorly differentiated ER+, PR+, Her2+ breast cancer requires pre-op docetaxel, carboplatin, trastuzumab, and pertuzumab, which is the standard of care. She was not able to receive the carboplatin because it is not available. This is a curative intent regimen but the lack of carboplatin could lead to a higher risk of recurrence of disease and death.

Female patient, 32 years old, with BRCA1+, stage IIIc (T3N1M0) triple negative invasive ductal carcinoma who needed to receive indicated treatment of carboplatin, paclitaxel, doxorubicin, cyclophosphamide, and pembrolizumab. Carboplatin has had to be held due to shortages resulting in a suboptimal regimen for this young mother of three children with an aggressive breast cancer.

Unfortunately, there are already way too many of these heartbreaking stories across the country now on a daily basis.

It is beyond unfortunate and unthinkable that now we have to resort to desperate measures to address drug shortages, including importation of these short-supply drugs from China and any other country that will provide them urgently, as well as rely on other means to procure these critical drugs.

COA stands ready to work with Congress on these recommendations and others. We want to provide meaningful input on ensuring that Americans with cancer have access to the highest quality, most appropriate treatments. We implore Congress to put aside politics and simple solutions, which are more feel-good sound bites, to fundamentally fix a deteriorating cancer drug shortages crisis.

We are all concerned about high drug prices but we are now paying an inordinately high cost for low-priced drugs that are simply not available.

I end by quoting recent remarks by FDA Commissioner Robert M. Califf, M.D. where he spoke of drug shortages⁸ and made the following point:

“One of the many reasons for drug shortages today involves manufacturers of older generic drugs and particularly injectables. These manufacturers face intense price competition, uncertain revenue streams, and investment requirements to maintain quality conditions. ***If the basic economics and contracting practices of the generic drug market are not fixed, more patients will be impacted by these shortages and we will miss this amazing global public health opportunity.***” (emphasis added)

I appreciate the opportunity to provide these comments.

Ted Okon
Executive Director

⁸ Remarks by Commissioner Robert Califf to the Healthcare Distribution Alliance Board of Directors meeting, November 15, 2023

PREPARED STATEMENT OF INMACULADA HERNANDEZ, PHARM.D., PH.D., PROFESSOR, DIVISION OF CLINICAL PHARMACY, SKAGGS SCHOOL OF PHARMACY AND PHARMACEUTICAL SCIENCES, UNIVERSITY OF CALIFORNIA, SAN DIEGO

Chairman Wyden, Ranking Member Crapo, and honorable members of the committee, thank you for the invitation to testify about drug shortages. My name is Inmaculada Hernandez, and I am a pharmacist and professor at the University of California, San Diego. My testimony is substantiated by the academic research I conduct on the drug reimbursement system in the U.S. The opinions I offer today are my own and do not reflect the opinions of the organization with which I am affiliated.

Mr. Chairman, I applaud you for holding this hearing. Drug shortages are an ongoing public health concern that threatens patients' access to essential medications. Drug shortages have devastating consequences, leading to delays or omission in the use of life-saving treatments or substitution with less effective drugs, all of which contribute to adverse health effects and even death in certain clinical circumstances.^{1, 2, 3} As such, the development of policy reforms that address drug shortages is a national public health priority.

In the U.S., drug shortages are disproportionately seen in the generic product market—84 percent of the drugs experiencing a shortage in 2017–2023 were generics.⁴ Shortages of generic drugs are a complex interaction of many factors, including: (1) the lack of adequate financial incentives for manufacturers to, (a) produce drugs with limited profit margins, and (b) invest in resilient and mature drug supply chains; and (2) the logistical and regulatory complexities associated with drug manufacturing.²

My testimony focuses on the economic factors underlying shortages of generic products rather than regulatory oversight. This does not mean, however, that reform of the regulatory oversight of the supply chain is not needed. To the contrary, effective policymaking to address drug shortages requires a combination of policy reforms that address both economic and regulatory drivers.

In what follows, I explain the generic supply chain and the reimbursement model under Medicare and Medicaid. I discuss how the generic reimbursement model generates a “race to the bottom” of prices, which reduces manufacturer profitability, jeopardizing sustainability. I outline the mechanisms through which limited profit margins for certain drugs contribute to drug shortages. Finally, I provide policy recommendations for addressing this major public health risk.

I. THE GENERIC DRUG SUPPLY CHAIN

Generic products make their way to patients through a complex, global supply chain. The supply chain involves manufacturers, wholesalers, group purchasing organizations, pharmacies, health-care providers, and ultimately the patient. Below is a brief explanation of the major players in the supply chain. A resilient supply chain necessarily requires all players in the manufacturing, packaging, and distribution process to remain financially stable.

Manufacturing

Generic sponsors submit abbreviated new drug applications to the Food and Drug Administration (FDA). After approval, manufacturers may produce the active ingredient and the final dosage form or may outsource production. Increasingly, generic manufacturers purchase the active ingredient from a supplier and outsource the manufacture of the dosage form to contract manufacturing organizations. Thus, ge-

¹Vail E, Gershengorn HB, Hua M, Walkey AJ, Rubenfeld G, Wunsch H. Association Between US Norepinephrine Shortage and Mortality Among Patients With Septic Shock. *JAMA*. 2017;317(14):1433–1442.

²US Food and Drug Administration. Drug Shortages: Root Causes and Potential Solutions. Published 2019. Accessed November 3, 2023. <https://www.fda.gov/media/131130/download?attachment>.

³Gross AE, Johannes RS, Gupta V, Tabak YP, Srinivasan A, Bleasdale SC. The effect of a piperacillin/tazobactam shortage on antimicrobial prescribing and *Clostridium difficile* risk in 88 US medical centers. *Clin Infect Dis*. 2017;65(4):613–618.

⁴IQVIA Institute Report. Drug Shortages in the U.S. 2023. Published November 15, 2023. Accessed November 21, 2023. <https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/drug-shortages-in-the-us-2023>.

neric manufacturers serve as a coordinating body of regulatory approval, distribution and sales, but may not actually perform any manufacturing.⁵

All generic products marketed in the U.S. must adhere to the Current Good Manufacturing Practices. Current Good Manufacturing Practices are the minimum level of requirements for drugs to access the U.S. marketplace but are not necessarily indicators of resilience and maturity of the supply chain, needed to ensure supply continuity.

The U.S. heavily relies on foreign manufacturing of generic drugs, with 87 percent of active ingredients and 60 percent of final dosage forms produced overseas.⁶ Foreign manufacturing of drugs is associated with increased quality issues—an analysis of warning letters issued by the FDA in 2010–2020 found that the majority of letters reporting violations of Current Good Manufacturing Practices were issued to manufacturers based in Asian countries.⁷

Oral and Injectable Products

The market and manufacturing of generic drugs are markedly different for oral and injectable products. Oral products consist largely of tablets, capsules, and liquid dosage formulations. Injectables include products that are administered subcutaneously (under the skin), intramuscularly (into a muscle), or intravenously (into a vein). Injectable products require specialized manufacturing to ensure sterility, among other requirements that oral products are not required to meet.⁸

The market size of generic oral products, as measured in sales, is 200 times the market for generic injectable products.⁹ Additionally, the market for injectable products is considerably more concentrated—2 years after loss of exclusivity, generics oral products in the highest third of sales had an average of 13 generic manufacturers, compared to 2 for those in the lowest third of sales. In comparison, injectable generics in the highest third of sales had an average of four manufacturers, and those in the lowest third, only one manufacturer.⁹

Purchasing of Generic Drugs by Pharmacies and Health-care Providers

Wholesalers purchase generic products from manufacturers and distribute them to pharmacies and health-care providers, including physician offices, ambulatory clinics, and hospitals. The wholesaler market is highly concentrated, with over 90 percent of drugs distributed through only three wholesalers.¹⁰ Given the large volumes of purchases, when wholesalers design their lists of preferred generics, they consider the manufacturer's ability to supply sufficient volume to meet customer demand. This ultimately leads to the concentration of the manufacturer market, as only manufacturers who consistently produce large volumes of products are competitive enough to have preferred relationships with the primary wholesalers dominating the market. This highly concentrated market leaves limited room for smaller firms who might otherwise create competition and provide an alternative source of supply.

Pharmacies, health-care providers, and the clinics or institutions they work for purchase drugs from wholesalers. Often, the prices at which pharmacies and providers purchase generic products are negotiated by group purchasing organizations. Group purchasing organizations are buying consortiums that, through the use of their aggregate purchasing power, achieve greater discounts than individual members would on their own. The market of group purchasing organizations is highly

⁵Hernandez I, Hershey TB, Donohue JM. Drug shortages in the United States: Are some prices too low? *JAMA*. 2020;323(9):819–820.

⁶Shivdasani Y, Kaygisiz NB, Berndt ER, Conti RM. The geography of prescription pharmaceuticals supplied to the USA: Levels, trends, and implications. *J Law Biosci*. 2021;8(1):lsaa085.

⁷Rathore AS, Li Y, Chhabra H, Lohiya A. FDA Warning Letters: A Retrospective Analysis of Letters Issued to Pharmaceutical Companies from 2010–2020. *J Pharm Innov*. Published online August 15, 2022;1–10.

⁸Center for Drug Evaluation, Research. Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice. U.S. Food and Drug Administration. Published September 29, 2023. Accessed November 30, 2023. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/sterile-drug-products-produced-aseptic-processing-current-good-manufacturing-practice>.

⁹Frank RG, McGuire TG, Nason I. The evolution of supply and demand in markets for generic drugs. *Milbank Q*. 2021;99(3):828–852.

¹⁰Deloitte 2019 Report: The Role of Distributors in the US Health Care Industry. Published August 9, 2019. Accessed September 22, 2023. <https://www2.deloitte.com/us/en/pages/life-sciences-and-health-care/articles/the-role-of-distributors-in-the-us-health-care-industry.html>.

consolidated, with the four larger group purchasing organizations accounting for 90 percent of the market.¹¹

II. GENERIC DRUG REIMBURSEMENT

Generic Drug Reimbursement Under the Medicare Program

For reimbursement purposes, we distinguish between two types of drugs: (a) drugs that patients receive from a pharmacy (“pharmacy-dispensed drugs”), and (b) drugs that are administered to a patient in the clinical setting, incident to a provider service (“provider-administered drugs”). Injectable drugs are more likely to be administered in the clinical setting, as only selected injectable formulations are designed for self-administration. In what follows, I provide a simplified summary of the reimbursement of each type of product under Medicare.

Reimbursement of Pharmacy-Dispensed Drugs

Generic drugs are interchangeable by law as they are therapeutic equivalent versions of the same drug but manufactured by different companies. Thus, when a patient presents a prescription for a generic drug, the dispensing pharmacist selects among all generic versions approved by the FDA. Pharmacy-dispensed drugs are covered under Medicare Part D, which is administered through private insurers called Part D organizations. Pharmacy benefit managers administer prescription drug coverage on behalf of Part D sponsors or may act as Part D sponsors themselves, offering their own stand-alone prescription drug plans. As part of their services, pharmacy benefit managers reimburse pharmacies for the submitted claims. Generic drug reimbursement is based on the rates specified on contracts between pharmacy benefit managers and pharmacies. Importantly, these rates are generally the same regardless of the manufacturer of the generic product dispensed. *Since pharmacies are reimbursed the same amount regardless of the generic version selected, pharmacies are incentivized to purchase generic versions with low acquisition costs.*

Reimbursement of Provider-Administered Drugs

The reimbursement of provider-administered generic drugs under Medicare depends on the clinical setting in which the drug is administered.

1. Medicare Part A payments for inpatient hospital services are bundles that cover all services provided under a hospitalization, including drugs. In other words, drugs administered during an inpatient admission are not separately reimbursed. The payments for bundles are based on Medicare severity diagnosis related groups (MS-DRG), which represent the average resources to care for cases that fall within the MS-DRG. This bundling of payments is meant to dissuade the provision of unnecessary care and improve efficiency. In some cases, there may be additional add-on payments for new high-cost technologies to correct for costs incurred before codes and payment rates are updated to reflect new technologies.
2. Drugs administered in hospital outpatient departments with an estimated per-day cost below the packaging threshold (\$135/day in 2023) are not reimbursed separately. Just like in the case of inpatient admissions, hospital outpatient departments receive a bundled payment that accounts for all procedures and services delivered.
3. Drugs that qualify for coverage under Medicare Part B,¹² are administered in hospital outpatient departments, and have estimated per-day costs above the packaging threshold (\$135/day in 2023) are reimbursed separately. This reimbursement follows the “buy and bill model,” under which providers purchase the drug product and then bill Medicare using Healthcare Common Procedure Coding System (HCPCS) codes. Medicare reimburses such drug products at 106 percent of the average sales price.¹³ The average sales price is a statutory price benchmark net of manufacturer discounts. Importantly, multisource products have a unique weighted average sales price that includes all branded and generic versions of a product. The average sales price

¹¹ Bruhn WE, Fracica EA, Makary MA. Group Purchasing Organizations, Health Care Costs, and Drug Shortages. *JAMA*. 2018;320(18):1859–1860.

¹² Includes drugs furnished incident to a physician’s service, drugs used with durable medical equipment, antigens, vaccinations, erythropoiesis-stimulating agents for end-stage renal disease, blood clotting factors, immunosuppressive agents, oral-antiemetic drugs, oral cancer drugs, par-enteral and enteral nutrition.

¹³ Because of sequestration, actual payment rates since 2013 are estimated at 104.3 percent of average sales price.

is calculated quarterly, and there is a 2-month lag in its application, meaning that reimbursement rates in Q4 2023 are based on Q2 2023 average sales price.

4. Drugs that qualify for coverage under Medicare Part B¹² and are administered in physician offices are reimbursed separately. This reimbursement also follows the “buy and bill model” and is calculated as 106 percent of the average sales price.¹³

Regardless of whether reimbursement for a generic provider-administered drug is based on a medical service bundle or a separate payment, providers are incentivized to procure drugs at the lowest acquisition cost. This allows them to maximize margin, as the reimbursement (if any) is the same for all generic versions of a drug. These reimbursement incentives are unlike those for single-source products, where providers are incentivized to select more expensive products, as the 6-percent mark-up results in larger margins for more expensive drugs.¹⁴ The reimbursement model for generic drugs is also different from the reimbursement of biosimilar products, which have their own average sales price, separate from originator biologics.

As all generics marketed in the U.S. must meet regulatory requirements for adherence to Current Good Manufacturing Practices, the partiality of pharmacies and providers towards less expensive generic versions should not compromise quality of the product dispensed.² However, as explained above, these regulatory requirements are considered a *minimum threshold* for accessing the U.S. marketplace and do not necessarily reflect the resilience and maturity of the supply chain.

Generic Drug Reimbursement Under the Medicaid Program

The reimbursement of generic drugs under the Medicaid program presents certain peculiarities:

1. State Medicaid agencies have flexibility in the administration of the pharmacy benefit and the reimbursement of both pharmacy-dispensed and provider-administered drugs. For example, some States “carve in” the coverage of pharmacy-dispensed drugs by including it as a benefit under Medicaid Managed Care Organizations, while others administer it on a fee-for-service basis.

When Medicaid directly administers the drug benefit on a fee-for-service basis, the reimbursement is estimated based on the ingredient cost and a dispensing fee. The ingredient cost is meant to reflect the pharmacy acquisition cost.

2. The Medicaid Drug Rebate Program requires manufacturers to enter a rebate agreement for covered outpatient prescription drugs in exchange for Medicaid coverage of the manufacturer’s drugs (§ 1927(a)(1)). Rebates are defined by statute, and for generic drugs, are estimated as the sum of:
 - a. A base rebate, which equals 13 percent of the average manufacturer price. The average manufacturer price is the average price paid to the manufacturer by wholesalers for drugs sold to retail pharmacies.
 - b. An inflationary rebate, which penalizes increases in prices above general inflation. The inflationary rebate on generic drugs was implemented in January 2017 under the Bipartisan Budget Act of 2015. For drugs brought to market after April 1, 2013, the inflationary rebate is estimated using as baseline the average manufacturer price for the fifth full calendar quarter after which the drug was marketed. For drugs marketed before April 1, 2013, it is calculated based on the average manufacturer price in Q3 2014.
3. For provider-administered drugs to be eligible for manufacturer rebates under the Medicaid Drug Rebate Program, they need to be billed separately (§ 1927(k)(3)). This policy has strongly incentivized the separate reimbursement of outpatient provider-administered drugs, which States generally esti-

¹⁴The Medicare Payment Advisory Commission. Report to the Congress: Medicare and the Health Care Delivery System. Chapter 3: Part B Drug Payment Policy Issues. Published June 2015. Accessed December 1, 2023. https://www.medpac.gov/wp-content/uploads/import_data/scrape_files/docs/default-source/reports/chapter-3-part-b-drug-payment-policy-issues-june-2015-report-.pdf.

mate using the average sales price.¹⁵ It should be noted that a 2023 CMS proposed rule would make drugs reimbursed as part of bundles eligible for rebates, as long as they are separately itemized in the invoice.¹⁶

The 340B Drug Pricing Program

Manufacturers that participate in the Medicaid Drug Rebate Program are required to offer covered outpatient drugs to safety net providers at a discounted price. The discounted price is estimated using the rebate calculated under the Medicaid Drug Rebate Program explained above. The 340B program has substantially expanded in recent years, driven by the expansion of contract pharmacy arrangements.^{17, 18} In recently published work, I documented large variation across therapeutic classes in the share of drug sales that are subject to 340B discounts, highest for antivirals and anticancer agents.¹⁷

Reimbursement Practices and Contribution to Shortages

Downward Pricing Pressure

As generic drug reimbursement is the same across all therapeutically equivalent versions of a product, generic manufacturers solely compete to sell their product at the lowest price, generating a “race to the bottom.” Price erosion is aggravated by the consolidation of purchasing entities.¹⁹ It should be noted that, unlike branded drugs, *prices of generic products are generally lower in the U.S. than other countries.*²⁰

Limited Ability to Raise Prices

Inflation penalties under the Medicaid Drug Rebate Program and the 340B program limit manufacturers’ ability to raise prices when manufacturing costs increase, especially for drugs with a large share of sales under these two programs. This is particularly problematic for the subset of generic products marketed before April 1, 2013, for which inflation penalties are estimated based on an arbitrary period (Q3 2014) instead of the fifth full calendar quarter after marketing. Some manufacturers may have lowered their prices to near marginal cost by this arbitrarily set baseline period, so any increase in production costs would generate a penalty.

The reimbursement of generic products by Medicare Part B puts manufacturers that raise prices at a competitive disadvantage. This is because there is a two-quarter lag in the application of the average sales price to Medicare reimbursement rates (for example, reimbursement rates for Q4 2023 are based on the average sales price in Q2 2023). As a result, providers would be less willing to purchase drugs that have recently raised prices, as reimbursement rates are not updated for two quarters.

Contribution to Shortages

Reimbursement practices that were meant to create an efficient marketplace for generics and keep costs down have led to marked price compression, threatening market sustainability and supply continuity:

1. According to experts, *price pressure induces manufacturers to engage in cost-reduction strategies*, such as reduced investments in factory maintenance,

¹⁵ U.S. Government Accountability Office. Physician-administered Drugs: Comparison of Payer Payment Methodologies. Published August 1, 2016. Accessed November 26, 2023. <https://www.gao.gov/assets/gao-16-780r.pdf>.

¹⁶ Medicaid Program; Misclassification of Drugs, Program Administration and Program Integrity Updates Under the Medicaid Drug Rebate Program. 88 F.R. 34238 (proposed May 26, 2023).

¹⁷ Dickson S, Gabriel N, Hernandez I. Trends in proportion of Medicare Part D claims subject to 340B discounts, 2013–2020. *JAMA Health Forum*. 2023;4(11):e234091.

¹⁸ Nikpay S, McGlave CC, Bruno JP, Yang H, Watts E. Trends in 340B Drug Pricing Program Contract Growth Among Retail Pharmacies From 2009 to 2022. *JAMA Health Forum*. 2023;4(8):e232139.

¹⁹ Sardella A. U.S. Generic Pharmaceutical Industry Economic Instability. Published April 21, 2023. Accessed November 29, 2023. <https://apicenter.org/wp-content/uploads/2023/07/US-Generic-Pharmaceutical-Industry-Economic-Instability.pdf>.

²⁰ Mulcahy AW, Whaley C, Tebeka MG, Schwam D, Edenfield N, Becerra-Ornelas AU. International prescription drug price comparisons. Accessed November 22, 2023. https://www.rand.org/content/dam/rand/pubs/research_reports/RR2900/RR2956/RAND_RR2956.pdf.

²¹ Wosinska ME, Frank RG. Federal Policies to Address Persistent Generic Drug Shortages. Published 2023. Accessed November 8, 2023. https://www.brookings.edu/wp-content/uploads/2023/06/20230621_ES_THP_GSI_Report_Final.pdf.

²² Sardella A. Testimony Before the House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations Examining the Root Causes of Drug Shortages: Chal-

equipment upgrading and off-shoring,^{21, 22, 23} which increase the risk of quality issues. Quality issues create vulnerabilities across the supply chain and ultimately contribute to shortages.^{23, 24}

2. *Limited profitability generates a lack of incentives for manufacturers to invest in drug supply redundancies and quality management systems.*² Redundancies enable manufacturers to quickly ramp up manufacturing at the back-up line while resolving issues affecting the primary line, and thus prevent manufacturing issues from ultimately disrupting product supply. Quality management systems proactively identify issues before they lead to shortages.²
3. *Reduced profitability may ultimately lead manufacturers to discontinue the production of less profitable drugs.*²³ Market withdrawals increase the concentration of generic manufacturers,²⁵ which limits the market ability to respond to disruptions in the supply chain by a single manufacturer.

Generic Injectable Drugs—The Perfect Storm

The peculiarities of the manufacturing and marketing of generic injectable drugs generate a “perfect storm” that explains their vulnerability to drug shortages—67 percent of drugs on shortage in recent years were generic injectable products.⁴

1. Generic injectables have reduced profit margins due to the small market size⁹ and the requirements for specialized manufacturing, which make them costlier to manufacture than oral drugs.
2. Generic injectable markets have fewer entrants than generic oral markets.⁹
3. Rates of market exit are markedly higher for generic injectable products.⁹ An analysis of molecules that lost patent production in 2010–2013 found that, for generic products with small markets, more than half of generic manufacturers had exited the market by the end of the fourth year after loss of exclusivity.⁹
4. The manufacture of generic injectable products is particularly vulnerable to maintenance cost-reduction strategies due to the requirement for specialized manufacturing processes that ensure sterility.²⁴
5. Supply redundancies are particularly uncommon for generic injectable drugs, which require specific facilities and rooms.^{23, 24}
6. The requirement for specialized manufacturing lines limits the ability of other manufacturers to ramp up production in the setting of a drug shortage.

The time needed to establish production of injectable drugs is one of the factors that has limited the role of 503B outsourcing facilities in filling supply gaps for drugs on shortage.^{26, 27} 503B compounding facilities, often denominated outsourcing facilities, compound drug products in large volume without the need for patient-specific prescriptions. 503B facilities are only allowed to compound products that include bulk drug substances for which the FDA has determined there is clinical need, or products that appear in the FDA drug shortage list. 503B facilities are required to follow Current Good Manufacturing Practices and to compound at least one sterile product.²⁸ The role of 503B facilities in the manufacturing of drugs on shortage has been limited.²⁷ This has been attributed to the unpredictability around the occurrence and duration of shortages, which generate uncertainty around the profit-

lenges in Pharmaceutical Drug Supply Chains. Published May 9, 2023. Accessed November 29, 2023. https://d1dth6e84htgma.cloudfront.net/Witness_Testimony_Sardella_5_11_23_b932ed112a.pdf?updated_at=2023-05-10T18:13:11.412Z.

²³ Drug Shortages. A report from The Pew Charitable Trusts and the International Society for Pharmaceutical Engineering. Published January 2017. Accessed November 22, 2023. https://www.pewtrusts.org/-/media/assets/2017/01/drug_shortages.pdf.

²⁴ Woodcock J, Wosińska M. Economic and technological drivers of generic sterile injectable drug shortages. *Clin Pharmacol Ther.* 2013;93(2):170–176.

²⁵ U.S. Government Accountability Office Report to Congressional Addressees. Drug Shortages: Public Health Threat Continues, Despite Efforts to Help Ensure Product Availability. Published February 2014. Accessed November 8, 2023. <https://www.gao.gov/assets/gao-14-194.pdf>.

²⁶ Drug shortages roundtable: Minimizing the impact on patient care. *Am J Health Syst Pharm.* 2018;75(11):816–820.

²⁷ Mattingly AN. The role of outsourcing facilities in overcoming drug shortages. *J Am Pharm Assoc* (2003). 2021;61(1):e110–e114.

²⁸ United States Code: Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 353b (2014).

ability associated with the reassignment of production lines to products on shortage.²⁶

Other Shortcomings Associated With the Current Generic Drug Reimbursement Model

The failure to incentivize pharmacies and providers to purchase products with resilient supply chains is a major shortcoming of the generic reimbursement model, but not the only one. Earlier this year, Chairman Wyden brought attention to the provision of unjustifiably high reimbursements for certain generic drugs by Medicare Part D sponsors, an issue that I recently studied.²⁹ In collaboration with colleagues at the University of Washington, I evaluated reimbursement rates for the top 50 generic drugs by Medicare spending. I identified 16 generic drugs reimbursed in 2021 at a markup of 1,000 percent or higher by at least one of the six leading Part D organizations. For instance, aripiprazole 5mg, an antipsychotic drug, was purchased by pharmacies at an average of \$0.17 per tablet in 2021. However, Rite Aid reimbursed pharmacies at point-of-sale at an average of \$11.7 per tablet (over 7,000 percent markup), Cigna at \$4.6 per tablet (over 2,700 percent markup), and CVS Health at \$4.5 per tablet (over 2,600 percent markup).

Due to the confidential nature of post-sale adjustments, it was not possible to study to what extent these unjustifiably high reimbursements were offset by clawbacks. Nevertheless, the described reimbursement practices are concerning because point-of-sale reimbursement rates are the basis for patient cost sharing. As a result, it is likely that the provision of these unjustifiably high reimbursements rates resulted in increased out-of-pocket costs for Medicare beneficiaries.

III. POLICY RECOMMENDATIONS

The drug supply chain heavily relies on foreign manufacturing, which is a national public health risk. The drug reimbursement model fails to generate sufficient incentives for the manufacturing of certain drugs with limited profit margins, yet allows intermediaries to unjustifiably inflate costs of generic products covered under Medicare Part D. These major shortcomings warrant policy intervention to reenvision the way how we pay for generic drugs. In what follows, I focus on the aspects of the reform that more closely relate to drug shortages. These are not, however, the only reforms needed to the generic reimbursement model. The recommendations proposed below should be complemented by reforms to the Medicare Part D program to align patient and payer financial incentives, ensure fair pricing and reimbursement practices, prevent and penalize anticompetitive behavior, foster pharmacy sustainability, guarantee pharmacy access, and promote transparency. I applaud the efforts of the committee in the drafting and passage of legislation to achieve these goals earlier this year.

Effective policymaking requires a combination of policy reforms that address both economic and regulatory factors underlying drug shortages. My discussion is limited to policy solutions that address economic drivers of drug shortages. These interventions should be accompanied by the strengthening of the FDA oversight of the supply chain.

Federal policy intervention is urgently needed to: (1) rebuild the domestic infrastructure for the manufacturing of generic drugs, and (2) create incentives for manufacturers to invest in resilient supply chains to ensure long-term sustainability.

1. *Government funding to rebuild the domestic manufacturing infrastructure.* The provision of government funding is a short-term solution to rebuild the domestic infrastructure for the manufacturing of both generic active ingredients and final dosage forms. Funds would be destined for the establishment or upgrading of domestic facilities, purchasing of equipment, development of supply chain redundancies, and development of quality management systems. As suggested by Wosińska and Frank, funds could be provided in the form of low-interest loans, which would be eligible for forgiveness based on performance. Performance would capture the manufacturer's ability to meet supply guarantees and the achievement of high levels of supply chain maturity and resilience, as monitored by the FDA.²¹ Funds destined to the establishment or upgrading of production lines for a list of eligible products would be fully forgivable. The list of eligible products would be assembled by the

²⁹Hernandez I, Gabriel N, Kaltenboeck A, Boccuti C, Hansen RN, Sullivan SD. Reimbursement to Pharmacies for Generic Drugs by Medicare Part D Sponsors. *JAMA* 2023 doi:10.1001/jama.2023.21481.

Department of Health and Human Services (HHS) based on prices per unit, market concentration, recent history of shortages, vulnerability of the existing supply chain, and criticality of the product.³⁰

2. *Revision of generic reimbursement models to reward supply chain resilience and maturity.* I recommend a revision of generic drug reimbursement models to incentivize the selection of products manufactured in resilient and mature supply chains. Supply chain resilience and maturity are crucial for supply stability and continuity. Supply stability and continuity are elements of value because, when we initiate a patient on a treatment, we not only value the product available for the initial dose, but also the continuity of supply so that a patient can complete the treatment course. The value of supply continuity differentiates the generic market from the common commodity market and justifies variable payment based on the resilience and maturity of the supply chain of the generic version selected.

The reform of the current generic reimbursement model to reward supply chain resilience and maturity would involve:

- a. *Development of a rating system measuring supply chain resilience and maturity for each generic product.* The rating system would be developed by the FDA and would measure key elements for supply chain resilience and maturity. Such elements may include factory maintenance, upgrading of equipment, presence of manufacturing redundancies, and monitoring of manufacturing variability.² This system would differentiate from the Current Good Manufacturing Practices in that it would measure attributes of the supply chain that are not needed to ensure minimum levels of quality but are relevant to supply stability and continuity.

The ratings would be measured at the manufacturer-generic product level, would be mandatory for all generic products marketed in the U.S., and would be made publicly available by the FDA. Measurement at the manufacturer-generic product level is preferred over manufacturer-level measures, as the latter would incentivize manufacturers to invest in resilient supply chains for high-utilization profitable products but not necessarily for generic drugs most vulnerable to shortages.

- b. *Application of the rating as a value-based modifier to generic products reimbursed under Medicare Parts A and B.* The manufacturer-generic product rating would be transformed into a value-based modifier applied to claims for generic products separately reimbursed by Medicare Parts A and B. Reimbursement would still be based on the weighted average sales price capturing all branded and generic versions of a product. The value-based modifier would be operationalized as the mark-up for the average sales price, with different tiers for different ratings. For instance, reimbursement could be calculated as 125 percent of the weighted average sales price for generic versions scoring three out of three stars, 115 percent for products with two out of three stars, and 106 percent for products with one out of three stars. (Note: these markups are provided for illustration purposes; the incorporation of value-based modifiers would necessitate further research to identify the optimal magnitude of modifiers that incentivizes providers to purchase products with high ratings while limiting budget impact).

Claims would incorporate national drug codes in addition to HCPCS codes to enable identification of the generic version selected, as is currently done in Medicaid for rebate collection. The value-based modifier would be applied at the claim level. The alternative—the derivation of average value-based modifiers capturing product mix for a given provider—would disproportionately incentivize providers to purchase high rating generic versions for high-utilization drugs, but not necessarily for drugs most vulnerable to shortages.

The incorporation of value-based modifiers would increase provider reimbursement rates when selecting generic versions with high ratings,

³⁰ Wosińska ME, Joseph Mattingly T II, Conti RM. A Framework for Prioritizing Pharmaceutical Supply Chain Interventions. *Health Affairs Forefront*. doi:10.1377/forefront.20230912.938681.

which would ultimately result into higher acquisition costs and higher profit margins for manufacturers of generic versions with resilient and mature supply chains.

- c. *Establishment of eligible drugs with daily costs under the packaging threshold as separately payable products under Medicare Part A and Part B, independent of clinical setting.* Drug shortages disproportionately affect low-priced generic injectable drugs, which are not separately reimbursed under Parts A or under Part B when administered in outpatient hospital departments, as further detailed above. The incorporation of value-based modifiers at the drug claim level would require the separate reimbursement of eligible drugs with daily costs under the packaging threshold under Medicare Parts A and B, independent of clinical setting. Eligible products would include those in a list elaborated by HHS based on prices per unit, market concentration, recent history of shortages, vulnerability of the existing supply chain, and criticality of the product.³⁰

I recognize that this proposal would only generate incentives for providers to purchase drugs with resilient and mature supply chains, and not pharmacies. The creation of similar incentives in Medicare Part D would necessitate legislation that requires pharmacy benefit managers to incorporate value-based modifiers into Part D reimbursement rates.

Other Policy Solutions to Generate Incentives for the Manufacture of Selected Generic Drugs

The incorporation of value-based modifiers to the reimbursement of generic provider-administered drugs is a major overtaking, yet the necessary step to reward supply chain resilience and maturity. In what follows, I offer less sophisticated policy solutions that would have a *limited* impact in generating incentives for the manufacture of selected generic products:

1. *Creation of incentives for generic manufacturing through regulatory benefits.* Regulatory benefits could be explored as incentives for investments in supply chain resilience and maturity and for the manufacture of less-profitable products. Examples of these benefits include:
 - a. Manufacturers could be rewarded for investments in supply chain maturity and resilience through the development of tiers for generic user fees based on supply chain maturity and resilience ratings.
 - b. Waiver of generic user fees, award of priority review vouchers, or conferral of extended market exclusivity periods could be considered as incentives for manufacturers who enter the market of eligible products and commit to supply guarantees. Eligible products would include those in a list elaborated by HHS based on prices per unit, market concentration, recent history of shortages, vulnerability of the existing supply chain, and criticality of the product.³⁰
2. *Reform of the inflation penalty.* Several reforms to the calculation of the Medicaid inflationary rebate could be considered to partially mitigate the inability of manufacturers to raise prices in the context of manufacturing cost increases:
 - a. One-time reestablishment of the inflation penalty baseline for eligible generic products contingent on investments in manufacturing upgrades. Legislation could allow a one-time reestablishment of the baseline period for the measurement of inflation penalties for selected generic products in exchange for manufacturers' investment in upgrading production lines to meet a predetermined threshold of resilience and maturity. Eligible products would be selected as discussed under section 1b.
 - b. Reestablishment of the baseline period for calculation of the inflation penalty for generic drugs marketed before April 1, 2013 to the fifth full calendar quarter after marketing. As explained above, the baseline period for the calculation of the inflation penalty for generic products marketed before April 1, 2013 was arbitrarily set to Q3 2014. Drugs marketed before April 1, 2013 may have had prices close to marginal costs by Q3 2014, and thus any increase in production costs would generate a penalty. The reestablishment of the baseline period to the fifth full calendar quarter after marketing would mitigate the differentiation with

drugs marketed after April 1, 2013 introduced by the Bipartisan Budget Act of 2015.

- c. Redesign of the inflation penalty for eligible generic products to a trigger-based model. As explained above, inflation penalties limit manufacturers' ability to raise prices when manufacturing costs increase, especially for drugs with large share of Medicaid and 340B sales. To mitigate this problem while preventing price hikes, the inflation penalty could be redesigned to only penalize large increases in prices, for instance, above 3 times the rate of general inflation in a year. Eligible products would be selected using parameters discussed under section 1b.

Comment

Drug shortages are not a problem of the masses, but a problem of the exceptions. Many drugs have no substitutes. The shortage of a single product can trigger a major public health disruption³¹ and have devastating consequences on population health.¹ Policy intervention should aim to prevent drug shortages across the entire therapeutic arsenal of drugs approved by the FDA. Policymaking should refrain from solutions that only incentivize supply chain resilience for high utilization products or for drugs within certain therapeutic classes.

Drug shortages are a terribly complex problem. My policy recommendations address economic drivers of drug shortages that can be influenced through reform of Federal health insurance programs. There are however many factors contributing to shortages that are outside of the influence of Federal health program policy levers, the subject of this hearing.

I acknowledge that the solutions proposed will likely result in increased government spending. I am unaware of any budget-neutral policy solutions that would effectively address the economic drivers of drug shortages. This spending is a necessary investment in our country's health and national security. Just as we invest in the construction and maintenance of roads and bridges for economic prosperity, we must invest in generic manufacturing infrastructure to further our health and well-being and protect national security.

QUESTIONS SUBMITTED FOR THE RECORD TO
INMACULADA HERNANDEZ, PHARM.D., PH.D.

QUESTIONS SUBMITTED BY HON. MARIA CANTWELL

Question. The American Medical Association and the Association for Accessible Medicines have noted that pharmacy benefit managers, or PBMs, may contribute to practices that hinder access to lifesaving medication. PBMs are middlemen in the prescription drug industry with powerful influence over the price and distribution of prescription medications. The three largest PBMs control 80 percent of the total market share. The four largest PBMs also own their own affiliate insurers and pharmacies, which creates a clear conflict of interest.

Even when drugs are not in shortage, patients may still face access barriers caused by PBMs. PBMs that own their own pharmacies use unfair tactics that steer patients to those pharmacies while reducing market access for other unaffiliated ones. This decreases competition, limits patient choice, and causes smaller independent pharmacies to go out of business.

That is why I introduced legislation to increase transparency in the PBM market and encourage them to stop using discriminatory and predatory practices.

My bill, the PBM Transparency Act, would prohibit deceptive practices like reimbursement claw backs and spread pricing, while requiring PBMs to disclose data including any discrepancies between what they reimburse their affiliate pharmacies compared to non-affiliate pharmacies.

Can you talk about the access barriers that PBMs impose on patients trying to obtain necessary medications?

Answer. There are multiple business practices of pharmacy benefit managers (PBMs) that create or exacerbate access barriers to medications.

³¹Choi Y, Santhireswaran A, Chu C, et al. Effects of the July 2018 worldwide valsartan recall and shortage on global trends in antihypertensive medication use: a time-series analysis in 83 countries. *BMJ Open.* 2023;13(1):e068233.

1. PBMs often favor medications with high list prices and large rebates over medications with lower list prices.^{1,2} These practices reduce premiums if, after discounts, the net costs of the high-list-price products are lower than those of alternatives with lower list prices. Nevertheless, this preference towards high-list-price high-rebate products translates to increased out-of-pocket costs for patients,^{1,2} as patient coinsurance is calculated using the list price. The magnitude of confidential rebates negotiated between PBMs and manufacturers has increased exponentially in recent years,^{3,4,5,6} supporting an increasingly opaque reimbursement system for branded products.
2. Some PBMs have been shown to pay unjustifiably high reimbursement rates to pharmacies for generic products.^{7,8,9} In a paper recently published in *JAMA*, my colleagues and I identified 16 generic drugs that were reimbursed in 2021 at a markup of 1,000 percent or higher by at least one of the leading Part D sponsors.⁷ As patient coinsurance is based on the point-of-sale reimbursement, this practice likely results in increased out-of-pocket expenses for patients.
3. PBMs have established preferred-pharmacy networks, which hinder pharmacy access and contribute to closures of independent pharmacies through two mechanisms: First, through preferred-pharmacy networks, PBMs can steer patients to fill prescriptions at PBM-owned pharmacies by offering lower out-of-pocket costs.¹⁰ Second, independent pharmacies who accept contracts to participate in preferred pharmacy networks often receive reimbursement rates that are insufficient to cover drug acquisition costs and operating expenses. Beyond contributing to closures of independent pharmacies, preferred-pharmacy networks limit patient access because beneficiaries need to opt between traveling further to access preferred pharmacies or pay increased out-of-pocket costs at non-preferred pharmacies.
4. PBMs engage in non-transparent reimbursement practices that threaten the sustainability of independent community pharmacies, as in some cases, after post-adjudication adjustments (clawbacks), pharmacies are reimbursed by PBMs less than the drug acquisition amount.^{10,11} It should be noted that, effective January 2024, the Centers for Medicare and Medicaid Services (CMS) eliminated PBM use of retroactive fees in Medicare Part D. Fees will instead be charged at point of sale. Commercial plans may however continue to apply fees retroactively.

¹U.S. Government Accountability Office Report to Congressional Requesters. Medicare Part D: CMS Should Monitor Effects of Rebates on Plan Formularies and Beneficiary Spending. Published September 2023. Accessed December 28, 2023. <https://www.gao.gov/assets/gao-23/105270.pdf>.

²Murrin S. U.S. Department of Health and Human Services Office of Inspector General. Medicare Part D and Beneficiaries Could Realize Significant Spending Reductions With Increased Biosimilar Use. Published March 2022. Accessed December 29, 2023. <https://oig.hhs.gov/oei/reports/OEI-05-20-00480.pdf>.

³Dickson S, Gabriel N, Hernandez I. Contextualizing the Price of Biosimilar Adalimumab Based on Historical Rebates for Humira. *JAMA Network Open*. 2023;6(7):e2323398.

⁴Dickson S, Gabriel N, Gellad WF, Hernandez I. Estimated Changes in Insulin Prices and Discounts following Entry of New Insulin Products, 2012–2019. *JAMA Health Forum*. 2023;4(6):e231430.

⁵Dickson S, Gabriel N, Gellad WF, Hernandez I. Assessment of Voluntary and Mandatory Discounts in the Gross-to-Net Bubble for Leading Insulin Products, 2012–2019. *JAMA Network Open*. 6(6):e2318145.

⁶Hernandez I, San-Juan-Rodriguez A, Good CB, Gellad WF. Changes in List Prices, Net Prices, and Discounts for Branded Drugs in the U.S., 2007–2018. *JAMA*. 2020;323(9):854–862.

⁷Hernandez I, Gabriel N, Kaltenboeck A, Boccuti C, Hansen RN, Sullivan SD. Reimbursement to Pharmacies for Generic Drugs by Medicare Part D Sponsors. *JAMA*. Published online December 5, 2023. doi:10.1001/jama.2023.21481.

⁸Sunshine in the Black Box of Pharmacy Benefits Management: Florida Medicaid Pharmacy Claims Analysis. Published January 27, 2020. Accessed March 3, 2023. <http://ncpa.co/pdf/florida-3aa-medicaid-pharmacy-analysis.pdf>.

⁹Maine Health Data Organization Prescription Drug Transparency Report. Published December 14, 2022. Accessed March 20, 2023. https://mhdo.maine.gov/_pdf/MHDO%20Rx%20Transparency%20Report%20221213.pdf.

¹⁰Surya S, Seeley E. Competition, Consolidation, and Evolution in the Pharmacy Market. Published August 12, 2021. Accessed January 19, 2023. <https://www.commonwealthfund.org/publications/issue-briefs/2021/aug/competition-consolidation-evolution-pharmacy-market>.

¹¹Oregon Health Authority Pharmacy Benefit Managers Poor Accountability and Transparency Harm Medicaid Patients and Independent Pharmacies. Published August 2023. Accessed December 28, 2023. <https://sos.oregon.gov/audits/Documents/2023-25.pdf>.

Question. How would bills that encourage transparency, like my PBM Transparency Act, improve patient access to prescription drugs?

Answer. I support the PBM Transparency Act, which includes important provisions to address the opacity of the drug reimbursement system. The PBM Transparency Act prohibits claw backs from pharmacies to PBMs and spread pricing (the practice of charging health plans or payers higher amounts for prescription drugs than what PBMs reimburse pharmacies for). PBMs would not be in violation of the Act if: (1) PBMs passed 100 percent of rebates to health plans or payers; and (2) PBMs fully disclosed to pharmacies and health plans or payers the cost, price, and reimbursement of drugs, and all fees, markups, and discounts imposed to health plans or payers and pharmacies; *or* PBMs disclosed to health plans or payers and Federal agencies aggregate remuneration fees from manufacturers.

Additionally, the PBM Transparency Act requires PBMs to report to the Federal Trade Commission: (1) the aggregate figure for the difference between the amount the health plan paid the PBM and the amount the PBM reimbursed pharmacies; (2) the aggregate amount of fees and clawbacks charged to pharmacies; (3) for PBMs that are affiliated with pharmacies, differences in reimbursement rates, fees, and clawbacks between affiliated and non-affiliated pharmacies. The passage of the PBM Transparency Act would be an important step towards increased transparency in the PBM industry. I have some additional recommendations that build on this important policy:

1. While prohibiting pharmacy clawbacks is important to improve transparency, it is insufficient to ensure pharmacy sustainability, as PBMs may simply respond by adjusting point-of-sale reimbursement rates accordingly. Additional legislation is needed to ensure that reimbursement rates are sufficient to cover drug acquisition costs and pharmacy operating expenses.
2. PBMs could game the requirement for the 100-percent rebate pass-through rate by redefining what counts as rebate. Recently, PBMs established group purchasing organizations (GPOs), which could be leveraged to recategorize rebates, ensuring compliance with the 100-percent rebate pass-through rate while deviating discounts through alternative income streams.¹² Provisions that prevent PBMs from using affiliated entities to circumvent this provision would be crucial for the effectiveness of the policy.
3. The mandatory disclosure of aggregate amounts of differences in reimbursement rates, fees, and clawbacks between affiliated and non-affiliated pharmacies is insufficient to address concerns around the consequences of PBM and pharmacy affiliation. Aggregate amounts can mask concerning reimbursement practices for certain products and market sectors. For instance, there is a concern that the over-reimbursement of generics may help PBMs affiliated with pharmacy chains shift profits to the pharmacy side of the conglomerate.⁷ The testing of this hypothesis requires claim- or product-level data for differences in reimbursement rates, fees, and clawbacks between affiliated and non-affiliated pharmacies. If only aggregate amounts are reported, any potential signal of differential reimbursement for generic drugs would be masked by data for branded and specialty products, which account for the largest share of spending.
4. The PBM Transparency Act could be strengthened if it regulated preferred pharmacy networks and directly addressed the preference of PBMs towards drugs with high list prices and high rebates.

I applaud the Senator's efforts to improve transparency on the business practices of PBMs. I encourage the introduction and support of legislation that (1) aligns the financial incentives of patients, health plans or payers, and PBMs, preventing practices that increase out-of-pocket costs for patients; (2) regulates preferred-pharmacy networks, and prevents anticompetitive behavior associated with PBM and pharmacy affiliation, guaranteeing pharmacy access and sustainability of independent pharmacies.

I remain at the service of the Senator to assist with legislative efforts that address these relevant goals.

¹²Joseph S. The Opportunity to Unbundle and Disrupt Pharmacy Benefit Managers (Part 1). *Forbes Magazine*. Published online November 13, 2022. Accessed January 2, 2024. <https://www.forbes.com/sites/sethjoseph/2022/11/13/how-to-get-away-with-corporate-murder-unbundling-and-disrupting-pharmacy-benefit-managers-part-1/?sh=2844dc137bc0>.

QUESTIONS SUBMITTED BY HON. BENJAMIN L. CARDIN

Question. In a 2019 report from the FDA on drug shortages, the agency notes that FDA heard from stakeholders that some contracts currently include “low-price clauses” that allow group purchasing organizations to unilaterally walk away from a contract if a competing manufacturer is willing to supply the same product or bundle of products for a lower price.

How do practices like “low-price clauses” impact drug shortages?

Answer. There are two key stakeholders in the purchasing of generic drugs: (1) generic drug buying groups; and (2) group purchasing organizations (GPOs). Both of them exert pressure on generic manufacturers, thus contributing to price erosion.

GENERIC DRUG BUYING GROUPS

Traditionally, large pharmacy chains directly contract with generic manufacturers to purchase drugs. In the last decade, large pharmacy chains have partnered with leading wholesalers to create joint ventures for generic sourcing. These entities include Red Oak Sourcing (Cardinal Health + CVS), Walgreens Boot Alliance Development (AmerisourceBergen + Walgreens), and ClarusOne/McKesson (McKesson + Walmart). The establishment of these entities has resulted into a highly concentrated market: it is estimated that, in 2018, these three buying groups accounted for over 90 percent of U.S. generic drug purchases.¹³ The large concentration of generic buying groups reduces prices¹³ and limits the ability of generic manufacturers to raise prices when costs of production increase.

Due to the lack of publicly available data on contracting practices, I am not able to comment on how the specific terms of agreements between generic manufacturers and buying groups contribute to shortages. It should be noted, however, that the Association for Accessible Medicines, which represents generic and biosimilar manufacturers, reports a long list of contract terms that contribute to generic price erosion.¹⁴ For example, they report that contracts often include failure-to-supply agreements that require generic manufacturers to pay penalties if they fail to supply product.¹⁴ These agreements may have incentivized manufacturers to discontinue the production of less profitable products, instead of bearing the risk of penalties in the setting of a shortage.

GROUP PURCHASING ORGANIZATIONS

GPOs negotiate purchasing rates for products on behalf of their members. Unlike the generic buying groups described above, GPOs do not take title to the product. Contracts between GPOs and generic manufacturers include low-price clauses that give GPOs the flexibility to purchase products from other manufacturers who may offer the product at a lower price than negotiated. Due to the lack of transparency around contracting practices, it is unclear with which frequency GPOs contract with manufacturers undercutting the market and offering lower prices than negotiated with the original supplier. It should be noted, however, that even if GPOs do not contract with generic manufacturers undercutting the market, these suppliers are accessible to health systems and providers via wholesalers. In other words, members of GPOs may purchase product from generic manufacturers with lower prices outside of the GPO contract. These purchasing practices are allowed by the infrequent inclusion of minimum purchase requirements in contracts.

In summary, low-price clauses included in GPO contracts with generic manufacturers are only one of multiple purchasing practices that create price pressure on manufacturers. Price pressure is exacerbated by the consolidation of purchasing entities, particularly of generic buying groups. Downward price pressure interacts with the limited ability to raise prices when costs of production increase, threatening market sustainability and continuity:

¹³Fein AJ. The Big Three Generic Drug Mega-Buyers Drove Double-Digit Deflation in 2018. Stability Ahead? (rerun). Accessed December 26, 2023. <https://www.drugchannels.net/2019/07/the-big-three-generic-drug-mega-buyers.html>.

¹⁴Association for Accessible Medicines. Comments to the Federal Trade Commission and Antitrust Division of the Department of Justice. Published March 21, 2022. Accessed December 26, 2023. <https://accessiblemeds.org/sites/default/files/2022-03/AAM-Public-Comments-RFI-Merger-Enforcement-Version-3-18-22.pdf>.

1. Price erosion foments the adoption of cost-containment strategies, which increase the risk of quality issues.^{15, 16, 17} Quality issues create vulnerabilities across the supply chain and ultimately contribute to shortages as production must be halted until issues are resolved.^{17, 18}
2. Limited profitability generates few incentives for manufacturers to invest on redundant manufacturing capacity and quality management systems, which can prevent and restore supply disruptions before they result in shortages.
3. Limited profitability may ultimately result in manufacturers' determination to discontinue production, increasing market concentration and limiting the ability of the market to respond to disruptions in the supply chain by a single manufacturer.

Now we hear that some PBMs have chosen to start group purchasing organizations even as PBMs use group purchasing organization services.

Question. How might these relationships impact drug shortages, particularly patients' ability to access low-cost drugs that typically do not provide much profit to manufacturers?

Answer. The establishment of GPOs by PBMs is a new example of increased vertical integration that gives the resulting conglomerates additional control over the drug supply chain. The primary reason underlying the establishment of GPOs by PBMs is to increase their ability to negotiate rebates with manufacturers for brand-name products.¹⁹ As noted above, the establishment of GPOs can also help redefine what counts as rebates, providing flexibility for PBMs to respond to potential new requirements for transparency.¹² Drug shortages disproportionately affect generic products.²⁰ As a result, it is unclear how the establishment of PBM-led GPOs focused on branded products could contribute to shortages of generic drugs.

It should be noted, however, that PBMs participate in generic drug buying groups through direct or indirect ways. For example, the PBM Express Scripts participates in the generic buying group Walgreens Boot Alliance Development through a subsidiary called Innovative Product Alignment.²¹ The alignment of wholesalers, large pharmacy chains, and PBMs increases control over the entire chain of distribution and reimbursement of generic drugs.

QUESTION SUBMITTED BY HON. SHERROD BROWN

Question. In its 2022 report, the United States-China Economic and Security Review Commission, or USCC, recommended that Congress direct the FDA and other Federal agencies to identify alternative sources for APIs and other ingredients, including utilizing Defense Production Act Authorities.

Recently, the administration announced its plans to implement some of these recommendations. Congress has already provided some resources to the administration to use Defense Production Act, or DPA, authorities to ramp up production of medical

¹⁵ Wosińska ME, Frank RG. Federal Policies to Address Persistent Generic Drug Shortages. Published 2023. Accessed November 8, 2023. https://www.brookings.edu/wp-content/uploads/2023/06/20230621_ES_THP_GSI_Report_Final.pdf.

¹⁶ Sardella A. Testimony Before the House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations Examining the Root Causes of Drug Shortages: Challenges in Pharmaceutical Drug Supply Chains. Published May 9, 2023. Accessed November 29, 2023. https://d1dth6e84htgma.cloudfront.net/Witness_Testimony_Sardella_5_11_23_b932ed112a.pdf?updated_at=2023-05-10T18:13:11.412Z.

¹⁷ Drug Shortages. A report from The Pew Charitable Trusts and the International Society for Pharmaceutical Engineering. Published January 2017. Accessed November 22, 2023. https://www.pewtrusts.org/-/media/assets/2017/01/drug_shortages.pdf.

¹⁸ Woodcock J, Wosińska M. Economic and technological drivers of generic sterile injectable drug shortages. *Clin Pharmacol Ther.* 2013;93(2):170–176.

¹⁹ Heron E. Peeking Behind the PBM-lead GPO Curtain. Eversana. Published April 13, 2023. Accessed December 26, 2023. <https://www.eversana.com/insights/peeking-behind-the-pbm-led-gpo-curtain/>.

²⁰ IQVIA Institute Report. Drug Shortages in the U.S. 2023. Published November 15, 2023. Accessed November 21, 2023. <https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/drug-shortages-in-the-us-2023>.

²¹ Express Scripts. Express Scripts Subsidiary to Join Walgreens Boots Alliance Development Group Purchasing Organization. PR Newswire. Published May 18, 2017. Accessed January 2, 2024. <https://www.prnewswire.com/news-releases/express-scripts-subsidiary-to-join-walgreens-boots-alliance-development-group-purchasing-organization-300459770.html>.

supplies—including generic pharmaceuticals. I fought to include this funding in the CARES Act.

One domestic company, National Resilience, has already secured a DPA loan to expand domestic manufacturing capacity of essential medicines in West Chester Township, OH.

What are additional authorities that the U.S. Government can use, similar to how the Defense Production Act is being used, to bolster the domestic manufacturing of pharmaceuticals?

Answer. This question is outside of my area of expertise. I applaud the Senator's efforts to leverage the Defense Production Act to support the expansion of domestic manufacturing of drug products. I am unable to speak from experience on this topic. However, anything that can be done to expand domestic manufacturing capacity to boost production of generic drugs would help alleviate shortages.

QUESTIONS SUBMITTED BY HON. JAMES LANKFORD

Question. My bill, the Ensuring Access to Lower-Cost Medicines for Seniors Act (S. 2129), aims to mitigate disincentives for favorable generic and biosimilar coverage. Currently, large Part D plans routinely exclude or disadvantage lower-cost biosimilars and complex generics and steer patients towards more expensive branded biologics and specialty drugs, exacerbating inflationary pressures currently facing seniors. These distorted dynamics also threaten the sustainability and long-term viability of competitive markets, as manufacturers confront the prospect of eroding returns, particularly for biosimilars—increasing consumer costs in the short term, as well as driving up health system spending in the long run.

How do current Part D plan and PBM benefit designs and coverage strategies impact uptake and access for low-cost alternatives to branded products, such as highly discounted biosimilars?

Answer. I wish to start with a very brief explanation of the economics of the biosimilar market in the U.S. First, a large share of biosimilar drugs marketed in the U.S. are provider-administered drugs, which are primarily covered under the medical benefit of an insurance policy (Medicare Part B). Second, in the biosimilar market, there are typically fewer competitors as compared to the generics market. Only in 2023 did the market see the entry of multiple biosimilars for adalimumab, the first biologic product with a number of competitors comparable to that seen in the small-molecule generics market. Third, according to the limited experience with self-administered biosimilars representing the period before the entry of biosimilar adalimumab, rates of price erosion are considerably lower than those observed for small-molecule generics.^{22, 23}

There are several reasons that explain these market dynamics. First, in the U.S., a large share of the biosimilar market is supplied by traditional brand-name manufacturers (e.g., Amgen, Biogen, Novartis, Pfizer, Roche).²⁴ These manufacturers have the manufacturing capacity and technical skill to produce and distribute biologic products, which require complex manufacturing processes and cold chain distribution and storage. Second, manufacturers of originator reference products offer increased rebates to payers in response to biosimilar competition.^{1, 25, 26} Thus, biosimilars compete not only among themselves but also with the originator product. This is a major difference with the behavior of small-molecule non-complex branded products, which rarely attempt to compete with generics.²⁷ Third, while the market share of small-molecule non-complex branded products falls by up to 90 percent in

²² Mulcahy AW, Hlavka JP, Case SR. Biosimilar cost savings in the United States: Initial experience and future potential. *RAND Health Q.* 2018;7(4):3.

²³ Stern AD, Chen JL, Ouellet M, et al. Biosimilars and follow-on products in the United States: Adoption, prices, and users. *Health Aff (Millwood).* 2021;40(6):989–999.

²⁴ Biosimilars: Top 10 pharma companies leading the way. *Clinical Trials Arena.* Published January 20, 2022. Accessed December 29, 2023. <https://www.clinicaltrialsarena.com/features/biosimilars-the-top-10-pharma-companies-leading-the-way/>.

²⁵ San-Juan-Rodriguez A, Gellad WF, Good CB, Hernandez I. Trends in list prices, net prices, and discounts for originator biologics facing biosimilar competition. *JAMA Netw Open.* 2019;2(12):e1917379.

²⁶ Maini L, Feng J, Hwang T, Klimek J. Biosimilar Entry and the Pricing of Biologic Drugs. Published online January 4, 2021. doi:10.2139/ssrn.3760213.

the year after generic entry,^{27,28} originator biologic products are able to retain substantial market share after biosimilar entry.^{2,23}

Several reports have documented the preference of Part D plans towards originator products with high list prices and large rebates over complex generic or biosimilar versions with lower list prices.^{1,2} These practices are the result of several factors:

1. The standard benefit parameters that define phases in the Part D program, including entry into the catastrophic phase, are determined by gross drug costs that do not account for discounts negotiated between manufacturers and payers. PBMs operating in the Part D market are incentivized to favor drugs with high list prices and high rebates, which shift spending into the catastrophic phase, where plans are only responsible for 15 percent of drug costs. This share will change with the passage of the Inflation Reduction Act: After 2025, Part D plans will be responsible for 60 percent of drug costs once beneficiaries reach the \$2,000 out-of-pocket cap.
2. Part D plans may also favor originator biologics because of the so-called “rebate trap.”²⁹ Often, manufacturers provide greater rebates to payers if their drug is the only one or one of two products with preferred status.¹ If payers include non-interchangeable biosimilar products in their preferred tier, they risk losing rebates from the reference biologics for all patients who fail to switch to the biosimilar.
3. Prices offered by biosimilar manufacturers may not be low enough to incentivize their preferred placement. At comparable net prices, Part D plans are expected to favor originator products, as, in addition to benefiting from the Part D benefit structure defined above, they also prevent patient and provider concerns around medication switching in chronic treatment regimens.

The preferred placement of originator drugs with high list prices and rebates on formularies reduces premiums and taxpayer spending if, after discounts, net costs of originator drugs are lower than net costs of biosimilar products. However, this practice results into increased out-of-pocket payments for Medicare beneficiaries, as coinsurance is calculated using the list price.²

It should be noted that preference for originator products with high list prices and high rebates is not unique to the Part D market. In a study published in the *Journal of Managed Care and Specialty Pharmacy*, I demonstrated that Medicaid programs that administer pharmacy benefits on a fee-for-service basis heavily favored originator products.³⁰ This was also the case for Medicaid programs that carved in pharmacy benefits under Medicaid Managed Care Organizations, but had preferred-drug lists. The preference towards drugs with high list prices and high rebates by Medicaid programs does not necessarily result in increased beneficiary cost sharing, as it is minimal in Medicaid, but also impacts uptake of biosimilar products.

Question. What impact might these types of coverage policies and formulary designs have on the viability of competitive markets with multiple entrants in the longer term?

Answer. Only a share of biosimilar products are self-administered drugs covered under the pharmacy benefit of an insurance policy (Part D in the case of Medicare). This is an important caveat, as the insurer factors described above do not apply to the provider-administered market, which concentrates a large share of the biosimilar products marketed in the U.S.

It is difficult to predict how preference for high-list-price high-rebate products will affect the uptake of self-administered biosimilars and the viability of a competitive market place in the long term. This is because it was not until earlier this year that the market saw the entry of multiple biosimilars for adalimumab, the first biologic product with a large number of biosimilar competitors.

²⁷ Grabowski H, Long G, Mortimer R, Boyo A. Updated trends in US brand-name and generic drug competition. *J Med Econ.* 2016;19(9):836–844.

²⁸ Berndt ER, Aitken ML. Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century After the 1984 Waxman-Hatch Legislation. Published online October 2010. doi:10.3386/w16431.

²⁹ Hakim A, Ross JS. Obstacles to the adoption of biosimilars for chronic diseases. *JAMA.* 2017;317(21):2163–2164.

³⁰ Hernandez I, Gellad WF. Differences between managed care and fee-for-service Medicaid in the use of generics for high-rebate drugs: The cases of insulin glargine and glatiramer. *J Manag Care Spec Pharm.* 2020;26(2):154–159.

Nevertheless, the preferred formulary placement of originator products in Part D plans cannot be solely attributed to PBM preference for products with high list prices and high rebates. As described above, manufacturers of originator products respond to biosimilar competition through increased rebates.⁴ It is possible that products offered by biosimilar manufacturers have not been low enough to incentivize their preferred placement. Part D plans are expected to favor originator products if manufacturers match the net prices of biosimilars through increased rebates. It is worth noting that, even if biosimilar uptake is modest, the increased rebates offered for originator products decrease net spending, and are evidence of a competitive market place on the rebate space. In other words, the long-term viability of a competitive biosimilar market is not solely dependent on the preference of PBMs for products with high list prices but also on the pricing strategies that biosimilar manufacturers adopt over time.

Question. Without a shift in these PBM and insurer practices, to what extent might current uptake challenges—such as those facing biosimilars and certain generics—signal or create shortage risks over time?

Answer. The primary economic driver of drug shortages is insufficient incentives for manufacturers to produce drugs with limited profitability. Commonly, drugs on shortage have prices near marginal cost after decades of competition. For biosimilars to be at risk of shortage, their prices would have to drop to near or below long-run marginal cost. There has not been any evidence to date of shortage risks for these biologic products.

There is insufficient data to speculate on the long-term sustainability of the self-administered biosimilar market. Before the entry of biosimilars for adalimumab, Part D biosimilars presented few market entries and rates of price erosion were considerably lower than those seen in the small-molecule non-complex generic space.^{22,23} It should be noted that, while the prices of biosimilars are compared to those of originator biologics at the time of entry, in many cases, the reference products sustained large increases over time since launch, which distorts the comparison. For instance, in a report published in *JAMA Health Forum*, my colleagues and I compared the price of Amjevita, the first biosimilar for adalimumab, to the net price of Humira after rebates.³ After accounting for rebates, the 2023 price of the discounted version of Amjevita was only 14 percent lower than the net price of Humira in 2020.³ Moreover, Amjevita's price was twice as high as the launch price of Humira.³

I share the Senator's concerns on the effect of preferred placement of high-list-price products on out-of-pocket costs faced by Medicare beneficiaries. However, the biosimilar experience to date is insufficient to discuss how these insurance dynamics could contribute to the long-term sustainability of the self-administered biosimilar market and the potential occurrence of drug shortages.

PREPARED STATEMENT OF JASON R. WESTIN, M.D., MS, FACP, DIRECTOR, LYMPHOMA CLINICAL RESEARCH PROGRAM, AND SECTION CHIEF, DEPARTMENT OF LYMPHOMA AND MYELOMA, M.D. ANDERSON CANCER CENTER

INTRODUCTION

Chairman Wyden, Ranking Member Crapo, and members of the committee, it is my pleasure to appear before you to discuss the ongoing drug shortage crisis facing patients today. I am Dr. Jason Westin, professor of medicine, director of Lymphoma Clinical Research and section chief at M.D. Anderson Cancer Center in Houston, TX. Today, I am speaking on behalf of the Association for Clinical Oncology (ASCO), the leading oncology professional organization representing nearly 50,000 oncology professionals, including physicians, researchers, and other health-care providers dedicated to improving cancer care. We appreciate the committee's bipartisan dedication to addressing the root causes of drug shortages.

Today, I aim to provide a firsthand account of the challenges faced by cancer patients and their health-care providers amid some of the worst oncology drug shortages to date. This crisis is impacting whether patients receive lifesaving and life-prolonging oncology drugs on schedule and in the established doses or whether we're left to use suboptimal alternatives, reduce doses, delay treatments, and in the worst situations, unable to provide any of the necessary therapies. Many of my colleagues have been forced to make impossible choices, including to choose which patients will

be prioritized to receive potentially curative therapy. Patients and their families look to their providers as a trusted source, and we're left with no explanation.

In the summer of 2022, I started to feel the impact of a potential shortage of a drug called fludarabine, a crucial component of CAR T-cell therapy—an innovative, lifesaving technology that teaches a patient's immune system to combat cancer. Fludarabine is a cheap and generic drug, initially approved over 30 years ago, and it is an essential component of CAR T-cell therapy. CAR T is a lifesaving, cutting-edge, “almost science fiction-like technology” that weaponizes the patient's own immune cells to fight their cancer by seeing the cancer cells, the wolf in sheep's clothing hiding in plain sight, but its efficacy is dependent upon being given with fludarabine. Unfortunately, fludarabine has no known effective substitutes.

My patients with rapidly progressing, aggressive blood cancers, oftentimes only get one chance at CAR T treatment because they may not be well enough to try treatment again. Due to the shortages, I don't know if CAR T will work without fludarabine, and we can't wait to try again when fludarabine is back in stock. Moreover, CAR T is a one-time treatment, and because it is expensive, insurance plans won't cover it twice. In other words, the absence of a generic and cheap drug like fludarabine can mean the difference between life and death.

I recently treated a young mother of three who was battling an aggressive refractory cancer that grew despite multiple chemotherapy lines. Contemplating hospice care, she joined my CAR T clinical trial and is now in a long-term remission, offering her the potential for decades of life and her children the security of having their mom alive and well. Her story—and others like it—would not be possible without common, affordable drugs currently in short supply nationwide.

A colleague in Ames, IA is treating a 21-year-old with testicular cancer. Cisplatin is essential for curing testicular cancer. When he first saw the patient in May of this year, he was able to treat him with Cisplatin, but by August, he had no drug and was forced to withhold care. It's not a situation where we don't know how to treat your cancer, it's that we can't get the drug because it's not being made. We have drugs that are lifesaving and shortages that are life-threatening.

Shortages force impossible choices. The oncology care team is forced to work outside of the recommended practice guidelines or must choose how to allocate scarce resources. When physicians must use treatments that may not be standard of care, prior authorization—already an untenable burden—becomes even more intrusive. This added stress to patients and their families is unacceptable.

The United States needs a more reliable generic drug supply chain to avert future shortages of lifesaving and life-prolonging medications. Most oncology drugs in shortage are old, generic injectables that sell for anywhere from \$1 to \$8 per dose, leaving these drugs with slim profit margins, sometimes to the point of production costs exceeding the selling price.¹ Many of these drugs do not have alternatives. There are few manufacturers of these sterile injectables, and the ones that remain in the market face significant costs to remain in business. The leading cause of drug shortages is manufacturing quality issues, which are largely driven by economic factors. Often, any disruptions from quality issues leave the manufacturer unable to ramp up production for several months and at significant expense, that is, if they even choose to resume production. When one experiences quality issues, it has an impact on the entire supply chain. Some manufacturers decide to leave the market completely, while others take weeks or months to make expensive repairs, or they shift production to other more profitable drugs. There is little incentive for companies to enter the market, knowing they may be unable to make any profit on these lifesaving drugs.

Fundamentally, current drug payment policies compound quality issues. Purchasers have limited information—typically only price data—and do not have access to quality or supply information. This creates adverse market incentives for manufacturers to prioritize cost cutting over quality improvements or capital investments. These are particularly challenging for oncology drugs in shortage, as generic manufacturers often operate on a slim or negative profit margin compared to brand drugs.

The current Medicare payment system bases drug reimbursement on average sales prices (ASP) plus 6 percent (ASP+6). These amounts are updated using data from previous quarters. Multiple-source drugs can experience artificially low reimbursement because of delays in updating ASP. This creates a barrier to entry for

¹ <https://accessiblemeds.org/resources/blog/2022-savings-report#:~:text=91%25%3A%20PorFon%20of%20U.S.,country%27s%20spending%20on%20prescripFon%20drugs.>

new manufacturers of multiple-source drugs, for increasing production, and potentially for correcting quality issues. Congress should consider alternative payment methodologies that would provide immediate relief from artificially low rates and encourage a more reliable supply of drugs.

While CMS is constrained by statute in how it pays for drugs, it could use its authority to investigate innovative reimbursement structures for sterile generic injectable drugs under the Center for Medicare and Medicaid Innovation's (CMMI's) current authority. For example, CMMI could develop and test demonstration projects that set a reimbursement floor on critical drugs that have been in and out of shortage; investigate novel methods of tying increased reimbursement to guaranteed supply by the manufacturer; or link increased reimbursement to the expansion of quality management maturity pilots already underway, such as the FDA's Center for Drug Evaluation and Research pilot program to promote quality manufacturing and minimize risks to reliable drug supply. At least one public-private utility has already shown proof of concept that purchasers will be willing to pay above spot market prices in return for guaranteed buffer supply.

Additionally, policymakers could incentivize changes to the drug supply chain in several areas:

1. Encourage the adoption of advanced manufacturing technology and the development of continuous manufacturing for critical drugs and active pharmaceutical ingredients (APIs). Incentives could include tax credits or government contracts for domestic manufacturing.
2. Consider coupling enforcement mechanisms to the existing requirement that manufacturers of certain drugs develop risk management plans.
3. Incentivize purchasers to realign contracts with manufacturers with reliable supply. This will require additional transparency in the drug supply chain.

The Department of Health and Human Services (HHS) could incentivize the creation of private-sector reserves of essential medicines, medical devices, and supplies. HHS recently proposed consideration of additional payments to hospitals that acquire and maintain a buffer supply of certain drugs. While such proposals are worthy of consideration, they should be implemented in a manner that does not promote hoarding or create additional shortages or supply chain challenges. They must also include independent and private practices, with consideration of their different needs. Any incentive programs should be enough to cover the cost of participation, focusing on improved reliability and quality, and should not be budget-neutral.

The proposed solutions are immediate steps toward a comprehensive solution. We recognize concerns around increased costs to the health-care system. But we will pay a greater long-term cost in the form of delayed or denied care if we do not address underlying economic forces driving shortages of generic drugs.

The shortage of critical cancer drugs is an urgent crisis. My patients, and their families, deserve to know that they will get the care they need without delay. Providers shouldn't have to make impossible choices about patient care.

Thank you for the opportunity to testify on this timely issue. We at ASCO appreciate the committee's continued efforts to enhance the pharmaceutical and medical supply chain to protect our Nation's most vulnerable patients. This is an urgent crisis, and we stand ready to collaborate with you to advance comprehensive solutions that ensure individuals with cancer receive the lifesaving and life-prolonging treatments they require.

QUESTIONS SUBMITTED FOR THE RECORD TO JASON R. WESTIN, M.D., MS, FACP

QUESTIONS SUBMITTED BY HON. CHUCK GRASSLEY

Question. I have heard from Iowans receiving cancer treatment about how cancer drugs in short supply have impacted their ability to access treatment. Some patients have even had to switch hospitals to maintain treatment, because another hospital was getting a more consistent supply.

Some hospitals seem to handle drug shortages better than others. Why do you think that is?

Answer. We are dealing with a chronic maldistribution of both resources and information across the U.S. health-care system in the context of shortages. Better-

resourced institutions and health systems have the human and financial capital to better plan for drug shortages. They are more likely to be able to afford to routinely keep more stock on hand, bundle purchases of shortage drugs along with other drugs, and have the staff dedicated to constantly monitor and manage patient workflow. This disadvantages smaller and less resourced practice settings, such as Iowa's rural hospitals, exacerbating inequities already present in our health-care system.

Question. Are there parts of the supply chain that weather shortages more effectively?

Answer. Much of the breakdown in the drug supply chain comes at the final stage: the final dose form sometimes referred to as "fill and finish." The majority of shortages are caused by quality issues identified either by the manufacturers themselves or by the Food and Drug Administration (FDA) via audits. While it is critical to ensure a steady, high-quality supply of upstream items, such as key starting materials and active pharmaceutical ingredients (APIs), the strongest upstream supply chain in the world will not matter if the final step in manufacturing is not functioning well.

QUESTIONS SUBMITTED BY HON. JOHN THUNE

Question. From your experience working in a health system, what challenges exist currently for hospitals to obtain information about manufacturers facing disruptions in drug production?

Answer. Hospitals are faced with nearly zero visibility regarding which specific drugs will go into shortage until a shortage is publicly announced. The only publicly available information is posted on the FDA website, the information provided by organizations, such as the American Society of Health System Pharmacists (ASHP), and what the manufacturer says publicly (sometimes in the form of a "Dear Healthcare Professional" letter). When there are adverse findings from an FDA inspection, communications from the FDA to the manufacturer are posted on the FDA website, which could increase the likelihood of a shortage. Further, these communications are redacted so that most of the time it is not possible to identify the specific drugs affected.

Question. Are there ways Congress can further promote increased transparency around generic drug production?

Answer. The pharmaceutical supply chain currently operates with a significant lack of transparency. While the FDA possesses information about finished product manufacturers and active pharmaceutical ingredients (APIs), it is not always aware of which API supplier(s) a manufacturer utilizes or the quantities involved. Moreover, visibility into earlier stages of the supply chain, such as key starting materials (KSMs) and refined chemicals, is severely limited. This opacity extends to manufacturers' quality improvement initiatives and investments in production quality.

To address these issues, there is a pressing need for enhanced reporting mechanisms concerning manufacturers' quality efforts. Establishing more robust quality reporting and risk assessments—overseen by external sources—would contribute to a more comprehensive understanding of the pharmaceutical supply chain. This proactive approach is crucial to fortifying the health-care system against potential disruptions in the availability of critical drugs.

Organizations like the Association for Clinical Oncology (ASCO) have long advocated for increased insight into the pharmaceutical supply chain. Their recommendations include compelling manufacturers to provide more actionable information to the FDA. This not only aids the FDA in obtaining a comprehensive and timely overview of the current and anticipated supply of specific drugs but also facilitates a holistic understanding of the entire manufacturing process. By implementing such measures, we can work towards creating a more transparent and resilient pharmaceutical supply chain, ultimately ensuring the consistent availability of vital medications in the healthcare system.

QUESTIONS SUBMITTED BY HON. TIM SCOTT

Question. Although America remains the world's top innovator in life sciences, it dramatically lags behind countries such as China and India in the manufacture of

antibiotics, active pharmaceutical ingredients (APIs) formulated into tablets, capsules and medicines, and vitamin C. While States like mine reap extraordinary benefits from foreign investment by international manufacturers, returning the manufacturing and sourcing of life sciences products to our country is not only a powerful economic driver—it's a path to national and global stability. My Manufacturing API, Drugs, and Excipients (MADE) in America Act would help bring pharmaceutical manufacturing back to the United States by incentivizing pharmaceutical manufacturing in designated "Opportunity Zones," using tax credits to encourage production of vital products and ingredients in America.

Incentivizing advanced manufacturing technology adoption and new continuous manufacturing processes is one of your proposed solutions to addressing critical drug shortages. How could these technological advancements contribute to a more resilient prescription drug supply chain, and what incentives would encourage their implementation?

Answer. In addition to the myriad financial pressures facing manufacturers of sterile generic injectable drugs, there are very practical considerations that impact their ability to ramp up production of drugs in shortage. It can take weeks or longer for a manufacturer to change production processes. This is especially true for chemotherapy drugs, as they are often highly toxic and require special handling to ensure high-quality, safe processes. Advanced manufacturing technologies would allow for a significant improvement in turnaround times, which would reduce the risk of or duration of shortages. Continuous manufacturing, a form of advanced manufacturing technology, allows a manufacturer to more easily adapt supply to demand and has the added advantage of a smaller footprint. However, to transition to these technologies, manufacturers will need to see a path forward to a return on investment before committing the necessary resources, as these changes require significant up-front investments. Given the critical nature of these drug shortages, ASCO has been supportive of trying several different incentive structures, whether they be linked to tax incentives, guaranteed volume contracts, pricing floors, and/or novel payment structures that could be tested through CMMI.

Question. For nearly a year, millions have experienced difficulty in accessing the prescribed medications they need. In some cases, doctors have been forced to choose less-effective treatment plans for patients whose need is deemed less critical.

Can you share specific examples from your experience as an oncology health-care provider where drug shortages have directly impacted patient outcomes, and what challenges did you face in finding suitable alternatives?

Answer. In the summer of 2022, I started to feel the impact of a potential shortage of a drug called fludarabine, a crucial component of CAR T-cell therapy. CAR T-cell therapy is an innovative, lifesaving technology that teaches a patient's immune system to combat cancer. Fludarabine, initially approved over 30 years ago, is an inexpensive generic drug—and it is an essential component of CAR T-cell therapy. CAR T's lifesaving, cutting-edge, "almost science fiction-like technology" weaponizes the patient's own immune cells to fight their cancer by seeing the cancer cells—the "wolf in sheep's clothing"—hiding in plain sight. To be effective, CAR T must be given in combination with fludarabine. There are no known effective substitutes for fludarabine.

My patients with rapidly progressing, aggressive blood cancers, often have only one chance at CAR T treatment because they may not be well enough to try a second time. I don't know if CAR T will work without fludarabine, and the disease won't wait for us to try again when fludarabine is back in stock. Moreover, CAR T is a one-time treatment, and because it is expensive, insurance plans won't cover it twice. In other words, the absence of a generic and cheap drug like fludarabine can mean the difference between life and death.

I recently treated a young mother of three who was battling an aggressive cancer that grew despite multiple chemotherapy lines. Contemplating hospice care, she joined my CAR T clinical trial and is now in a long-term remission, offering her the potential for decades of life and her children the security of having their mom alive and well. Her story—and others like it—would not be possible without common, affordable drugs currently in short supply nationwide.

Question. Hospitals typically make their purchases on a just-in-time instead of a just-in-case basis. Earlier this year, the Centers for Medicare and Medicaid Services (CMS) proposed reimbursing hospitals for creating a 3-month stockpile of essential medicines; however, industry has voiced multiple concerns. One such concern is that reimbursement would, in reality, likely only support well-financed hospitals that

could afford a 3-month stockpile—otherwise, it will be a significant expense for hospitals with limited liquidity and (in worst case) exacerbate existing access disparities.

Can you discuss incentivizing the private sector to establish and maintain reserves, and what safeguards should be in place to prevent unintended consequences like hoarding?

Answer. CMS proposed consideration of additional payments to hospitals that maintain a buffer supply of certain drugs. While such proposals are worthy of consideration, they must be implemented in a manner that does not promote hoarding or create additional shortages or supply chain challenges. It is also important that they include independent and private practices, with consideration of their different needs.

It requires resources for hospitals and oncology practices to acquire and store drugs, including both financial and human capital. If CMS were to pursue reimbursement for strategic reserves, special consideration would have to be given to smaller physician practices that administer chemotherapy but may lack the space or resources to take advantage of such a program. These practices especially rely on just-in-time inventory and are often the first and hardest hit when shortages emerge.

QUESTIONS SUBMITTED BY HON. BENJAMIN L. CARDIN

Question. In a 2019 report from the FDA on drug shortages, the agency notes that FDA heard from stakeholders that some contracts currently include “low-price clauses” that allow group purchasing organizations to unilaterally walk away from a contract if a competing manufacturer is willing to supply the same product or bundle of products for a lower price.

How do practices like “low-price clauses” impact drug shortages?

Answer. In addition to the existing opacity of the supply chain, the market for prescription drugs is incredibly complex and likewise lacking in transparency. Many institutions and practices join group purchasing organizations (GPOs), which negotiate drug prices on their behalf. Because they can leverage the purchasing power of scale, GPOs often obtain more favorable pricing than that available on the “open” market. The specifics of each contract are confidential and proprietary and often involve the “bundling” of drugs and rebates for specific preferred drugs. Manufacturers may sell certain drugs at very thin margins, or even at a loss, to procure guaranteed purchasing for other drugs. Finally, much of this purchasing power has been consolidated into just three GPOs, which serve most of the market, giving them yet more leverage. All these forces are at work behind the scenes, compounding the “race to the bottom” inherent in our current generic market competition. This reduces the competition and resilience in the underlying supply chain and market.

The “race to the bottom” for pricing regardless of quality forces manufacturers to deprioritize investments in improving their manufacturing resilience, thus increasing the risk of shortages. Therefore, issues like “low-price clauses” directly increase the risk of drug shortages.

Now we hear that some PBMs have chosen to start group purchasing organizations even as PBMs use group purchasing organization services.

Question. How might these relationships impact drug shortages, particularly patients’ ability to access low-cost drugs that typically do not provide much profit to manufacturers?

Answer. The market for purchasing prescription drugs is heavily consolidated. This consolidation gives a small handful of powerful purchasers the ability to negotiate favorable pricing, which is effective in lowering prices. In the context of sterile generic injectable shortages, however, it has the effect of making manufacturing of generic sterile injectable medications like essential chemotherapies less and less economically viable. Today, purchasers of these medications prioritize the lowest price possible, regardless of other factors like manufacturing quality. End users of these drugs (hospitals, clinics, etc.) should be incentivized to purchase drugs based not on price alone, but instead based on price and quality and reliability of supply. ASCO has long advocated for a framework in which quality and reliability of supply is reflected in drug pricing; the current FDA pilot programs in quality management maturity (QMM) is a step in the right direction of laying the groundwork.

QUESTION SUBMITTED BY HON. SHERROD BROWN

Question. In its 2022 report, the United States-China Economic and Security Review Commission, or USCC, recommended that Congress direct the FDA and other Federal agencies to identify alternative sources for APIs and other ingredients, including utilizing Defense Production Act Authorities.

Recently, the administration announced its plans to implement some of these recommendations. Congress has already provided some resources to the administration to use Defense Production Act, or DPA, authorities to ramp up production of medical supplies—including generic pharmaceuticals. I fought to include this funding in the CARES Act.

One domestic company, National Resilience, has already secured a DPA loan to expand domestic manufacturing capacity of essential medicines in West Chester Township, OH.

What are additional authorities that the U.S. Government can use, similar to how the Defense Production Act is being used, to bolster the domestic manufacturing of pharmaceuticals?

Answer. Congress could use its authority to incentivize advanced manufacturing technology and develop new continuous manufacturing technology for critical drugs and active pharmaceutical ingredients (APIs), including support for advanced manufacturing grant appropriations. We need to improve drug and device manufacturing quality and focus on outcomes that improve the overall resilience of our Nation's medication and device supply chains. Congress could require the FDA to provide ratings of the quality management processes of medication and device manufacturers that are predictive of supply chain and manufacturing vulnerabilities and to make the ratings publicly available.

While CMS is constrained by statute in how it pays for drugs, it could use its authority to investigate innovative reimbursement structures for sterile generic injectable drugs under the Center for Medicare and Medicaid Innovation's (CMMI's) current demonstration authority. For example, CMMI could develop and test demonstration projects that set a reimbursement floor on critical drugs that have been in and out of shortage; investigate novel methods of tying increased reimbursement to guaranteed supply by the manufacturer; or link increased reimbursement to the expansion of quality management maturity pilots already underway, such as the FDA's Center for Drug Evaluation and Research pilot program to promote quality manufacturing and minimize risks to reliable drug supply. At least one public-private utility has already shown proof of concept that purchasers will be willing to pay above spot market prices in return for guaranteed buffer supply.

QUESTION SUBMITTED BY HON. ROBERT P. CASEY, JR.

Question. You spoke about the impacts that cancer drug shortages have on providers and their patients. The FDA has 16 cancer drugs classified as currently in shortage, and I've heard from hospitals in Pennsylvania that these shortages are impacting patient access to care. We've even heard of providers in several States having to ration cancer drugs by rounding down doses. We must do everything we can to ensure that while patients are struggling with terrible illnesses like cancer that they aren't also worried about if there's enough of a drug for them and their neighbor.

What are some of the challenges hospitals face in procuring drugs that treat cancer and the impact that these shortages have on patients seeking lifesaving treatments?

Answer. In 2022, approximately 100,000 Americans were diagnosed with ovarian, bladder, and testicular cancers, cancers which may rely on Cisplatin or Carboplatin for potentially lifesaving treatment, where shortages could have dramatic consequences. In addition to ovarian, testicular and bladder cancers, these chemotherapies are also frequently used in cervical, endometrial, lung, head and neck, bladder, esophageal, gastric, breast, and more cancers, impacting up to 500,000 Americans each year. Even worse, these shortages impact children with cancer: 80 percent of drugs to treat acute lymphoblastic leukemia—the most common curable childhood cancer—were temporarily unavailable between 2010 and 2020. Americans with cancer should get the best treatments possible, but shortages force impossible choices.

For example, a colleague in Ames, IA is treating a 21-year-old with testicular cancer. Cisplatin is essential for curing testicular cancer. When he first saw the patient in May of this year, he was able to treat him with Cisplatin, but by August, he had no drug and was forced to withhold care. It's not a situation where we don't know how to treat your cancer, it's that we can't get the drug because it's not being made.

Beyond drugs, shortages in medical devices and supplies have also caused barriers to delivering high-quality care. In oncology, we have experienced shortages of glass vials, IV tubing, saline bags, and more. Device shortages include fluid containers to dilute medications for infusion.

The cause of breakdowns in the drug and medical supply chain are multifaceted and require a comprehensive approach. Factors such as manufacturing disruptions, quality control issues, regulatory challenges, supply chain vulnerabilities, and market dynamics contribute to the persistent shortage of critical cancer medications. While some shortages may be short-lived, others last and leave American lives at risk.

PREPARED STATEMENT OF MARTA E. WOSIŃSKA, PH.D., SENIOR FELLOW,
SCHAEFFER INITIATIVE ON HEALTH POLICY, THE BROOKINGS INSTITUTION¹

Chairman Wyden, Ranking Member Crapo, and members of the committee, thank you for inviting me here today. My name is Marta Wosińska, and I am an economist and a senior fellow in economic studies at the Brookings Institution, where I am affiliated with the Schaeffer Initiative on Health Policy. My research explores the economics and regulation of prescription drug markets. Much of my work focuses on the topic of this hearing—drug shortages.

I would like to begin by thanking Chairman Wyden and Ranking Member Crapo for holding this hearing. As I will discuss, the persistence of drug shortages is primarily rooted in economics, driven by how we pay for and buy generic drugs. This is not the first time we have had cancer drug shortages, and it will not be the last unless Congress steps in to address the economics through CMS. Getting at drug shortages through CMS is critical because CMS is much better positioned than FDA to address the economics driving the issue.

But as I will discuss, CMS needs support from Congress, and this committee in particular.

In this testimony, I focus on low-cost generic sterile injectable (GSI) drugs. These drugs are the staple of hospital care, with almost every inpatient stay involving treatment with at least one GSI drug. Shortages of these drugs can affect patients in emergency rooms, ICUs, cancer clinics, and outpatient elective surgery departments.

I begin this testimony by describing why GSI drugs are the most likely drugs to experience shortages. I then describe how Federal health-care programs affect GSI drug profitability, followed by a specific set of recommendations for how this committee can support CMS in addressing drug shortages. I conclude with a discussion of other areas where Congress can make the greatest impact.

My testimony is based on over a decade of research and extensive engagement with stakeholders on all sides of the issue: manufacturers, wholesalers, group purchasing organizations (GPOs), hospital executives, clinicians, and hospital pharmacists. Much of what I describe in this testimony is contained in a recent analysis² published through The Hamilton Project³ at the Brookings Institution.

In short, I recommend that the Senate Finance committee take three actions:

- Establishing a CMS pay-for-performance program that would shift hospital purchase decisions towards more reliable manufacturers;
- Enabling Medicaid rebate exemptions for certain drugs; and
- Strengthening the authority that CMS used for the domestic N95 rule.

There are also many actions that other congressional committees should take, the most important of which I describe in this testimony and summarize here:

¹The views I express in this testimony are my own and do not necessarily reflect the views of other Brookings staff members, officers, or trustees of the Institution.

²<https://www.brookings.edu/articles/federal-policies-to-address-persistent-generic-drug-shortages/>.

³<https://www.hamiltonproject.org/>.

- Properly funding the CMS efforts;
- Allowing FDA to disclose the culprit of each shortage;
- Supporting FDA's efforts to improve signals about manufacturing quality and reliability;
- Supporting the HHS supply chain coordinator role;
- Supporting forgivable loans (not tax credits) for strengthening key drug infrastructure; and
- Supporting well-targeted buffering mechanism proposals.

Where and why are shortages occurring?

Drug shortages occur when demand exceeds available supply. Drug shortages can result from a rapid demand increase, as we saw with ventilator drugs during the early months of COVID and what we currently see with Ozempic and related diabetes drugs as their use for weight-loss skyrockets. Shortages can also occur when supply disruptions are significant enough that available inventories or ramping up production on existing lines do not suffice.

Supply disruptions due to manufacturing quality problems dominate⁴ as a cause of drug shortages. The share of other causes varies over time, but generally manufacturing quality problems have been followed by increases in demand, natural disasters, product discontinuations, and disruptions in availability of inputs, not necessarily always in this order.

GSI drugs have persistently represented the largest share of drugs⁵ in shortage, many lasting⁶ months if not years. Although no detailed statistics exists, it is well understood that GSI shortages primarily result from manufacturing quality problems at facilities where the final product is made.

Unlike shortages caused by natural disasters or pandemics, shortages caused by manufacturing quality problems are essentially self-inflicted and thus avoidable. They result not from external shocks, but from choices in how hospitals buy GSI drugs and the underinvestment in reliability of manufacturing operations that results.

As I describe in next section, GSI drug reimbursement mechanisms across all payers give hospitals incentives to use the lowest price GSI available. These reimbursement mechanisms rest on the assumption that two versions of the same generic drug are therapeutically equivalent (TE) and therefore can be readily substituted. This assumption is not without merit—these products met bioequivalence requirements at the time of FDA approval. But reliability of production is much more than meeting bioequivalence at the time of approval.

These reimbursement mechanisms also rest on the presumption that FDA can assure that all approved products are made to exact specifications. However, FDA is not able to continually monitor facilities, instead relying on manufacturers to report problems. If problems are identified, whether by FDA or the manufacturer, FDA may find itself in a bind—to prevent disruptions in production of medically necessary drugs, FDA will be compelled⁷ to allow product release from noncompliant facilities that make large share of medically necessary drugs, often GSIs. That FDA does everything to mitigate an impending shortage is expected by Congress and by the American public, even though those actions send the wrong signal to manufacturers.

The price pressures, coupled with inconsistent FDA oversight, create a dynamic for manufacturers where there is little room for and return on investing in facilities, staffing, and oversight. This is particularly problematic with GSI drugs because there is less room for error in the final production stage than in production of oral dose products—the drugs are injected into the body, often directly into the blood stream, and therefore they must be sterile and free of particulates. This lower margin for error requires that the final fill-and-finish manufacturing stage be done in specialized facilities with employees following complex manufacturing processes and controls.

Running such complex operations in a cost-cutting environment challenges the reliability of GSI facility operations. If problems with systems or product batches are

⁴ <https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions>.

⁵ <https://www.brookings.edu/articles/drug-shortages-and-rebates/>.

⁶ https://healthpolicy.duke.edu/sites/default/files/2020-02/presentation_slides_0.pdf.

⁷ <https://pubmed.ncbi.nlm.nih.gov/23337525/>.

uncovered, often after FDA inspections, companies may need to discard or recall large batches of compromised product, and temporarily or permanently shut down lines or entire facilities. Any of these scenarios can result in shortages.

How do Federal programs affect profitability of GSI drugs?

There are two ways in which CMS programs affect profitability of GSI drugs: by enhancing price competition and by penalizing input cost pass-through.

REIMBURSEMENT MECHANISMS

Most hospital payment arrangements for GSI drugs encourage hospitals to minimize spending on them. Medicare, the largest payer for hospital stays, bundles reimbursement for GSI drugs with other hospital services provided during an inpatient stay, which incentivizes hospitals to keep cost for the inputs to the service low. Such incentives also exist in outpatient settings. In some outpatient settings, payment rate is based on the average cost across manufacturers, providing incentives to buy the lowest cost version. In other outpatient settings, GSI drugs are bundled if the daily drug cost is under \$135 and otherwise separately payable on average cost. Other payers create similar reimbursement schemes.

These reimbursement mechanisms incentivize hospitals to find the lowest price available at a given time. Hospitals typically do that by pooling their bargaining power through GPOs. The contracts GPOs negotiate for GSI drugs typically have terms of 1 to 3 years. Those contracts generally neither provide a purchase guarantee to the manufacturer nor do they fix the price over the contract term. Instead, the contracts frequently include best-price guarantees that allow the contract price to drop if the GPO finds a better price elsewhere. GPO contract participation is voluntary for hospitals so hospitals can buy off contract.

One place where GPO contracts are not used is 340B hospitals because of a prohibition⁸ in place since the ACA. 340B hospitals will still hold GPO contracts for their inpatient use, but will use the 340B vendor, Apexus, to obtain 340B drugs at 340B prices. The GPO prohibition need not be a disadvantage to hospitals from a cost perspective because 340B discounts can be larger than the GPOs discounts.

Whether or not GPOs are involved, hospital purchasing practices encourage cost cutting on the part of manufacturers. In a highly competitive environment with limited demand stability, companies have little incentive to buffer supply chains through dual sourcing or maintaining buffer inventory. The instability of demand means that manufacturers switch between products more often—a risk factor in complex sterile facilities. To cut costs, companies have opened operations in lower-cost environments such as India. Some companies have continued to invest in U.S.-based facilities, but other facilities have closed. Less-profitable products continually are discontinued.⁹

INFLATION REBATES AND DISCOUNT PROGRAMS

Even if product price can stay above marginal cost, well-intentioned rebate and discount programs may push a product into unprofitable space. Consider for example a GSI drug selling for \$2 per unit with input and production costs totaling at \$1.80. Suppose that this product experiences a \$1 cost increase. If the manufacturer were to pass on the full cost increase, which is what we would expect in a highly competitive market, the resulting price increase would be 50 percent (*i.e.*, the full \$1), well above the CPI. This means an inflation rebate—which requires manufacturers to rebate the price increase—could make the product unprofitable depending on the market share to which that penalty applies. This could lead a manufacturer to phase out the product or drop it entirely.

Medicare and Medicaid handle inflation rebates for competitive generics markets differently.

In its concern about drug shortages, Congress exempted drugs facing fierce price competition from Medicare inflation drug rebates. Specifically, all multiple source drugs are exempt from Part B inflation rebates and all multiple source generics are exempt from Part D inflation rebates. In addition, Congress directed CMS to reduce the newly required Medicare inflation rebates for single-sourced drugs in shortage.

⁸ <https://www.hrsa.gov/sites/default/files/hrsa/opa/prohibition-gpo-participation-02-07-13.pdf#:~:text=340B%20covered%20entities%20subject%20to%20the%20GPO%20prohibition,drugs%20and%20listed%20on%20the%20OPA%20340B%20database.>

⁹ [https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.](https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm)

Elsewhere, I have written¹⁰ how CMS should use the flexibilities afforded under the IRA to balance amelioration of shortages of non-exempt drugs with the risk that waiving rebates might exacerbate shortages.

In contrast, Medicaid inflation rebates cover all drugs. The Medicaid inflation rebate affects manufacturers of the same product asymmetrically—products on the market in 2016 have a benchmark set for that year but more recent products have a benchmark set near their market entry date when the market dynamics and equilibrium prices may have also been different. The program includes no exceptions or waivers.

If the Medicaid share of the market is sufficiently low, profit losses from Medicaid sales can potentially be absorbed. However, Medicaid rebates become the basis for the 340B price. This means that for GSI drugs that have large presence in the 340B program, such as cancer drugs, the Medicaid inflation provision can have significant profitability implications that go beyond Medicaid.

The mechanism by which Medicaid inflation rebates affect GSI drug break-even does not directly cause shortages. Instead, the effect is indirect: as manufacturers find certain products to be unprofitable, they phase them out and ultimately drop production entirely. The products are more likely to be unprofitable and therefore dropped when there are many competitors. If a product is dropped when its share is low, there will be no shortage, but fewer competitors will be left in the market, making it less resilient to a future shock.

How should the Senate Committee on Finance support CMS's role in addressing shortages?

Solutions to drug shortages need to reflect the nature of those shortages. For shortages caused by external events, such as pandemics or natural disasters, any actions are largely limited to buffering strategies such as identifying ways to scale up production and creating buffer inventories. But for shortages where triggers are economic, it is imperative that the root causes be addressed.

Here I present three proposals that the Senate Finance committee should undertake to support CMS in addressing the economic drivers of GSI drugs. As I will describe below, these proposals can also support a government response to offshoring, which also has its roots in economics.

ESTABLISH A CMS PAY-FOR-PERFORMANCE PROGRAM TO SHIFT HOSPITAL PURCHASE DECISIONS

To address the root cause of persistent GSI drug shortages, hospitals must reorient the overt emphasis on low prices in favor of manufacturing quality and reliability.

As the largest payer for hospital stays and outpatient visits, CMS is well positioned to influence how hospitals buy. Specifically, CMS should encourage hospitals to place more weight on reliability of manufacturing supply through a pay-for-performance program under Medicare. Below, I summarize key elements of such a program, referring readers for more detail to a June 2023 report¹¹ from The Hamilton Project at the Brookings Institution.

Under the proposed pay-for-performance program, hospitals would be scored on their behavior on two measures: do they buy from reliable manufacturers and do they buffer their inventory. Hospitals would be measured on their performance retroactively, on their behavior *before* the first signal of each shortage that occurs. The scorecard would then feed into an end-year sliding-scale payment adjustment based on a hospital's performance relative to its peers. Hospitals should largely expect to cover their participation costs, with top performing hospitals exceeding those cost.

Under the proposal, hospitals would not need to take the responsibility for identifying which manufacturer's products are less likely to be in shortage, instead relying on their GPOs to do this work for them. GPOs already conduct such assessments but have strong financial incentives to continue heavily weighing low-cost producers because otherwise hospitals buy off contract. But if hospitals weigh reliability more, they will not only encourage GPOs to assess reliability, but be willing to buy higher-priced but more reliable on-contract products. By putting at least two GPOs in each

¹⁰ <https://www.brookings.edu/articles/drug-shortages-and-rebates/>.

¹¹ <https://www.hamiltonproject.org/publication/policy-proposal/federal-policies-to-address-persistent-generic-drug-shortages/>.

hospital peer group, GPOs would be incentivized to perform better on predicting reliability and securing product through quantity commitments.

One nuance in the proposal is that GPOs cannot play the envisioned role for outpatient drugs in 340B hospitals because of the GPO prohibition I described in the previous section. Unless this prohibition is lifted or waived for high-risk shortage drugs of which GSI drugs are part, 340B hospitals would have the first-line responsibility for assessing which drug manufacturers selling 340B products are more reliable.

To start purchasing from reliable manufacturers, hospitals could leverage current but underutilized programs that vet manufacturers on reliability. Greater interest from hospitals in identify which manufacturers are reliable would also drive development and utilization of tools to identify reliability of different suppliers and the vulnerability of specific products to shortages—some of which exist today but are underutilized. The program would also incentivize greater adoption of currently underutilized programs hold buffer inventory through wholesalers or manufacturers (as in the case of Civica Rx or through a GPO private-label program).

The proposed pay-for-performance program would build on a long history of such programs in Medicare. If there is one lesson learned from those programs is that the financial incentive must be sufficiently large to change behavior. For this reason, the proposed program should not be budget-neutral. The June 2023 Hamilton Project proposal identifies ways to assess the level of necessary support.

There are important reasons why I propose a pay-for-performance proposal instead of the oft-recommended “add-on payment,” which would add a fixed reimbursement percentage to what CMS reimburses or a “payment adjustment” program that reimburses CMS share of a difference between two alternatives. One reason add-on payments are not workable is that such payments require separately billable items, which is not the case with inpatient setting where the majority of GSI drugs are used. Second, both add-on and payment adjustment programs require clear identification of where the additional payment applies. However, CMS is not well positioned to identify which manufacturers are more reliable.

To address the latter shortcoming, some propose waiting for FDA to develop a system of metrics on which CMS could rely. However, even with funding (which FDA does not currently have), that system will likely take several years to develop. In addition, the FDA’s proposed system of metrics will focus on measures of facility reliability and not product reliability. However, products from the same facility can be at different risk of shortages because of their upstream supply chains and other factors not currently envisioned in FDA’s quality management maturity program.

In turn, GPOs already have various tools at their disposal and therefore a pay-for-performance program can be implemented before FDA’s quality metrics system is ready. FDA’s ratings can be added to the pay-for-performance program later. But even there the proposed pick-right measures should continue to exist in the pay-for-performance program because facility reliability is not the only predictor of product supply reliability.

Currently, CMS does not have the authority to stand up the pay-for-performance program I described here, but this committee can change that.

CREATE MEDICAID REBATE EXEMPTIONS FOR CERTAIN DRUGS

As I described above, well-intentioned rebate programs can have adverse impact on the profitability and therefore availability of products in highly competitive markets. To address this issue, I recommend that this committee authorizes Medicaid drug rebate exemptions for multisource drugs. GSI drugs, due to their shortage risk, are at the front of the list for exemptions.

STRENGTHEN THE PROVISION ON WHICH THE N95 DOMESTIC MASK RULE RELIES

As I described above, payment adjustments are not well suited for identifying which manufacturer is more reliable in supplying a product. However, payment adjustments can be helpful in other settings where eligibility for the adjustment can be easily ascertained. For example, payment adjustments can be a straightforward way to incentivize hospitals to purchase products that the HHS in collaboration with DOD and State Department may deem important from a national security perspective, giving specific guidance to CMS to which products it applies.

I recommend this committee strengthen sections 1886(d)(5)(I)¹² and 1833(t)(2)(E)¹³ of Social Security Act because the authorities that enable adjustment payments have significant shortcomings. Below, I identify those shortcomings using two examples where CMS has leaned on that authority: domestic production of N95 masks¹⁴ and a now-abandoned hospital buffer inventory¹⁵ of select essential drugs.

First, the IPPS authority can only reimburse the IPPS share¹⁶ of the expense, meaning that a typical hospital purchasing domestic N95 masks will only be reimbursed for about half of the added spending. Under these circumstances, a rational economic agent (such as hospital), would choose the less expensive non-domestic N95 mask, even before the hospital considers administrative burdens to file paperwork. I have not seen statistics on the uptake of the N95 mask rule, but my analysis suggest that it should be very limited if non-domestic masks have been widely available.

Another problem with the IPPS provision is the seeming inability to target IPPS supplemental payments. Recently a colleague and I argued against¹⁷ CMS implementing the buffer inventory proposal because the proposal would provide insufficient incentives to hospitals that currently suffer most from shortages (see above), instead buffering hospitals that already have much greater ability to procure product during shortages. If CMS could target the program to independent clinics and smaller, independent, and often rural, hospitals face inventory program, the program would get closer to reaching its primary goal.

For OPSS, payment adjustment also needs to be prorated. There also appears to be the added complication that any such reimbursement programs be budget-neutral. However, there appears to be room for targeting.

To address these shortcomings, I recommend that Congress allow CMS to target the IPPS authority. Additionally, Congress should consider allowing CMS to pay more than IPPS and OPSS share because properly subsidizing products in the program is key to their uptake.

As indicated above, these payment adjustments are not a substitute for a pay-for-performance program described above. In fact, the proposed pay-for-performance program may be necessary for supplementing the payment-adjustment program described in this section because the payment-adjustment, even if reimbursing the full cost differential, falls short of accounting for administrative costs. CMS could work payment adjustment program participation rate into the pay-for-performance program, with it adding further incentives to participate in the payment adjustment program.

Where do the CMS recommendations fit in the broader response plan to shortages?

I consider empowering CMS with a pay-for-performance program authority as the most important step that Congress can take to address the persistent shortages that have plagued our health-care system for well over a decade.

There are other opportunities for congressional involvement that may fall outside the jurisdiction of this committee, but which I highlight here for context. Some of those efforts complement and support the pay-for-performance program I described. Other efforts are concerned with risks that have not thus far caused shortages but may.

EFFORTS TO SUPPORT THE CMS PAY-FOR-PERFORMANCE PROGRAM

In addition to appropriations to set up the pay-for-performance program, Congress should support FDA's efforts to improve signals about manufacturing quality and reliability, with it aiding hospital and GPO decision-making. There are a variety of

¹² https://www.ssa.gov/OP_Home/ssact/title18/1886.htm.

¹³ https://www.ssa.gov/OP_Home/ssact/title18/1883.htm.

¹⁴ <https://www.cms.gov/files/document/mm13052-new-payment-adjustments-domestic-n95-respirators.pdf>.

¹⁵ <https://www.govinfo.gov/content/pkg/FR-2023-07-31/pdf/2023-14768.pdf>.

¹⁶ <https://www.govinfo.gov/content/pkg/FR-2022-11-23/pdf/2022-23918.pdf#page=298>.

¹⁷ <https://www.brookings.edu/articles/cms-hospital-payment-proposal-for-maintaining-a-buffer-stock-of-critical-medicines/>.

steps FDA can take,¹⁸ all of which are within FDA's current authorities. However, FDA cannot take these steps without additional congressional appropriations.

To further support hospital decision-making, Congress should also authorize public disclosure of which manufacturer had a production disruption that triggered a given shortage. Because the proposed scorecard creates measures based on multiple shortages—in recent years around 30 to 40 a year—the pay-for-performance proposal minimizes inadvertent disclosure of what could be considered business-confidential data. Congress should formalize disclosure by CMS of the shortage trigger, however, so that there is a feedback mechanism to hospitals for when they picked right and when they did not.

EFFORTS TO ADDRESS OTHER SUPPLY CHAIN VULNERABILITIES

To address the deterioration of the domestic GSI infrastructure, Congress should set up partially forgivable loans. The proposed loan program does not direct manufacturers to specific technologies, instead focusing on establishing a path to quality operations. To reinforce quality outcome goals, part or entire loan is forgiven if the company achieves agreed-on milestones that reflect manufacturing quality principles of proper employee processes and controls.

The main alternative, tax credits, which are within this committee's authority, are not well suited to address this problem for two reasons. First, it is difficult to identify eligibility criteria that will yield the desired outcome: neither do all companies have the same path for enhancing quality nor is purchasing equipment sufficient because most failures ultimately are human error. Second, tax credits provide meaningful incentives only if there is sufficient taxable profit. But manufacturers that could benefit from such investments have very low profitability and sometimes are making no profits at all.

Tax credits for building new facilities on U.S. soil have a different concern: there are simply so many foreign facilities to potentially move that it would be fiscally irresponsible to allow for such credits without prioritizing carefully. Not only could the expense be immense, but onshoring without a broader strategy could be ineffectual. For example, if the U.S. Government subsidizes an API facility in the U.S. but all the key starting materials and reagents still come from a country with high geopolitical risk, then the investment did little to lower that risk. In this example, not the whole upstream chain needs to be onshored, but consideration needs to be given to alternate sources of key starting materials and reagents.

The enormity and complexity of U.S. drug supply chains means that the U.S. Government must take a strategic approach in its dealing with broader drug supply chain and medical product supply chain issues. This requires assessing which drugs and medical products are essential, which of these are vulnerable and how. For more information on what such a strategic framework could look like, I refer readers to the following *Health Affairs Forefront* article: "A Framework for Prioritizing Pharmaceutical Supply Chain Interventions."¹⁹

These strategic efforts are broader than pandemic and CBRN threats preparedness and therefore fall outside of ASPR's authority. The recently announced position of an HHS supply chain coordinator²⁰ is an encouraging step that can only yield results with a statutory mandate and resources.

Lastly, I will comment on the role of buffer inventories. Such inventories are generally recognized as an important buffering strategy therefore many proposals have been put forward. What those proposals generally do not address is the panic buying that ensues at the first sign of a potential shortage. Such panic buying has two effects. First, stockpiling during a shortage amplifies the shortage. Second, the "bank run" on product is uneven, usually with the large hospital systems able get to the product first. For this reason, any government-funded stockpile should have allocation mechanisms in place, even if they are simply historical allocations. Otherwise, providers most likely to currently suffer from shortages will continue to suffer.

¹⁸ <https://www.hamiltonproject.org/publication/policy-proposal/federal-policies-to-address-persistent-generic-drug-shortages/>.

¹⁹ <https://www.healthaffairs.org/content/forefront/framework-prioritizing-pharmaceutical-supply-chain-interventions>.

²⁰ <https://www.hhs.gov/about/news/2023/11/27/biden-harris-administration-announces-actions-bolster-medical-supply-chain.html>.

CONCLUSION

To address the root cause of persistent GSI drug shortages, hospitals must be encouraged to reorient the overt emphasis on low prices in favor of manufacturing quality and reliability. Without significant progress on that front, we will continue to experience shortages of these drugs. The CMS pay-for-performance program is our best chance for changing the tide.

Beyond persistent GSI drug shortages, Congress must empower the administrative branch of the government to be strategic in its approach to secure drug and medical product supply chains, prioritizing supply chains for greatest impact. Without a strategic approach to prioritize the immense yet vulnerable supply chains, the United States will be vulnerable to potentially wide-reaching shortages.

 QUESTIONS SUBMITTED FOR THE RECORD TO MARTA E. WOSIŃSKA, PH.D.

QUESTIONS SUBMITTED BY HON. RON WYDEN

Question. Your testimony recommends Congress create new performance-based payment incentives for hospitals related to drug shortage prevention and mitigation.

Please list examples of specific measures that you recommend including in the scorecard, along with a rationale for why each measure should be included.

Answer. Under the proposed program¹ in question, CMS would score hospitals on purchasing based on vendor reliability and inventory practices during *non-shortage* times. The scorecard would then feed into an end-year payment adjustment based on a hospital's performance relative to its peers.

The Medicare drug shortage scorecard would reflect a combination of two measures: a hospital inventory index and a reliable manufacturer index. The inventory index would measure the level of buffering in which a hospital would engage in advance of potential shortages. The reliable manufacturer index is meant to shift the average reliability of manufacturers by rewarding those that are more reliable. The former would help mitigate shortages, the latter would get at the root of the problem, preventing shortages.

As described in the proposal, “the hospital inventory index would measure the level of inventory when a supply disruption occurred. This index would be a retroactive measure for shortages added to the FDA’s drug shortage website in the relevant year. The eligible inventory would be inventory held at the hospital, committed wholesaler inventory (other than historical allocation), or committed inventory held by the contracted manufacturer (as in the case of Civica Rx or through a group purchasing organization [GPO] private-label program).

“At the end of each calendar year, hospitals would report inventory at [a trigger date determined at the end of the year by CMS, with FDA’s input]. That trigger point date, different for each shortage, would be the earlier date of the manufacturer’s report of disruption to FDA in 21 U.S.C. 356c² or other public signals of the shortage. We recommend that Medicare structure the index with greater weights for drugs that are used more and for drugs that do not have therapeutic substitutes.

“The reliable manufacturer index we propose is a composite measure comprising two elements: whether a hospital is picking manufacturers that are not having production disruptions (picked-right) and whether a hospital is procuring product from manufacturers rated above a certain level of the yet-to-be-developed FDA QMM measure (QMM measure).

“Like the hospital buffer inventory index, the picked-right measure would look back to the trigger point date of an FDA-listed shortage and then assess the *share* of purchases that the hospital procured from manufacturers other than the one triggering the shortage (as reported under 21 U.S.C. 356c). In some cases, there may be no at-fault manufacturers (as with a demand shock) or there could be multiple (as with an active ingredient shortage). In contrast, the QMM measure would apply to all GSI drugs throughout the full year, irrespective of whether any of them ends in shortage, also looking at the share of sales coming from QMM manufacturers.”

¹<https://www.brookings.edu/articles/federal-policies-to-address-persistent-generic-drug-shortages/>.

²<https://www.law.cornell.edu/uscode/text/21/356c>.

Question. How might these measures need to be adapted if the FDA Quality Management Maturity (QMM) program is not fully operationalized?

Answer. As we describe in our proposal, Medicare could set up the scorecard based solely on the inventory and picked-right measures because GPOs already have various tools at their disposal to assess the likelihood of a supply disruption. We also anticipate rapid development of such tools if there is demand for them.

It might be, however, beneficial to give CMS flexibility to supplement the picked-right measures with additional indicators of quality. For example, CMS could work with FDA to develop a set of metrics for high-risk suppliers from which hospitals would be advised not to purchase. Such suppliers might include those that refused an FDA inspection, have no inspection history in last 3 years preceded by concerning inspection history, or a particularly problematic combination of violations (specific violations found during inspections, import alerts, and poor history of efforts to remedy problems).

As an outcome measure, the picked-right measure will remain the most accurate measure of performance because it encompasses all forms of vulnerability: manufacturing disruptions, reliability of vendors, risk of discontinuation, and vulnerability to natural disasters. For that reason, we recommend keeping it even if other measures (such as QMM) are developed.

Question. What special considerations should Congress keep in mind to create a fair program for small independent and rural hospitals?

Answer. The proposed pay-for-performance (P4P) program has two features that make it a fair program for small independent and rural hospitals. First, it leverages the role that GPOs already play in assessing manufacturers during contracting process. Small hospitals using GPOs can benefit from these assessments, with the only decision left to the hospital is whether to follow those recommendations (as a reminder, the picked-right metric is about the share of volume procured from more reliable manufacturers). Small hospitals not affiliated with GPOs can leverage programs such as Civica Rx.

Second, the payment is relative to performance of the hospital's peers. In this case, a small rural hospital would be compared to like hospitals, not large teaching hospitals part of a health system.

To further support the needs of smaller, independent hospitals, Congress should consider three additional flexibilities:

1. Give CMS flexibility to assign different weights in the scorecard for different peer groups. Large hospitals and systems should be weighted more on the picked-right measure, while smaller independent hospitals should be encouraged to buffer against shortages.
2. Allow the payment adjustment to deviate from prescription volume. For smaller entities, administrative costs associated with this P4P program may represent a greater share of participation cost than for larger entities that leverage sophisticated data systems and can spread administrative costs across many units.
3. Allow for a phased-in approach, with peer groups that include small independent hospitals to be phased in a year or two later.

Question. In addition, if Congress were to try to create a similar model for clinic and physician office settings, how might the scorecard and the specific measures you identify need to be adapted?

Answer. The pay-for-performance model can be readily extended to the outpatient settings that are part of health systems and perhaps physician practice networks. Such systems and networks have integrated data, which improves adoption of the P4P program and lowers reporting costs. The same scorecard measures could work, but for drugs only used on the outpatient side of 340B entities, wholesalers would need to take over the assessment role from GPOs because of GPO prohibition in the 340B program. Motivating wholesalers to perform well for this narrow set of outpatient-only set of generic sterile injectable drugs would necessitate structuring outpatient payment peer groups with at least two major wholesalers per peer group (in addition to the two GPOs per peer group).

When it comes to smaller independent outpatient providers, such an arrangement is more complicated operationally and would benefit from a different arrangement that would focus solely on buffering. This focus is appropriate because with small market power, independent outpatient clinics and physician practices are less likely

to influence the quality equilibrium in the market. This could be done by strengthening the authority previously used for the domestic N95 mask rule.³ In my written testimony, I recommend Congress adjust sections 1886(d)(5)(I) and 1833(t)(2)(E) of Social Security to cover not just the Medicare share of qualified expenses, but all the qualified costs that relate to supply chain resilience.

One consideration is whether the outpatient setting requires financial bonuses or penalties. Unlike under a DRG payment, doctors and clinics under Medicare Part B collect margins on their purchases, not even considering 340B. This means that there is less concern with resilience requirements leading to financial losses and therefore policy instruments may reasonably encompass both bonuses and penalties.

A final consideration is how Medicaid inflation rebates may affect the effectiveness of the program on the outpatient side. Medicaid inflation rebates (and by extension the 340B discounts that follow) penalize manufacturers on any cost increases beyond CPI (which for a low-cost product might be on the order of a few dollars or less). The P4P, if implemented on the outpatient side, could change hospital behavior, but the impact on manufacturer behavior may be limited as there is no incentive to invest in reliability if those costs cannot be passed on to buyers. To address this structural problem, my written testimony⁴ includes the recommendation to exclude multisource generic sterile injectable drugs from Medicaid inflation rebates.

Question. Are there unique challenges around shortages for controlled substances we should consider from a Finance Committee perspective?

Answer. The policy challenge with controlled substances used for treating ADHD or pain is that there is, at the same time, both “overuse” (inappropriate use) and “underuse” of these products. This complicates responses to shortages and public health policy generally. To address overuse and underuse, policymakers need to distinguish appropriate from inappropriate use and then develop mechanisms that steer utilization towards the former and away from the latter.

In the opioids context, CMS addressed Medicare Part D over-prescribing by instituting a set of utilization management “edits” to its approval of prescription drug payment processes. Simple indicators related to dosages and durations of prescriptions were used to create the edits, and the result was a significant reduction in high-risk prescribing. Likewise, some commercial and State Medicaid health plans have instituted requirements that for controlled substances (like stimulants for ADHD) that were initiated via telehealth, a face-to-face visit take place within a prescribed period.

Because reducing inappropriate use when a shortage arises serves to boost the effective supply of the product, similar approaches hold promise for improving appropriate use of controlled substances generally and when shortages arise. The impact of above-described efforts should be more fully assessed, pointing way towards broader implementation of such tools.

QUESTIONS SUBMITTED BY HON. CHUCK GRASSLEY

Question. Given the persistence and scale of drug shortages, does there need to be more transparency within the supply chain?

If so, by whom and how could this improve the situation?

If not, who in the supply chain should do more with the information they have to address drug shortages?

Answer. The first step toward transparency is assessing who needs which information and for what purpose. Not all information sharing is equally useful and, in some cases, could be counterproductive.

There are many stakeholders we could consider, but here I discuss two key ones: the Federal Government and hospitals and providers.

On the Federal Government side, there are two areas of need I would like to highlight.

³ <https://www.cms.gov/files/document/mln8990453-new-domestic-n95-respirator-payment-adjustments.pdf>.

⁴ <https://www.brookings.edu/articles/marta-wosinskas-testimony-before-the-senate-finance-committee/>.

First, FDA would benefit from greater transparency into when manufacturers face a demand spike to implement prevention or mitigation efforts. I describe my recommendations on such notifications in my response below.

Second, the Federal Government needs better transparency into the vulnerability of various supply chains, so that it prioritizes where to engage, thereby maximizing the impact on taxpayer dollars. In my response below, I describe my recommendations regarding the strategic approach that should be deployed and the role that Congress should play there.

On the hospital and provider side, I would distinguish between three different needs.

First is the need to know how the shortage is likely to progress and when it is likely to end. This need however is difficult to fulfil because shortages are dynamic, potentiated through panic buying, and with the path to recovery often taking weeks if not months to assess by the companies involved. Congress could improve what FDA can share by improving the transparency of the notifications that manufacturers currently submit to FDA under 21 U.S.C. 356c. I further describe this recommendation in my response below.

Second is the hospitals' interest in early warning systems that identify impending shortages. This kind of transparency, however, is one that policymakers should be extremely cautious about providing. It is critical that FDA knows as early as possible that a manufacturer has a disruption in production so it can work with that manufacturer to restore production and with others. It would be important for wholesalers to know the same so they could put product on allocation. However, to a hospital, an early warning signal of shortage is a signal to start stockpiling, precipitating the shortage.

Third is transparency to hospitals about which manufacturer is reliable. More transparency on this front is a common recommendation, as review⁵ of literature suggests. I agree that information about manufacturing quality can be improved and have proposed various ways FDA can help on that front with support of congressional appropriation. But I emphasize that currently there is sufficient information available to enable resilience purchasing. Individual hospitals do not directly contract with manufacturers, but the GPOs that contract on their behalf can leverage their market power, can compel manufacturers to share confidential business information that is otherwise not publicly available. Similarly, GPOs can do the homework on behalf for hospitals by tapping into reliability and risk measures through syndicated sources such as Redica Systems,⁶ Medicine Supply Map,⁷ or RISC Ratings.⁸ Hospitals can also rely on the vetting (and contracting) of organizations such as Civica Rx.⁹

Much relevant information already exists, but it is underutilized because hospitals are reluctant to pay for resilience. Congressional priority, especially with Senate Finance, should be on incentivizing hospitals to utilize the wealth of information and the programs that already exist. Only then will additional transparency measures help. For recommendations on priority transparency measures that FDA should provide, please see "Federal policies to address persistent generic drug shortages," Brookings.

Question. Drug companies harden their manufacturing facilities to be resilient against natural disasters like hurricanes and tornadoes.

What role do drug companies have in preparing for drug shortages caused by economic factors or a pandemic?

Do they do enough to prepare for the unexpected?

Answer. Perhaps the most basic premise in economics is that rational economic actors balance the costs and benefits of the actions they take. Along these lines, it is rational for companies to balance the costs and benefits of investing in risk mitigation against potential supply chain disruptions.

This cost-benefit calculus looks very different for manufacturers of branded and generic drugs. For high-margin branded products, losing production capacity for any

⁵ <https://www.healthaffairs.org/content/forefront/building-resilience-into-us-prescription-drug-supply-chains>.

⁶ <https://redica.com/>.

⁷ <https://www.usp.org/supply-chain/medicine-supply-map>.

⁸ <https://riscratings.com/home/riscs>.

⁹ <https://civicarx.org/>.

reason means lost profits in the short term and a potential longer-term loss of market share to competitors. In contrast, for generic products, foregone profits due to production disruptions of low-margin products would not be significant.

For these reasons, branded manufacturers work to lower the risk of disruptions by investing more in manufacturing quality oversight than their generic counterparts. Manufacturers also buffer supply chains of branded products more: they will vet their suppliers more closely, diversify their supply chain with multiple suppliers and multiple production sites, carry greater inventory of raw materials and finished product, and maintain a lower utilization rate on production lines. But the low margins resulting from price competition makes these kinds of steps economically prohibitive for manufacturers of generic drugs.

Given the impact that shortages have on patients, their families, and communities, it is also worthwhile to compare the manufacturers' risk calculus with that from a social perspective. For one, neither branded manufacturers nor generic manufacturers fully internalize the harm that results from poor supply chain resilience. Private manufacturers also do not internalize such concepts as national security.

To the extent that policymakers want manufacturers to make their supply chains more resilient than their economic circumstances dictate, they will need to provide economic incentives. They can be in the form of subsidies or penalties, but it is important to consider that penalties (requirements) imposed on low-cost producers can lead to market exit if those additional costs make production unprofitable.

Question. Can alternative payments for drugs under Medicare reduce the number of shortages?

Answer. To address the persistent shortages of generic sterile injectable drugs, we need to change how hospitals buy such drugs. By modifying how CMS pays for drugs most at risk for shortage, CMS can steer hospitals away from their heavy emphasis on price and towards reliability of supply.

It matters greatly how Congress implements such programs—not every alternative payment system will be equally effective or could be made functional in the same time frame. Some proposals could even make things worse. For example, paying hospitals more when drugs are in shortage would do nothing to encourage hospitals to buy from more reliable manufacturers. In fact, hospitals might see buffering and other prevention efforts not worth the effort when the hospital can get a higher payment during a shortage.

The payment models needed to improve reliability of generic sterile injectable supply are procurement-based. In that way, they differ from standard alternative payment models (APMs) that give an added incentive payment to provide high-quality and cost-efficient care. Ultimately preventing shortages is about preventing patient harm but designing proper quality measures would be challenging given adverse health outcomes vary greatly for each of the many dozens of drugs in shortage, with outcomes often not observable in the time frame observed within a hospital.

There are two primary proposals for how to incentivize hospitals to buy reliably: an add-on payment for purchasing from reliable manufacturers and a pay-for-performance program that adds a year-end payment based on hospital's relative performance on shortage prevention and shortage mitigation measures.

The add-on payment would apply to manufacturers qualifying as reliable. The effectiveness of such an add-on payment in preventing shortages would depend on CMS's (or FDA's) ability to identify which manufacturers are reliable. The better the predictive power of such measures, the greater the impact of an add-on payment program tied to such a list. If those measures are not reliable, CMS would be increasing government spending without making a difference on the shortage front.

Currently no validated measures of supply reliability exist. FDA has been developing a set of forward-looking metrics. However, even with funding (which FDA does not currently have), that system will likely take several years to develop and would only be a general facility measure and not the specific product supply reliability measure that is needed. Another alternative is to use FDA compliance records to construct a measure of reliability. Just as with QMM, the predictive ability of such measures would need to be established.

An alternative mechanism—one that I explained in my written testimony—is a pay-for-performance program, under which hospitals are scored on their behavior on two measures: what share they buy from what turned out to be (in retrospect) reliable manufacturers and did they buffer their inventory for the affected drugs. Hos-

pitals would be measured on their performance retroactively, on their behavior *before* the first signal of each shortage that occurs. The scorecard would then feed into an end-year payment adjustment based on a hospital's performance relative to its peers. Hospitals should largely expect to cover their participation costs, with payments to top performing hospitals exceeding those costs.

Unlike an add-on payment where CMS needs to identify which manufacturers are reliable, the pay-for-performance program harnesses market ingenuity. To start purchasing from reliable manufacturers, hospitals could leverage current but underutilized programs that assess manufacturers on reliability, including those done by their GPOs. Greater interest from hospitals in identifying which manufacturers are reliable would also drive development and utilization of new tools. The program would also incentivize greater adoption of currently underutilized programs that hold buffer inventory through wholesalers or manufacturers (as in the case of Civica Rx or through a GPO private-label program).

I should also add that any drug shortage resilience project should be separate from other hospital quality programs. It would be possible, perhaps, to expand the Hospital Value-Based Payment (HVBP) program to encompass procurement measures. Bundling shortage with other measures would lower the visibility that the shortage measures deserve and require. Also, HVBP is budget-neutral, but the shortage proposal needs a strong financial boost across the board.

QUESTIONS SUBMITTED BY HON. MARIA CANTWELL

Question. Do you agree that the current GPO business model is ultimately unsustainable and weakens the drug supply chain in the long run?

Answer. Because generic versions of the same drug are therapeutically equivalent and therefore can be readily substituted, buyers can place tremendous pressure on manufacturers to lower price. The resulting race to the bottom leads manufacturers to shift production to lower-cost environments and challenges manufacturers' ability to invest in maintenance, upgrades, staffing, and oversight. This dynamic leads to a fragile supply chain, with potential for highly disruptive drug shortages.

GPOs play a significant role in driving prices down, enabled by the market power they represent—three GPOs represent around 80 percent of hospital beds. Generally, the contracts GPOs negotiate neither provide a purchase guarantee to the manufacturer nor do they fix the price over the contract term. Instead, the contracts frequently include best-price guarantees that allow the contract price to drop if the GPO finds a better price elsewhere.

It is important to note that GPOs are incentivized to weigh price heavily over reliability of supply because their hospital customers demand that. Currently, while GPOs assess supply reliability of many manufacturers, they will be hard pressed to contract with a higher-priced but more reliable manufacturer because GPO contract participation is voluntary for hospitals. Hospitals can and do buy off contract if they find a lower price. GPOs try to incentivize hospitals to buy through the contract (which is the way the GPO makes money) but the strongest tool GPOs have for contract compliance is securing the lowest price possible.

Question. Is it possible to find a balance between keeping costs down for providers and using the GPOs' market leverage to enforce the resiliency of the drug supply chain? What would that look like?

Answer. Under the pay-for-performance proposal described in my written testimony, hospitals would not need to take the responsibility for identifying which manufacturer's products are less likely to be in shortage, instead relying on their GPOs to do this work for them. GPOs already conduct such assessments but have strong financial incentives to continue heavily weighing low-cost producers because otherwise hospitals buy off contract. If hospitals weigh reliability more, they will change GPO's incentives for how to award contracts to manufacturers. By putting at least two GPOs in each hospital peer group, GPOs would be incentivized to perform better on predicting reliability and securing product through quantity commitments.

Leveraging GPO's market power is helpful in that three GPOs can do the assessment for virtually all hospitals and then compete for hospital business by excelling at these assessments.

QUESTION SUBMITTED BY HON. JOHN THUNE

Question. Some individuals have asserted that the 340B program is causing drug shortages. In your testimony, the drugs you state are most commonly in shortage are generic sterile injectables. 340B purchases make up only 7 percent of total U.S. purchases of generic sterile injectables.

With such a low volume of overall drug spending, is there evidence that 340B has a direct effect on drug shortages?

Answer. Because of lack of data transparency around the 340B program, there are no well-designed studies of the impact of that program on drug supply chain resilience and drug shortages. This does not mean, however, that there is not a problem.

It is indeed the case that drug shortages disproportionately affect generic sterile injectable drugs used in the inpatient setting. But this is due to the preponderance of those drugs in that setting, not the fact that somehow outpatient generic sterile injectable drugs are at less risk.

Just like inpatient generic sterile injectable drugs, outpatient generic sterile injectable drugs (including generic injectable cancer drugs) can face fierce price competition, with prices trending towards marginal cost. However, outpatient drugs face an additional pressure: manufacturers of those drugs are limited in their ability to pass on cost increases, including input costs increases driven by supply shocks, and infrastructure improvements, maintenance, quality oversight, and staffing investment.

With low margins, manufacturers have little ability to absorb these costs, and with 340B, they have limited ability to pass on costs, however legitimate they might be. The cost increases need not be high to hit the penalty threshold—the penalty threshold can be less than \$1 for a \$20 generic sterile injectable drug. The penalty will then apply not to the 7 percent mentioned in the question, but to the drug's volume of 340B sales. For a cancer drug, a third or half of volume could be going through the 340B program—a potentially consequential financial hit that could lead the manufacturer to phase out and ultimately discontinue the product. This in turn makes the market more vulnerable to future shortages.

The inability of manufacturers to pass on legitimate costs becomes even more consequential if Congress attempts to change the hospitals' existing emphasis on price towards reliability of supply. The only reason that paying hospitals more for reliability helps prevent shortages is that such a system enables manufacturers to differentiate therapeutically equivalent products on reliability, carrying a price premium for that added reliability. However, in the outpatient setting, a manufacturer cannot pass any quality improvements on to the prices of 340B products.

To address this structural problem that constrains generic manufacturers from passing on legitimate costs, my written testimony recommends excluding multi-source generic sterile injectable drugs from Medicaid inflation rebates.

On the hospital side, the potential financial losses to 340B entities are lower than the 7-percent volume statistic might suggest. First, single-source generic sterile injectables should not be included in the calculation because those are not included in my recommendations to Congress. Second, the loss in the 340B dollar savings will be less after adjusting for the fact that per unit 340B savings on a \$10,000 drug will quite likely be much larger than on a \$20 drug. Third, relevant losses should net out compliance burden relating to 340B requirements, particular in mixed-use areas such as emergency rooms. Fourth, the losses would be even lower if Congress were to eliminate the GPO 340B prohibition for drugs that are exempt from Medicaid inflation rebates. In that case, hospitals would be swapping 340B savings for GPO rebates.

Given the limited financial consequences for improving supply chain resilience, I strongly question the rationale for the strong pushback from 340B providers regarding Medicaid inflation rebates for multiple-source generic sterile injectable drugs.

QUESTIONS SUBMITTED BY HON. BENJAMIN L. CARDIN

Question. My legislation, the Drug Shortages Prevention and Quality Improvement Act, would require manufacturers to notify the FDA no later than 30 days after the manufacturer knows of an increase in demand for a drug that is likely to lead to a shortage.

How would this kind of authority impact the drug shortages and wholesale alerts?

Answer. Notifying FDA about supply or demand shocks is helpful to the extent that it gives FDA time to work with manufacturers to restore or ramp up production.

Demand increase reporting (or rather reporting in the number of orders a given manufacturer receives) can be grouped in two categories. First are across-the-board demand increases, such as what we saw with ventilator drugs in early COVID or with amoxicillin early last year. Second are spillover demand increases when orders for a given manufacturer's product increase because another manufacturer (for the same drug or a substitute drug) had a supply disruption. In the latter case, manufacturers that experienced disruptions should be reporting, but reporting of spillover can serve as backup and another market signal.

To maximize the effectiveness of the demand notification requirement, I would recommend that FDA be authorized to require that a manufacturer report when orders exceed by a certain level what the manufacturer can fulfill. This is different from reporting a demand increase within 30 days because the signal to the manufacturer can occur much earlier than 30 days. If a manufacturer waits the full 30 days, the information might not be useful to the FDA. Congress should determine the level which triggers reporting in consultation with FDA and industry.

I am not aware of the existence of wholesaler alerts from the FDA to wholesalers or vice versa. However, FDA would benefit from information sharing from wholesalers when they see unusual order patterns. I would recommend FDA set up a pilot program to test this kind of information sharing.

Question. Are there other data gaps that exist regarding the causes of drug shortages that would be important for providers to have as they plan to care for patients who may need a drug that is in shortage?

Answer. Congress should improve the transparency around the causes of shortages. FDA knows the precipitating events leading to each shortage, but they are unable to share them publicly because it interprets the information as business confidential. Instead, FDA discloses what category specified in 21 U.S.C. 356c the manufacturer chose to select. Those categories, however, are not helpful, especially the "Other" category.

Enabling FDA to share more information could help providers plan better for patient care. Such sharing would also be important for supporting the pay-for-performance program that I presented in my written testimony. It is possible for CMS to protect manufacturer confidentiality and score hospitals on whether they picked right across 30–50 shortages, however, hospitals and GPOs should have a clear feedback mechanism for whether they are indeed picking right.

Question. In a 2019 report from the FDA on drug shortages, the agency notes that FDA heard from stakeholders that some contracts currently include "low-price clauses" that allow group purchasing organizations to unilaterally walk away from a contract if a competing manufacturer is willing to supply the same product or bundle of products for a lower price.

How do practices like "low-price clauses" impact drug shortages?

Answer. Those kinds of contracts may exist for hospital and retail drugs alike, but given the focus of FDA's drug shortage report on generic sterile injectables, I will focus my answer on the latter. I am unable to comment on the frequency with which such contracts (sometimes called best-price clauses or MNF clauses) are deployed for drugs administered in hospitals, but I have heard those contracts exist.

Standard economics suggests such contracts terms would push prices down between contract cycles. They also decrease demand predictability for manufacturers because a manufacturer may not be able to match the lower price. Without guarantees for stable demand, manufacturers have little incentive to buffer their supply chains. Frequent changes in demand for specific products also lead to more frequent changes on production lines, which is a key risk factor in manufacturing.

I should note that the importance of "low-price" provisions is lower than it would be if hospitals were committed to buy through GPO contracts. But GPO contracts are not binding, so hospitals can and often will buy off contract if they find a more attractive price. If "low-price" provisions were banned from GPO contracts, hospitals would simply buy off contract if a more attractive price were available elsewhere. For this reason, elimination of such provisions would be consequential for manufacturers only if hospitals were also prohibited from buying off contract.

Question. Now we hear that some PBMs have chosen to start group purchasing organizations even as PBMs use group purchasing organization services. How might these relationships impact drug shortages, particularly patients' ability to access low-cost drugs that typically do not provide much profit to manufacturers?

Answer. The GPOs that have been set up by PBMs are very different than the GPOs that operate in the hospital setting. In the hospital setting, GPOs negotiate contract terms on behalf of hospitals, which hospitals then can use to purchase products at negotiated prices or buy off contract if they find a better price through the wholesaler. In turn, the role of the retail GPOs is not well understood. The ongoing FTC section 6b study will hopefully shed more light on those new entities.

QUESTIONS SUBMITTED BY HON. SHERROD BROWN

Question. Can you comment on how consolidation among purchasers of generic drugs has led to "race to the bottom pricing" and is driving drug shortages?

Answer. Price competition in the generics industry can be fierce. At the heart of this competition is therapeutic equivalence, meaning that different manufacturer's versions of the same drug can be readily substituted. Using therapeutic equivalence, buyers can play manufacturers against each other to obtain better prices and better contract terms. Concentration on the buyer side, be it through GPOs, wholesalers, pharmacy chains, or mail pharmacies, means that buyers have more bargaining power in that negotiation.

This price competition drives manufacturers to cut costs. The price pressures create incentives to move operations to lower cost environments. They also create a dynamic where there is little room for and return on investing in facilities, staffing, and oversight.

These price pressures, however, have different consequences for injectable and oral dose generics.

With generic sterile injectables, there is little room for error in the final production stage. The drugs are injected into the body, often directly into the blood stream, and therefore they must be sterile and free of particulates. This lower margin for error requires that the final fill-and-finish manufacturing stage be done in specialized facilities with employees following complex manufacturing processes and controls.

In contrast, oral dose products, by definition, need not be sterile because our digestive system can get rid of most microbes and impurities. The manufacturing footprint is less concentrated and the manufacturing technologies more fungible. Even if manufacturing problems arise and a facility must close, the supply chain for these products is more resilient and can absorb the manufacturing disruption.

For these reasons, generic oral dose products are less likely to be in shortage due to manufacturing problems than generic sterile injectable products. On the other hand, vulnerability to geopolitical disruptions may not differ much between oral dose and injectable products because key starting materials for all drugs primarily are sourced outside of the United States.

Question. In a 2019 House Energy and Commerce Committee hearing, the FDA outlined competitive cost "advantages" that China and India have over the U.S.

Would speeding up implementation of advanced manufacturing approaches in the pharmaceutical manufacturing industry help lower drug prices?

Answer. The short answer is "no" for branded products and highly unlikely for generics. As for any product, manufacturers of branded products set prices based on demand elasticity, which reflects how sensitive buyers are to price changes. Because branded products are patent protected, they do not have close substitutes and therefore face inelastic demand, with profit maximizing prices far above the cost of production. Changing the marginal cost of production for patent-protected brand-name products could increase profit margins for those manufacturers but would have no discernable impact on drug prices.

In turn, manufacturers of generic products face highly elastic demand, which drives prices close to marginal cost. In this setting, lowering marginal cost would drive prices down. However, advanced manufacturing—continuous manufacturing in particular—does not, in its current state, appear to provide a cost advantage in manufacturing of generics. For one, the technology has great advantages when used

continually for one product. But this advantage does not translate well to generic manufacturing, where the unstable nature of the demand can lead to 20–30 products being run on a single line over a course of a year, leading to frequent switchovers. The up-front costs of these technologies are also prohibitive at this stage, making the return on investment quite unclear.

For more information about the potential role of advanced manufacturing technologies in addressing generic drug supply chain resilience, please see the summary from the proceedings of a workshop, which colleagues and I organized in March 2023 (<https://www.brookings.edu/articles/workshop-summary-technology-solutions-for-improving-the-resilience-of-generic-prescription-drug-manufacturing/>).

Question. What can we do to encourage the implementation of advanced manufacturing, and are there other ways to help reduce the cost of manufacturing drugs?

Answer. Given the offshoring context of this question, I presume the question is about making domestic manufacturing sustainable, whether through lowering the cost of production in the U.S. or through other means.

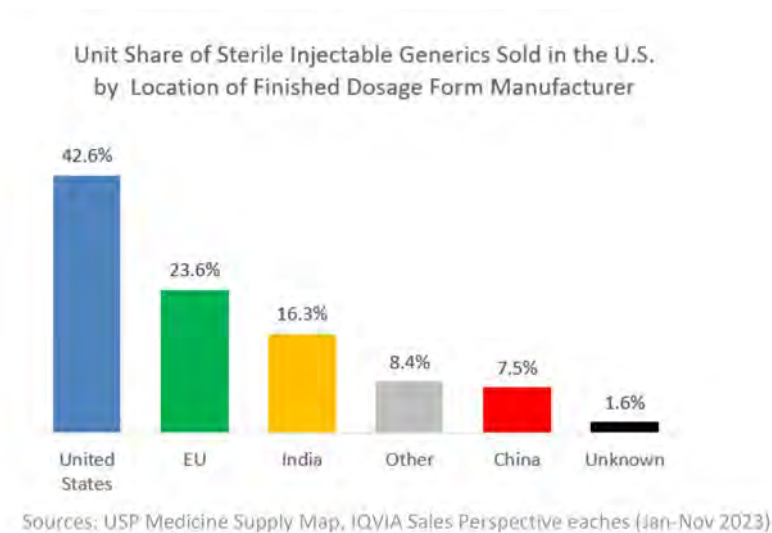
As I describe in my response below, economics is what has driven production offshore, so countering these economic forces would require the U.S. Government to subsidize any reversal of offshoring. Similarly, manufacturers lack economic incentives to adopt technologies that would improve reliability of manufacturing (for which advanced manufacturing is oft touted)—the return on investment is not there for them. For these reasons, if policymakers want greater supply chain resilience, they will need to subsidize manufacturers, ultimately passing on the cost either through higher taxes, higher health-care premiums, or higher generic drug prices.

There are many ways to do it, but all come with a cost. First, the government can provide grants or loans for upgrading or building new infrastructure, keeping in mind that sometimes the highest return on investment can be through relatively low-cost improvements and not through sophisticated advanced manufacturing technologies. Second, even with subsidies of fixed costs, manufacturers may struggle to keep the marginal cost of production competitive and therefore may require marginal subsidies. In my written testimony, I describe how the statutory provisions used to create the N95 domestic mask rule could be leveraged in this space if Congress were to enhance those provisions. The government could also strategically use direct purchasing (such as through the VA or DOD) to support domestic manufactured products or to fund buffer inventories of drugs using domestic manufacturers (all these with the caveat that those manufacturers meet appropriate manufacturing quality standards).

Question. What are additional authorities that the U.S. Government can use, similar to how the Defense Production Act is being used, to bolster the domestic manufacturing of pharmaceuticals?

Answer. Before considering authorities, it is critical that we first establish the role that domestic manufacturing should play in creating greater supply chain resilience. This analysis will then inform possible policy solutions and whether and which new authorities are needed. In that context, it is important to distinguish between current persistent drug shortages of generic sterile injectable drugs and potential shortages due to geopolitical conflicts.

Generic sterile injectable shortages are primarily caused by manufacturing quality problems at the final stage of production. As indicated in the graph below (courtesy of USP Medicine Supply Map), that stage of production for generic sterile injectable drugs is primarily done in the United States, followed by Europe. Although the recent cancer drug shortage was caused by a production disruption at a site in India, U.S. facilities, which produce 2.5 times as many units of generic sterile injectable drug units, are also plagued by manufacturing quality problems that lead to shortages.



Building more domestic capacity in the U.S. is not an appropriate solution to the persistent shortages of generic injectables, but improving the existing U.S. infrastructure can be. Even there, improving infrastructure with government support will be reversed if there is no change in how hospitals buy drugs. For this reason, changing how hospitals buy should take precedence in addressing persistent shortages of generic sterile injectables, with some supplemental infrastructure funding. For more information, I recommend reviewing the discussion of infrastructure funding in this report: “Federal policies to address persistent generic drug shortages,” Brookings.

In turn, addressing potential geopolitical threats requires a different approach. A major geopolitical conflict could expose many more supply chains, potentially quite different from the ones currently at high risk of shortage. It may also expose production sites along many different stages of production, unlike the more limited set of finished dose facilities that are at the heart of most current shortages.

Decreasing reliance on countries that pose geopolitical threats is key to lowering the risk of shortages that could result, but how it is done matters greatly. The pharmaceutical and chemical industries are immense and global. We have many thousands of drug products, each with dozens of inputs made in facilities spanning the globe.

Economics is what drove this expanding web of production, so countering these economic forces would require the U.S. Government to subsidize any reversal of offshoring. But given the size of the pharmaceutical industry and the chemical industry that feeds the key starting materials for drugs, government subsidies should be based on a highly strategic approach—otherwise, with limited resources, government intervention can easily become a feel-good strategy that does little to lower geopolitical risk to supply chain resilience where it matters most.

The strategic approach requires the following:

1. **Reconsidering which supply chains to support.** The FDA Essential Medicines list focuses on pandemics and CBRN treats, but our health-care system could be readily disrupted if drugs or components not on the list were unavailable.
2. **Thinking about all stages of production.** Much attention has been given to Active Pharmaceutical Ingredients (API) but moving API production to the U.S. will not address geopolitical risks if all the key starting materials and reagents still come from a country with high geopolitical risk.

3. **Supporting strategic diversification.** Lowering geopolitical risk means lowering exposure to certain countries, not moving all production onshore. Not all countries have the same risk, and therefore a proper risk mitigation strategy would consider the differential risk across countries. Friend-shoring and near-shoring should be an integral part of U.S. government strategy in response to geopolitical threats.
4. **Not assuming that domestic production equates with quality.** The economic incentives to drive costs down for generic drugs exist for domestic manufacturers as well, especially if they continue to compete with manufacturers from lower-cost environments. For this reason, any government subsidies to bolster domestic manufacturing should come with strings attached on quality outcomes.

The recently announced HHS Supply Chain Coordinator¹⁰ is in the best position to lead this strategic approach to U.S. Government engagement, helping to implement a data analytic approach to prioritizing supply chains for intervention (an approach we describe in “A Framework for Prioritizing Pharmaceutical Supply Chain Interventions,” *Health Affairs*).¹¹ However, to be effective, this role will require congressional support through a statutory mandate and resources. The MAPS bill is an important step in that direction.

In terms of authorities, my written testimony includes a discussion on why tax credits are a less effective tool for accomplishing greater supply chain resilience than loans or grants.

PREPARED STATEMENT OF HON. RON WYDEN,
A U.S. SENATOR FROM OREGON

This morning the Finance Committee gathers to discuss the drug shortages that are harming Americans in communities around the country. In America today, if you receive a cancer diagnosis, chances are scientists and doctors have developed effective treatments to fight or beat this awful disease. While most of the spotlight tends to fall on new, cutting-edge innovations, some of the most vital treatments for millions of Americans suffering from cancer and other chronic diseases are lower-cost generic medicines that have been around for many years. These are the products where the shortages are felt the most, and it’s threatening the health and wellness of the country.

Earlier this year the Finance Committee began to investigate what was causing a widespread shortage of ADHD medications in Oregon and around the country. What we found shocked me. The supply chains for these prescriptions that millions of Americans count on to work and learn were bogged down in what can only be called a bureaucratic bedlam. Manufacturers, the Drug Enforcement Agency, and the Food and Drug Administration all offered conflicting explanations for why the shortages for Adderall and its generics have persisted, and patients were left in the dark without clear answers. We’re pushing to resolve these shortages and add transparency and flexibility so it doesn’t happen again.

Today the Finance Committee will examine the causes of these devastating drug shortages. In particular, the committee needs to look to the power of Medicare and Medicaid, which covers millions of Americans and pays for hundreds of billions in health spending each year. It is urgent business for the Finance Committee to find bipartisan solutions that will get at the causes of a persistent and tragic problem.

The consequences of drug shortages are not abstract. I hear about them at pharmacies in Oregon and town halls all over the State, landing especially hard in rural communities. There has been story after story of drug shortages resulting in rationing, inappropriately low doses, or alternative treatments that aren’t as safe or effective as the product that’s experiencing a shortage. These shortages can be life or death for children, especially when it comes to cancer drugs.

The evidence shows that the vast majority of drug shortages are caused by market failures. Right now they exist across the prescription drug supply chain, from manufacturers to providers, as well as middlemen like PBMs and drug wholesalers. A

¹⁰ <https://www.hhs.gov/about/news/2023/11/27/biden-harris-administration-announces-actions-bolster-medical-supply-chain.html>.

¹¹ <https://www.healthaffairs.org/content/forefront/framework-prioritizing-pharmaceutical-supply-chain-interventions>.

substantial portion of these market failures are driven by the consolidation of generic drug purchasing among a small group of powerful health-care middlemen.

There are many companies that manufacture generic drugs, but they must compete for the attention of highly consolidated middlemen, such as drug wholesalers and hospital group purchasing organizations (GPOs), to gain access to the market. In the case of drug wholesalers, three companies control 90 percent of the pharmaceutical market in this country, and all three of those companies are among the top 15 largest businesses in America by revenue. The generic manufacturers that are awarded contracts by these middlemen do so by offering penny-on-the-dollar prices that mean they can't invest in the capacity or equipment needed to make reliable, high-quality medications. This "race to the bottom" price war for generics leads to quality control problems and factory shutdowns, which leads to shortages of generic drug products that are in high demand.

The Finance Committee is in a prime position to adopt policies to correct this mess. The committee oversees Medicare Parts A and B, which pay for services in doctors' offices and hospitals, including prescription drugs that are administered there, like chemotherapy treatments and related injectable drugs. Some of these injectable products are facing the most severe shortages. In Part D, 90 percent of prescriptions dispensed are generics.

As the committee has found through its work on pharmacy benefit managers, even if manufacturers are selling generics at low prices, middlemen have free rein to mark up prices along the way, leaving seniors with high costs. While middlemen get rich and consumers pay more than they ought to for these generics, manufacturers may decide it's not worth the trouble to produce these medicines and exit the market altogether.

In my view, there are a lot of possibilities to work in a bipartisan way to resolve drug shortages, and I look forward to continuing the productive partnership Democrats and Republicans have demonstrated on this committee this Congress with respect to health care.

COMMUNICATIONS

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December 14, 2023

U.S. Senate Committee on Finance
Rm. SD-219 Senate Dirksen Office Bldg.
Washington, DC 20510-6200

Dear Chairman Wyden and Ranking Member Crapo:

The Alliance for Pharmacy Compounding (APC) appreciates the opportunity to provide input to the Senate Committee on Finance on the subject of the hearing on December 5, 2023, entitled “Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective.”

APC is the voice for pharmacy compounding, representing more than 600 compounding pharmacies and facilities, including compounding pharmacists and technicians in both 503A and 503B settings, as well as prescribers, educators, researchers and suppliers. Pharmacists’ ability to compound medications from pure ingredients is authorized in federal law and for good reason: manufactured drugs don’t come in strengths and dosage forms that are right for everyone, and prescribers need to be able to prescribe customized medications when, in their judgment, a manufactured drug is not the best course of therapy for a human or animal patient.

Beyond its role in providing customized medications when a commercially available drug is not suited to a patient, *pharmacy compounding can play an essential role in addressing disruptions in our nation’s drug supply chain—and empowering pharmacy compounders to alleviate temporary drug shortages must be a component of any drug shortage legislation.*

In this era of rampant drug shortages, the focus of Congress has rightly been on root causes and long-term fixes. But we urge that Congress also attend to alleviating supply chain gaps in the near-term—the shortages that are resulting here and now in patients not receiving urgently needed medications. There already exists a system for addressing such temporary shortages—the components are in place—but certain restrictions hinder the ability of those components to act. What is needed—and what we propose—is a regulatory framework that facilitates rapid and urgent response by compounding pharmacies and outsourcing facilities, in tandem, to meet the *immediate* medication needs of patients in hospitals and clinics when those drugs are commercially unavailable.

Here are four ways Congress and/or the FDA could safely expand the ability of compounding pharmacies to alleviate drug shortages in the short term while longer term, broader supply chain issues can be addressed:

1. Update the statutory definition of drug shortages to include regional shortages and input from hospitals and other health care practitioners.

There is widespread agreement among health care providers that there are problems with the current process used by FDA to establish the agency’s drug shortage list. In addition to taking substantially longer for drugs in shortage to make it on the FDA list than the list established by the American Society of Health System Pharmacists (ASHP), the FDA list also fails to consider regional shortages and to consider direct input from health care practitioners.

This lag between the FDA list and the ASHP list was unfortunately recently illustrated by a July 19, 2023 tornado that damaged the Pfizer manufacturing facility in Rocky Mount, NC. Most of the damage caused by the tornado was not to the production area of the facility but to the warehouse facility where raw materials, packing supplies, and finished medicines were stored. In a July 21, 2023 letter to customers, Pfizer identified drugs manufactured at the facility for which they anticipate supply disruptions due to the damage caused to the facility by the tornado.¹ Of the 66 drugs identified in the Pfizer letter to customers many of the drugs appeared on the ASHP drug shortage list days or weeks prior to making it onto the FDA drug shortage list.

The delay and limited scope of the process to establish the FDA list created an unnecessary gap in patient access to critical medications for the patients of health systems relying on drugs from the Rocky Mount Pfizer facility. The vast majority of the drugs impacted were intended for distribution to hospitals or other clinical settings for administration to patients without a patient-specific prescription. While 503B outsourcing facilities would have been authorized under the FDCA to compound those drugs once they made it onto the FDA shortage list and distribute to hospitals and other clinical settings, 503A pharmacies would be limited under current law to only compounding pursuant to a patient-specific prescriptions, and only under the enforcement discretion granted through FDA guidance.

For these reasons, APC recommends amending the FDCA definition of “drug shortage” to include regional shortage and input from health care practitioners to better align the process used by the FDA to establish the shortage list with that used by ASHP and to expedite and improve that process at FDA. Specifically, we request and recommend the following amendment to the FDCA:

“(a) IN GENERAL.—Section 506C(h)(2) (21 U.S.C. 356c(h)(2)) of the Federal Food, Drug, and Cosmetic Act is amended by striking “exceeds the supply of the drug” and inserting “or a region of the United States exceeds the supply of the drug as reported by manufacturers and health care practitioners.”

2. Codify FDA’s current guidance that states 503A pharmacies can compound drugs on FDA’s shortage list without violating rules against copying FDA approved drugs.

As discussed above, in FDA’s January 2018 Guidance for industry entitled “Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act” the agency clarifies that they “do not consider a drug product to be commercially available if the drug product has been discontinued and is no longer marketed or if the drug product appears on the FDA drug shortage list in effect under section 506E of the FD&C Act. A drug ‘appears on the drug shortage list in effect under section 506E’ if the drug is in ‘currently in shortage’ status (and not in ‘resolved’ status) in FDA’s drug shortage database.”²

The guidance includes FDA’s interpretation of what they consider “commercially available” under the conditions established by 503A for compounding, specifically the provision that states that “(t)he licensed pharmacist or licensed physician does not compound regularly or in inordinate amounts any drug products that are essentially copies of commercially available drug products (section 503A(b)(1)(D) of the FD&C Act).”³ 503A traditional compounding pharmacies compounding drugs on the FDA shortage list to meet critical patient needs should be able to rest assured that they are performing a legal activity specifically authorized by the FDCA. Indeed, the uncertainty of this provision was recently cited in patent litigation pursued by Novo Nordisk against compounding pharmacies, arguing that the guidance did not carry the weight of law and therefore the provision about compounding drugs on the shortage list should not be considered as a valid exception to the statutory prohibition on compounding inordinate amounts of what are essentially copies of commercially available drugs.

Page one of the guidance states clearly the standard disclaimer each guidance contains for the industries regulated by the FDA. “In general, FDA’s guidance docu-

¹See Pfizer Inc. customer letter.

²See FDA Guidance for Industry “Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act,” page 5.

³See FDA Guidance for Industry “Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act,” page 2.

ments do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in Agency guidances means that something is suggested or recommended, but not required.⁴ Stamped at the top of that page and each subsequent page are the words, in bold and italicized, "***Contains Non-Binding Recommendations.***"

For these reasons, APC recommends amending the FDCA to codify the agency policy now expressed in guidance that drugs on the FDA shortage list are not "commercially available" and therefore compounding of those drugs does not violate the FDCA provision against compounding "drug products that are essentially copies of commercially available drug products." Specifically, we request and recommend the following amendment to the FDCA:

Paragraph (2) of section 503A(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353a(b)(2)) is amended to read as follows:

"(2) DEFINITION.—For purposes of paragraph (1)(D), the term 'essentially a copy of a commercially available drug product' does not include—

"(A) a drug product in which there is a change, made for an identified individual patient, which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product; or

"(B) At the time of compounding, distribution, or dispensing, the drug product appears on the drug shortage list in effect under section 506E."

3. Establish a narrow pathway, through law or policy guidance, allowing 503As to compound shortage and other drugs urgently needed for treatment of patients by practitioners when unavailable from 503B outsourcing facilities.

APC understands and supports the system created by the DQSA whereby 503B outsourcing facilities are subject to more stringent cGMP standards and FDA registration and are allowed under the statute to compound shortage and other drugs needed by hospitals and other practitioners for administration to patients. But 503Bs alone have not been sufficient to address temporary drug shortages. Traditional 503A compounding pharmacies must also be empowered in law to assist—a sort of cascading system in which the 503A fills the temporary gap in supply until the 503B can ramp up production. Currently, the FDA does not seem to recognize the simplicity of such a systematic approach to temporary drug shortage. The agency touts 503Bs, but without seeming to recognize the lengthy ramp up time to produce certain drugs in shortage. What about in the interim? Also, earlier this year the agency very publicly engaged a Chinese manufacturer to provide urgently needed cancer drugs and did so without conversation with or consideration of what 503Bs, much less 503As, could do to help.

That must change.

APC supports the inclusion of additional provisions in any drug shortage legislation developed by the committee that will improve the ability of compounding pharmacies to help respond to drug shortages, including those that will undoubtedly occur with the next public health emergency.

There is clear precedent for the approach we propose. In the early days of the COVID pandemic, gravely ill patients began to fill America's hospitals. Hospitals ran short of essential treatment medications and were unable to source those drugs from manufacturers or from the outsourcing facilities that had been authorized by Congress in 2013 to "fill the gap" in such situations. At the urging of the APC, FDA issued temporary guidance (citation to guidance) allowing traditional 503A compounding pharmacies to prepare 13 COVID drugs, within tight regulatory guardrails, from pure ingredients to meet hospitals' urgent need.⁵ That action al-

⁴See FDA Guidance for Industry "Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act," page 1.

⁵See FDA Guidance for Industry "Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Pharmacy Compounding not Registered as Outsourcing Facilities During the COVID-19 Public Health Emergency."

most certainly saved hundreds of lives, and an FDA official has indicated that no adverse events were reported.

Last autumn, as a triple-threat epidemic afflicted America's children and resulted in a shortage of amoxicillin suspension, APC asked FDA for a pathway to allow 503A pharmacies to compound amoxicillin suspension and other beta lactam antibiotics from FDA-approved tablets or capsules—something that existing FDA guidance made very difficult for compounders to do without risking disciplinary action. Three weeks later, FDA issued a guidance document that provided such a pathway, and compounding pharmacies and hospital pharmacies across the country were better able to prepare urgently needed treatments for children.⁶

More recently, many children suffered as pharmacies across the country were unable to stock FDA approved, over-the-counter ibuprofen and acetaminophen suspension. Compounding could have helped here, too, easily creating compounded ibuprofen and acetaminophen suspension from pure ingredients—but they could not because ibuprofen and acetaminophen never appeared on the FDA Drug Shortage List, and FDA did not relax temporarily its requirement that pharmacies only dispense compounded medications pursuant to a prescription. Few prescribers even knew to write a prescription for a compounded version of those over-the-counter medications.

While 503B outsourcing facilities are ramping up testing and production of a shortage drug, 503A pharmacies must be allowed to compound urgently needed drugs, in limited quantities and within tight regulatory guardrails, and to distribute those to prescribers when urgently needed for administration to patients—but only until such time that the outsourcing facilities are able to provide the drug. This model is quite similar to the framework established under FDA temporary emergency guidance during COVID. And, as we have indicated, the components are already in place: 503A sterile compounding pharmacies are already *equipped* to do this if *allowed* to do so under the law.

It is a common-sense solution that would make an immediate impact on this unnecessary gap in patient access in the current legal and regulatory framework.

Amid continuing drug supply chain disruptions, we know pharmacy compounding can play an essential role in alleviating shortages of urgently needed medications if allowed to do so. These examples we've shared demonstrate that. But it shouldn't take a plea from a trade association and then a weeks-long lapse in time for FDA to act when patient health is at stake. Changes to federal law are needed so that when shortage drugs are urgently needed, compounders may assist immediately, without bureaucratic delays and impediments.

That's why we urge the committee to include in any legislation addressing drug shortages and drug supply chain issue provisions to equip state-licensed pharmacy compounders to provide urgent-use medications to hospitals and for in-clinic administration—within tight regulatory guardrails similar to those in FDA's temporary COVID-era guidance—when those drugs are in shortage or otherwise unavailable from a traditional drug manufacturer or a licensed outsourcing facility. We also urge that FDA's Drug Shortage list, which tends to lag the market, be supplemented by the shortage list maintained by the ASHP, which has proven to be a much better real-time indicator of national and regional drug shortages. (If the ASHP list was currently a legal indicator of shortages, pharmacies would already be compounding many of these drugs to meet the need).

Legislation has been introduced in the House, H.R. 167, the Patient Access to Urgent-Use Pharmacy Compounding Act of 2023, that would put this framework into federal law to help address temporary drug shortages like those discussed above, but not only those above. As the recent pandemic has shown, there are patient access gaps in our health care system that occur when critical drugs go into shortage, including those needed for administration to patients in hospitals and other clinical settings. We ask that the Senate Committee on Finance consider including the provisions of this important legislation in the drug shortage legislation now under consideration.

FDA has interpreted Section 503A of the FDCA to require pharmacies to obtain a patient-specific prescription for each drug they compound before the drug leaves the pharmacy. This requirement for a patient-specific prescription for an urgent patient need is hampering patient care. For instance, certain patients may need anti-bacterial, anti-fungal, and anti-viral compounded medications to treat eye-infections

⁶See FDA Guidance for Industry "Compounding Certain Beta-Lactam Products in Shortage Under Section 503A of the Federal Food, Drug, and Cosmetic Act."

in immediate if not emergency circumstances. These drugs are often unavailable commercially or from 503B outsourcing facilities authorized to compound without a patient-specific prescription.

Because a delay in providing the medication can result in patient harm, in limited circumstances when a drug is in shortage it is appropriate and necessary for 503A pharmacies to compound the medication without having a patient specific prescription—and ensure that within seven days after the fact the patient-specific information is relayed from the provider to the compounding pharmacy. The patient information can then be married to the pharmacy’s records. When the FDA published its temporary COVID-related guidance document⁷ the agency acknowledged that urgent patient need should outweigh prescription requirements for 503A compounding, provided that other safeguards are in place. So, there is precedent for what this bill does. It strikes that critical balance.

4. Provide flexibility in the manufacturing standards that apply to 503B outsourcing facilities for drugs on the FDA shortage list so they can react more quickly when shortages occur.

As discussed above, although 503B outsourcing facilities, which are subject to cGMP standards and are registered with FDA are the appropriate facilities to compound larger batches of shortage and other drugs for distribution to hospitals and other providers for administration to patients. However, those cGMP requirements, including lengthy testing and validation periods, strict limits on the bulk ingredients they can use, along with longer production ramp-up periods means that outsourcing facilities are often unable or unwilling to make the economic investment required to help alleviate short term drug shortages.

To this end, APC is supportive of the inclusion of language in any drug shortage legislation developed by the committee that would allow 503B outsourcing facilities to distribute and dispense compounded drugs within 180 days of such drug appearing on the drug shortage list. This provision would strengthen the economic incentive for outsourcing facilities to make the time and financial investment and undertake testing required under current Good Manufacturing Practices (cGMP)—which is why it often takes several months for 503Bs to begin production—with a higher level of assurance that they will be able to distribute or dispense those shortage drugs with a longer lag period.

Again, we thank you for this opportunity to provide input to the Senate Committee on Finance. We urge you to develop and pass legislation intended to address drug shortages that will put a permanent framework into law that will allow 503A and 503B compounding pharmacists to help address drug shortages within tight guardrails that protect patient safety.

Please contact me at Scott@A4PC.org with questions or if the committee would like additional input from APC.

Sincerely,

Scott Brunner, CAE
Chief Executive Officer

Resources

- Pfizer Inc. customer letter.
- January 2018 GFI “Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act”—<https://www.fda.gov/media/98973/download>.
- April 2020 GFI “Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Pharmacy Compounders not Registered as Outsourcing Facilities During the COVID–19 Public Health Emergency”—<https://www.regulations.gov/document/FDA-2020-D-1136-0006>.
- November 2022 GFI “Compounding Certain Beta-Lactam Products in Shortage Under Section 503A of the Federal Food, Drug, and Cosmetic Act”—<https://www.fda.gov/media/163367/download>.

⁷ See FDA Guidance for Industry “Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Pharmacy Compounders not Registered as Outsourcing Facilities During the COVID–19 Public Health Emergency.”

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Chairman Wyden and Ranking Member Crapo, on behalf of the more than 17,000 U.S. members of the American Academy of Dermatology Association (Academy), thank you for the opportunity to submit a statement for the record regarding your hearing, *Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective*.

Dermatologists diagnose and treat more than 3,000 diseases, including skin cancer, psoriasis, immunologic diseases, and many genetic disorders.¹ They are committed to delivering high-value, cost-effective, and innovative care to patients. As dermatologists are at the forefront in the fight against skin cancer and treating numerous skin diseases, the Academy appreciates the Committee's efforts to understand the root cause of drug shortages in the United States and improve the resilience of the current supply chain.

The limited drug supply and rising drug prices have made it increasingly difficult for dermatologists to prescribe cost-effective and life-saving medications and for their patients to access affordable treatment. Generic oral and topical prescription drugs and drugs administered intravenously, such as antibiotics, flu therapeutics, saline, morphine, and certain cancer drugs, are the most vulnerable to shortages because of manufacturing and quality issues, the lack of incentives for manufacturers to produce less profitable drugs, and unique market dynamics.²

Patient access and physician practices are significantly impacted by a dermatologist's ability to obtain local anesthetics due to critical shortages. For several years, dermatologists have faced reduced access to essential drugs for dermatological procedures due to the national shortage of vital medications, like lidocaine. Currently, numerous solo and small group dermatology practices, including those in medically underserved areas, have reported limited to no supplies of lidocaine and lidocaine with epinephrine, two local anesthetics essential for dermatologic procedures. Some dermatologists are also facing limited supplies of sodium bicarbonate, which is often used for buffering lidocaine to decrease the pain of injection.

This ongoing drug shortage has resulted in the delay of medically necessary procedures for patients with critical needs, like skin cancer patients undergoing curative surgery in the office to remove cancerous cells from their skin using a local anesthetic. Without the requisite dosage of lidocaine or lidocaine with epinephrine, there will be increased pain and bleeding at the surgical site prolonging the procedure and increasing potential post-operative complications, or an inability to perform these curative office procedures at all.

In recent years, the shortage of drugs has only been exacerbated by limited production capacity and lack of competition in the pharmaceutical industry. The lidocaine shortage has worsened since a July 2023 tornado caused damage to the Pfizer manufacturing facility in Rocky Mount, NC. Now, dermatologists are running out of stock before they can obtain replacements. Drug manufacturers and suppliers are filling backorders at an unpredictable and slow pace, leaving many patients without the medications they need. It is troubling that commonplace medications that are used in physicians' offices every day are no longer available in the United States.

On behalf of the Academy and its member dermatologists, we urge Congress to put patients' health and well-being first and use its authority and influence to have more oversight of drug manufacturers and the Food and Drug Administration (FDA). Congress must direct the FDA to implement additional processes that require manufacturers to provide more information on the circumstances surrounding the shortage. These data points and their justification for a reduction of supply will help inform policymakers as they seek to provide long-term solutions to the shortage.

Thank you for holding this hearing and providing the opportunity for stakeholders to submit a statement for the record, and for your commitment to maintaining timely access to affordable and effective medications for patients. The Academy looks for-

¹The Academy's *Burden of Skin Disease* briefs are a set of informational resources that capture the scope and importance of various skin conditions, and can be accessed at <https://www.aad.org/about/burden-of-skin-disease/burden-of-skin-disease-briefs>.

²<https://www.fda.gov/media/131130/download>.

ward to working with you and asks you to consider policies to improve the drug supply chain and ensure the physician's perspective on helping patients access needed and affordable treatments.

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December 5, 2023

The Honorable Ron Wyden
Chairman
Committee on Finance
United States Senate
219 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Mike Crapo
Ranking Member
Committee on Finance
United States Senate
219 Dirksen Senate Office Building
Washington, DC 20510

Dear Chairman Wyden and Ranking Member Crapo,

On behalf of the American College of Emergency Physicians (ACEP) and our nearly 40,000 members, thank you for holding today's critical hearing entitled, "Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective." Shortages of everyday, lifesaving emergency medications are one of the most significant and persistent problems that emergency physicians encounter, and unfortunately, they have been dealing with these shortages for years. ACEP appreciates the opportunity to share our perspective on this critical issue that adversely affects emergency physicians' ability to provide the life-saving emergency care our patients need and deserve.

Drug shortages pose numerous challenges in the practice of emergency medicine, requiring emergency physicians to actively monitor what medications may be available on any given day, constantly find alternatives for drugs that are not available (if alternatives even exist), and train and retrain on what drugs to use and what new protocols may be in place each time a new drug shortage is announced. Exploring the viability of alternative treatments and medications diverts clinicians from the bedside (*e.g.*, using a computer, consulting, or coordinating with other experts, etc.) when that time could otherwise be devoted to direct patient care. This exacerbates already-substantial stresses on emergency departments (EDs) throughout the country that are overwhelmed due to the ongoing "boarding" crisis, where patients continue to occupy an ED bed even after being seen by a physician while they wait to be admitted to an inpatient bed. This has led to significant strain on emergency physicians, emergency nurses, and other staff, draining limited and critical resources and resulting in more delays in care. Particularly in emergency medicine where life or death can be a matter of minutes or even seconds, changes or delays in treatment can be life threatening. Furthermore, medication substitutes often prove less effective or induce different side effects, potentially compromising the quality of care, patient comfort, and satisfaction. Unfortunately, in many cases, there are simply no substitutes that exist.

This been a persistent issue for emergency medicine for years. In 2018, ACEP conducted a survey¹ of our membership and found that 9 out of 10 emergency physicians had experienced shortages or absence of critical medicines in their EDs within the last month. Additionally, nearly all respondents (93 percent) indicated that their EDs were not fully prepared for patient surge capacity in the event of a natural or man-made disaster or other mass casualty incident, and with fewer than half reporting that they were "somewhat" prepared. Unfortunately, these theoretical disaster scenarios would become all too real just a few short years later as the COVID-19 pandemic pushed our health care system to a breaking point (or beyond, in many cases).

Also in 2018, ACEP supported a bipartisan, bicameral congressional letter, led by Representatives Brett Guthrie (R-KY) and Mike Doyle (D-PA) and Senators Bill Cassidy, M.D. (R-LA) and Chris Murphy (D-CT), urging U.S. Food and Drug Administration (FDA) Commissioner Scott Gottlieb to identify the root causes of drug

¹ <https://www.emergencyphysicians.org/press-releases/2018/5-22-2018-90-percent-of-Emergency-Physicians-have-Experienced-Drug-Shortages-in-Past-Month>.

shortages, develop recommendations for Congress to address them, and take appropriate action to ensure these medications remain available. In response, Commissioner Gottlieb announced the creation of the FDA Drug Shortages Task Force in June 2018. ACEP was invited to participate in a listening session with the Task Force, attended the public meeting it convened, and submitted comments² to the Task Force. In October 2019, the Task Force issued a report entitled, “Drug Shortages: Root Causes and Potential Solutions.”³ This report (revised February 2020) found three major, foundational root causes for drug shortages: a lack of incentives to produce less profitable drugs; no recognition or reward for manufacturers for investing in and implementing mature quality management systems; and logistical and regulatory challenges that make it difficult for the market to recover after a disruption. The report further notes that these root causes are driven by a wide variety of economic factors driven both by the public and private sector.

With respect to emergency medicine, drug shortages exist across the spectrum of emergency care, including pre-hospital emergency care and emergency medical services (EMS). Shortages of commonly-used but essential medications remain an acute problem and tend to disproportionately affect emergency medicine due to its reliance upon generic medications for rapid sequence intubation, seizures, antidotes, resuscitation, as well as analgesics, antiemetics, and anticoagulants. EMS systems and hospital systems track and report shortages, adapting protocols in real-time to mitigate the effects of these challenges. Drug shortage reports typically include the drug/preparation in shortage, possible substitutes, and estimates of when the shortage will be resolved or when backorders are expected to clear (as reported by the manufacturer). In tracking shortages, what has become clear over the last decade, is that these shortages are not only severe but also *persistent*. One study conducted in 2015 found that half of all reported drug shortages from 2002 to 2014 involved acute care drugs used in ED, and these shortages are increasingly frequent and prolonged.⁴

Drug shortages can often last for several months or longer, constituting a significant risk to patients. While there is a mostly predictable demand for essential emergency medications, the supply is becoming increasingly unpredictable. Not having access to critical life-saving medications and drugs such as local anesthetics, injectable pain management drugs for acute pain and trauma, anti-nausea drugs, and even sterile intravenous (IV) fluids is disastrous and potentially devastating in terms of patient outcomes. There should never be shortages of essential and life-saving, but simple, products such as sterile saline, sodium bicarbonate, or epinephrine.

The clinical impact of a shortage is highly variable, depending on the drug. For example, amoxicillin is a common antibiotic to treat bacterial infections and is used across the entire age spectrum, but shortages particularly affect pediatric populations. While there is a current nationwide shortage of amoxicillin, fortunately, this appears to be improving somewhat in recent weeks. Shortages of common topical anesthetics, frequently referred to as the “caines”—lidocaine, bupivacaine, etc.—have existed for years, but are worsening throughout the country. These drugs are used every single day in EDs everywhere to numb lacerations and other similar injuries, but their availability is so unpredictable that supply can change daily. And recent, well-documented shortages of albuterol, an inhaled bronchodilator used for treatment of asthma, chronic obstructive pulmonary disease (COPD), and other lung diseases, limit both patients’ and clinicians’ ability to treat exacerbations of their conditions, which can result in ED visits and longer stays that would otherwise be preventable. Shortages of opioids and sedatives persist in the palliative care space, impacting the ability to relieve acute pain and discomfort.

In many cases, shortages may not be due to a lack of the medication itself, but rather the container. Some emergency physicians are currently reporting shortages of sodium bicarbonate syringes both in the 4.2 percent syringes used for pediatric patients and 8.4 percent syringes. As an alternative, their hospital pharmacy will likely supply vials, rather than syringes, until the shortage resolves. However, this also requires an additional layer of precaution to avoid medication errors, with the facility placing the pediatric vials in a separate location to prevent any possible confusion between the two concentrations. This is the currently the case for many other

² <https://www.acep.org/siteassets/new-pdfs/advocacy/acep-comments-on-fda-meeting-on-drug-shortages.pdf>.

³ <https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions>.

⁴ Chen, S.I. et al. (2015). National Shortages of Drugs Used in the Emergency Department, 2002–2014, *Annals of Emergency Medicine*, Volume 66, Issue 4, S64.

medications, where the container itself is in shortage and the medication may be available in different volumes or concentrations—but constantly changing protocols and different container sizes and concentrations increase the risk of medication errors and negative patient outcomes.

Consider the following example from just several years ago. In June 2017, there were 69 preparations of 28 emergency care medications in shortage, including most forms of adenosine, atropine, bicarbonate, calcium, dextrose, dopamine, epinephrine, fentanyl, furosemide, labetalol, magnesium, lorazepam, and paralytic agents.⁵ The shortages were exacerbated by the devastation wrought by Hurricane Maria on Puerto Rico in late 2017. The damage resulted in the largest drug manufacturing hub in the country grinding to a halt, with nearly all of the more than 50 pharmaceutical manufacturing facilities located on the island knocked offline by the storm. With little to no redundancy in the supply chain, manufacturers were not able to produce many of the essential products need throughout the health care system. By July of 2018, those shortages peaked at 170 emergency medication preparations and 50 intravenous fluid preparations that were not available. By December 2018, more than 110 drugs for emergency care remained in shortage. These conditions have not improved since—as of June 2023, there are 117 essential emergency medications in shortage.

Even before Hurricane Maria, sterile saline solution was already in short supply. Again, this is a simple, inexpensive product used every single day in every hospital in the country for nearly any patient, including countless patients in the ED. Saline typically comes in either small- or large-volume bags, both of which were in shortage prior to Hurricane Maria. The U.S. health care system relies on just three suppliers for saline (Baxter International, B. Braun Medical, and ICU Medical), with Baxter supplying small-volume bags to half of all U.S. hospitals alone.⁶ As any manufacturing problems for just one producer can overwhelm the system, Baxter's Puerto Rico facility going offline was extraordinarily disruptive—there was no redundancy built into their supply chain, other facilities cannot simply convert production lines for one product to another, and other manufacturers were not able to increase production capacity to meet the increased demand.

Another more recent example (Fall and Winter 2022) of how shortages can contribute to complications and worsen outcomes throughout the health care continuum are the severe shortages of commonly-used medications, such as liquid formulations of ibuprofen, acetaminophen, and amoxicillin. Shortages of these drugs left many parents unable to manage mild symptoms for their children's illnesses, resulting in increased visits to the ED and prolonged stays that could have been avoided with proper access to necessary medications. It also contributed to countless phone calls from pharmacies to EDs, urging emergency physicians to change prescriptions as they could not fill the orders.

Additional reasons for drug shortages cited by the Government Accountability Office (GAO), the FDA, Pew Agency for Charitable Trusts, and others, include greater scrutiny and regulatory oversight on the manufacturing process and quality controls, as well as additional factors such as consolidation of manufacturers (especially for generic injectables), low profit margins, shortages of raw materials, absences of redundancies in the supply chain, increased demand, and product discontinuations. The 2017 Pew report on drug shortages for example found that while quality factors are one of the most significant driving factors, it is not the only issue leading to shortages, and that other key factors are market withdrawals, supply chain design, purchaser-manufacturer incentives, limited market insights into future demands, and managing regulatory expectations.⁷

The 2016 GAO report, "Drug Shortages: Certain Factors Are Strongly Associated with This Persistent Public Health Challenge," also found that two factors were strongly associated with shortages of sterile injectable anti-infective and cardiovascular drugs—a decline in the number of suppliers, and failure of at least one es-

⁵Augustine, James J. (2017). "Emergency Departments Need Plan to Deal with Drug Shortages." ACEPNow <https://www.acepnow.com/article/emergency-departments-need-plan-deal-drug-shortages/?singlepage=1&theme=print-friendly>.

⁶Mazer-Amirshahi, M. & Fox, E. (2018). Saline Shortages—Many Causes, No Simple Solution. *The New England Journal of Medicine*. 378:1472–1474. <https://www.nejm.org/doi/full/10.1056/NEJMp1800347>.

⁷The Pew Charitable Trusts, "Drug Shortages An exploration of the relationship between U.S. market forces and sterile injectable pharmaceutical products: Interviews with 10 pharmaceutical companies," January 2017, https://www.pewtrusts.org/-/media/assets/2017/01/drug_short_ages.pdf.

establishment making a drug to comply with manufacturing standards resulting in an FDA warning letter.⁸ According to the GAO, this suggests that “. . . shortages may be triggered by supply disruptions.” The report also indicates that a third factor, drugs with sales of a generic version, is associated with shortages in that low profit margins for generic drugs mean that “manufacturers are less likely to increase production, making the market vulnerable to shortages.”

The ongoing price increases of certain essential medications also present a major challenge to the budgets of emergency care providers, such as EMS organizations. For example, a critically-needed drug for emergency care is naloxone, the rescue medicine for patients suffering respiratory depression due to an opiate overdose. As you well know, this frequently-used medication has been employed as a first-line response for opioid overdose treatment for more than 50 years but has recently become prohibitively expensive or difficult to source, especially at the higher doses or in formulations now needed to treat many patients with opioid use disorder (OUD) or individuals who have overdosed on fentanyl or fentanyl analogues that are significantly more potent. Various factors may contribute to this particular price increase: higher overall rates of opioid overdoses, increased awareness and promotion of naloxone as an overdose reversal agent, or even recent state and federal policies enacted to encourage co-prescribing of naloxone.

In the FDA Drug Shortages Task Force report, logistical and regulatory challenges are identified as one of the three key root causes of drug shortages, as they hinder the market’s ability to recover after disruptions in production or elsewhere in the supply chain. Many of these regulatory considerations fall under the purview of the FDA. However, like nearly any modern supply chain, the drug manufacturing supply chain has grown increasingly complex and is a global enterprise. As a result, manufacturers not only have to seek FDA approvals for things such as alternative manufacturing sites or alternative suppliers of active pharmaceutical ingredients (API), but also “. . . many post-approval changes to regulatory filings require prior approval by the regulatory authority of every country individually, and this can be over 100 countries for globally marketed products.” Additional details on the various regulatory considerations are included in the report.

Innovative payment models can help encourage the development of new drugs to address future needs, better prepare us against emergencies, disasters, and mass casualty events, or better equip our health care system to resolve drug shortages of essential emergency medications in a timely manner. As Congress considers any such approaches, ACEP believes a key piece of any new solution or payment model should ensure that essential emergency medications are prioritized and made available for emergency departments and EMS that maintain the health care safety net. EMS agencies in particular have still not fully recovered from the effects of the pandemic and struggle to respond to steep price increases or price gouging for everyday medications like naloxone or epinephrine autoinjectors (EpiPens), so Congress should consider policies that ensure EDs and EMS units are protected and not left to absorb severe price increases.

The FDA report noted that consolidation of group purchasing organizations (GPOs) resulted in the four largest GPOs accounting for approximately 90 percent of all medical supplies in the U.S., adding that as a result of this growing consolidation, GPOs are able to exert control over the market and “. . . have been able to negotiate low prices, especially for multi-source generics.”⁹ With manufacturers unable to raise prices or compete with other manufacturers seeking to gain market share, this often results in a “race to the bottom” where manufacturers sell a drug at or below cost. As the report states, this is a contributing factor to unfavorable pricing dynamics that discourage manufacturers by limiting their profitability:

When market conditions limit manufacturers’ profitability, they reduce a firm’s motivation to maintain a presence in, or enter the market for older prescription drugs, and to invest in manufacturing quality and redundant capacity. Manufacturers of older generic drugs, in particular, face intense price competition, uncertain revenue streams, and high investment requirements, all of which limit potential returns. Current contracting practices contribute to a ‘race to the bottom’ in pricing.

⁸United States Government Accountability Office, “Drug Shortages: Certain Factors Are Strongly Associated with This Persistent Public Health Challenge,” July 2016, <https://www.gao.gov/assets/680/678281.pdf>.

⁹Drug Shortages: Root Causes and Potential Solutions.

Many GPOs include “failure to supply” clauses in contracts with manufacturers, ostensibly intended to provide an incentive for manufacturers to invest in efforts to ensure a reliable and consistent supply chain for drugs. However, even despite growing GPO consolidation and outsized market presence, the report further notes that these clauses are “generally weak,” and that manufacturers face few or no repercussions beyond minimal revenue losses or reputation impacts.

As the FDA Drug Shortages Task Force, the Government Accountability Office (GAO), and numerous other analyses and studies have found, drug shortages are complex and multifactorial, and the issues described here are only pieces of a larger puzzle. There is only limited understanding and study of the broader, system-wide impacts of GPO contracting practices, including on how they may contribute to drug shortages. Given the already challenging economics of producing generic drugs, especially generic sterile injectables, it is possible that the significant downward pressure exerted by GPOs on already-low margin generic products could force manufacturers out of the market. Additionally, “sole-source” exclusive contracts could prevent some facilities, particularly drug compounders, from mitigating drug shortages.¹⁰ While not a key driver of drug shortages, it could potentially be an underlying factor. One issue Congress could examine in more detail is any role of GPOs in drug shortages, including whether the safe harbor provisions under federal antitrust statutes afforded to GPOs contribute to shortages, and consider repeal of the provisions if so.

With respect to business practices, many stakeholders throughout the health care system—drug manufacturers, GPOs, distributors, and health systems alike—have employed “just-in-time” inventory management practices, driven by financial incentives and potential operational efficiencies. While this may provide short-term benefits in normal, day-to-day operations, the Task Force noted that there is “. . . little redundancy in the supply chain when a disruption occurs,” and that resulting shortages cannot be easily addressed because of difficulties in ramping up production, expanding capacity, or sourcing necessary components including API.

Given that drug shortages are complex and multifactorial, and that there are numerous stakeholders involved in manufacturing, distribution, and utilization, we must be strategic and intentional about determining aligned incentives and cooperative initiatives that focus on providing quality patient care.

Any solutions should look at both short- and long-term needs—resolving existing shortages and insulating our health care system from future shortage scenarios. As ACEP has noted in responses to Congress regarding efforts to reauthorize the Pandemic and All-Hazards Preparedness Act (PAHPA), growing antimicrobial resistance and the reduction of remaining effective antimicrobial armamentarium represent a critical threat to public health and the health of patients in emergency departments throughout the U.S. and the world.

The Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) noted in a 2021 letter to HHS Secretary Xavier Becerra that the U.S. continues to face a “. . . severe lack of new antimicrobial drugs.” This growing deficit is exacerbated by increasing antimicrobial resistance to existing treatment options, leaving health care professionals more limited ability to treat infections. To help address the investment and development pipeline challenges for new antimicrobial drugs, ACEP urges Congress to include the Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (PASTEUR) Act in PAHPA. The PASTEUR Act would establish an innovative, subscription-based payment model for novel antimicrobials, allowing the federal government to enter purchasing contracts with companies that delinks payment from sales volume. This will help reduce risks for companies seeking to develop new antimicrobials, while also ensuring the federal government only pays for successful FDA-approved treatments that are available to patients and meet unmet antimicrobial resistance needs. The PASTEUR approach is similar to Project Bioshield, which helps support the development and procurement of medical countermeasures for other biological and radiological threats. Similar approaches for essential emergency medications or other drugs frequently in shortage could be employed as well.

Ensuring redundancy and resiliency within the pharmaceutical supply chain is critical for everyday needs as well as emergency preparedness needs, and as we have experienced directly, major natural disasters or disease outbreaks have pushed our

¹⁰Barlas S. (2019). Do GPOs Play a Role in Drug Shortages? Long-Standing Allegations Disputed by the GPOs. *Mar*;44(3):94–121. PMID: 30828227; PMCID: PMC6385730 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6385730/>.

health care system to or beyond its breaking point. Further incentives are undoubtedly essential to encourage manufacturers, primarily to ensure a consistent supply of essential medications at all times, particularly for low-cost/low-margin drugs. Additionally, these incentives should promote investment in equipment and technologies to facilitate efficient and rapid scalability of medication production. Moreover, they should incentivize domestic production and sourcing of active pharmaceutical ingredients (APIs) to reduce dependence on intricate and fragmented global supply chains. Overall, ACEP believes there are several overarching objectives that federal agencies should focus upon:

1. Routine measurement in the way of inventory surveillance
2. Broadly applied transparency as related to manufacturing and distribution practices to ensure adequate competition (including how existing federal laws may affect transparency and competition)
3. Flexibility in terms of granting authority to adjust protocols to fit the needs of real-time circumstances
4. Incentives or requirements to promote greater redundancy and resiliency
5. Comprehensive strategies to increase the manufacturing of drugs in shortage, especially generic sterile injectables (such as developing regulatory or process incentives to accelerate the development of new manufacturing sites)

Once again, thank you for holding this important hearing and for the opportunity to share our comments and experiences with how drug shortages affect care for our patients in need of lifesaving emergency care. ACEP remains hopeful that we can build upon our collective efforts to ensure stable, predictable, and affordable supplies of emergency medications for both everyday operation and disaster preparedness and response. Should you have any questions, please do not hesitate to reach out to Ryan McBride, ACEP Congressional Affairs Director, at rmcbride@acep.org.

Sincerely,

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On behalf of our nearly 5,000 member hospitals, health systems and other health care organizations, and our clinician partners—including more than 270,000 affiliated physicians, 2 million nurses and other caregivers—and the 43,000 health care leaders who belong to our professional membership groups, the American Hospital Association (AHA) thanks you for the opportunity to submit comments to the Senate Committee on Finance regarding the important topic of drug shortages.

America's hospitals and health systems have long been concerned about shortages of a wide range of drugs used to treat patients. Of particular concern to hospitals are the cascading impact of drug shortages on patients and the heightened stress on scarce hospital resources. Shortages can adversely affect patient care by causing delays in treatment, increasing the risk of medication errors and requiring the use of less effective alternative treatments. As a result, diseases that are curable or manageable for most patients, such as childhood leukemia, may not be able to be treated effectively.

When a drug is in shortage, hospitals must find an alternative drug to provide their patients. This process of finding and procuring an alternative drug can result in significant costs to the hospital. An analysis published in 2019 estimated that drug shortages result in at least \$359 million annually in additional labor costs to hospitals.¹ Due to the increased cost and necessity of treating patients in a timely manner, especially in cases of cancer and other serious illness, it is important to ensure the pharmaceutical supply chain is protected and priority drugs are identified and given special attention so that continual access is ensured for patients.

However, it has become increasingly clear that our national pharmaceutical supply chain is fragile; this fragility poses significant risk to the patients and communities

¹ <https://wreck-vizient-production.s3.us-west-1.amazonaws.com/page-Brum/attachment/c9dba646f40b9b5def8032480ea51e1e85194129>.

served by America's hospitals and health systems. Various businesses make up the pharmaceutical supply chain, including suppliers, manufacturers, distributors and group purchasing organizations. A disruption anywhere in the chain can create prolonged difficulties in pharmaceutical supply acquisition for providers, which can directly affect their ability to treat patients.

Exacerbating these difficulties is the "lean" or "just-in-time" framework of supply chain operations. There is effectively little buffer when disruptions occur. Distributors, manufacturers and health care providers have pursued this just-in-time supply chain approach with the goal of lowering costs so that health care is more affordable; however, during large scale emergencies and other disruptions in supply, the risks and added costs of such a strategy is clear. When those disruptions occur, providers often have little or no notice and can be left scrambling to acquire products necessary to care for the sick and injured.

To mitigate these challenges, strengthening the supply chain is crucial. A focus on increasing manufacturing redundancy, diversifying where raw materials are sourced and where products are manufactured, and "fattening" the overall supply chain will provide significant improvements. It will allow the supply chain to withstand expected and unexpected fluctuations in the supply of, and demand for, pharmaceutical products and protect it against future public health emergencies and natural disasters.

This year, the AHA has supported multiple bills in the Senate that take steps to address drug shortages and shore up the pharmaceutical supply chain, including the following.

Mapping America's Pharmaceutical Supply (MAPS) Act (S. 2364). A critical step in protecting America's drug supply chain is understanding its vulnerabilities from the beginning of production to the moment a drug is administered to a patient. The MAPS Act creates a plan for the Food and Drug Administration and the Department of Defense to map the U.S. pharmaceutical supply chain. The act also includes use of data analytics to identify and predict supply chain vulnerabilities and other national security threats. With the information collected and analyzed through the MAPS Act, it will be possible to begin addressing weaknesses in the pharmaceutical supply chain.²

Rolling Active Pharmaceutical Ingredient and Drug (RAPID) Reserve Act (S. 2510). Pharmaceutical shortages and supply chain failures can have a devastating impact on patients. The RAPID Reserve Act would establish a program to improve supply chain resiliency for critical generic drug products, ensuring adequate supply is available even in the event of a shortage. The legislation awards contracts to eligible drug manufacturers requiring them to maintain a 6-month buffer of these critical drugs and their active pharmaceutical ingredients to ensure continuous production flow. With adequate supply of necessary drugs, providers will be equipped to administer necessary, often lifesaving, drugs to patients.³

Pharmaceutical Supply Chain Risk Assessment Act of 2023 (S. 1961). The Pharmaceutical Supply Chain Risk Assessment Act of 2023 would require a comprehensive risk assessment of the entire U.S. pharmaceutical supply chain. This overarching project will help provide critical information necessary to mitigate and prevent drug supply shortages. A disruption anywhere in the supply chain can create prolonged difficulties in pharmaceutical supply acquisition for providers, and avoiding these disruptions before they occur will benefit providers and the patients they serve.⁴

We thank you for the opportunity to submit comments the Senate Committee on Finance regarding drug shortages and look forward to continuing to work with you on this important issue.

²AHA Letter of Support for the Mapping America's Pharmaceutical Supply Chain, or MAPS, Act of 2023|AHA.

³AHA Letter of Support for the Rolling Active Pharmaceutical Ingredient and Drug, or RAPID, Reserve Act of 2023|AHA.

⁴AHA Letter of Support for the Pharmaceutical Supply Chain Risk Assessment Act of 2023|AHA.

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The Honorable Ron Wyden Chair The U.S. Senate Committee on Finance 219 Dirksen SOB Washington, DC 20510	The Honorable Mike Crapo Ranking Member The U.S. Senate Committee on Finance 219 Dirksen SOB Washington, DC 20510
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Chair Wyden, Ranking Member Crapo, and Members of the Committee:

On behalf of our nation's over 310,000 pharmacists, the American Pharmacists Association (APhA) is pleased to submit the following Statement for the Record to the U.S. Senate Committee on Finance hearing "Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective."

APhA is the largest association of pharmacists in the United States advancing the entire pharmacy profession. APhA represents pharmacists and pharmacy personnel in all practice settings, including community pharmacies, hospitals, long-term care facilities, specialty pharmacies, community health centers, physician offices, ambulatory clinics, managed care organizations, hospice settings, and government facilities. Our members strive to improve medication use, advance patient care, and enhance public health.

APhA applauds the Committee's ongoing leadership and recognition of the need to address ongoing drug shortage issues. APhA has recently responded to congressional requests for information,¹ proposed legislation,² and the FDA³ on ways to partner with our nation's pharmacists to address ongoing drug shortages.

APhA also supports the recommendation from today's pharmacist witness, Inmaculada Hernandez, PharmD., Ph.D. for "reforms to the Medicare Part D program to . . . ensure fair pricing and reimbursement practices, prevent and penalize anti-competitive behavior, foster pharmacy sustainability, guarantee pharmacy access, and promote transparency."

Drug shortages impact pharmacy teams and patients in all practice settings. Health systems across the country have dedicated staff that focus specifically on addressing and mitigating the impact of potential and current drug shortages. They scour the country for short-supply drugs and develop protocols and allocation schemes for precious drugs, such as those for cancer and emergency care.

Impact of Drug Shortages on the Vital Role of Community Pharmacies

The effect on community pharmacies of drug shortages, particularly small independent pharmacies, is often hardest because they lack the buying power that larger chains or health systems have to purchase or stock up on short-supply drugs. During the recent amoxicillin and children's fever drug shortages, many chain pharmacies had drugs available for weeks and months after independent pharmacies, who have smaller on-hand inventories, quickly ran out and could not restock. This left many parents scrambling from pharmacy to pharmacy to find medicines for their sick children. While compounding pharmacies could have alleviated this issue, FDA did not implement APhA's recommendations, which could have mitigated the shortage, including: adding ibuprofen and acetaminophen pediatric oral suspensions to the FDA drug shortage list, issuing temporary guidance for the compounding of acetaminophen and ibuprofen pediatric oral suspensions, and providing enforcement discretion regarding the essential copies and prescription requirement provisions for these products until sufficient supply was available across the country.

Amend the FDCA Definition of "Drug Shortage" and What Goes on the Drug Shortage List to Enable Faster and Broader Prevention and Mitigation Response

The term "drug shortage" is defined in the Food, Drug, and Cosmetic Act (FDCA) in section 506C(h)(2) as: "the term 'drug shortage' or 'shortage,' with respect to a drug, means a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug;" FDA's drug shortage re-

¹ <https://www.pharmacist.com/DNNGlobalStorageRedirector.ashx?egsfid=lShzV4LvadQ%3d>.

² <https://www.pharmacist.com/DNNGlobalStorageRedirector.ashx?egsfid=BuDhOnzBpk%3d>.

³ https://www.pharmacist.com/DNNGlobalStorageRedirector.ashx?egsfid=sY1w_PYlpZ8%3d.

sponse is commendable. FDA can reach into their drug shortage toolbox and use various tools to deflect or mitigate drug shortages. There are many times when a demand exceeds supply throughout the country or in pockets of the country, however, the product does not appear on the FDA drug shortage list. This limits FDA's ability to use some of the effective tools in its toolbox.

The University of Utah/ASHP drug shortages list is broader and more reflective of what's happening in the marketplace. It contains drug shortage information that is reported by healthcare professionals around the country and is investigated and verified before it is added to their list. FDA uses information that is provided by manufacturers to determine whether the product is in shortage or at risk of shortage. Although FDA does query the marketplace, significant reliance on this narrow source of information unnecessarily keeps the bar high for a product to get on the drug shortage list and, consequently, slows prevention and mitigation response efforts.

APhA recommends that the scope of the FDA drug shortage list required under section 506E of the FDCA be broadened to reflect more sources of information. The list should be nimbler and resilient in identifying drug shortages in the U.S., whether widespread or in pockets of the country. Additionally, as experience shows, it takes a while for availability to stabilize across the country. Therefore, we recommend that the definition incorporate a stabilization period to ensure that the drug shortage has resolved and is not still in a fragile state. For example, the definition of what is reported and what goes on the list could be amended in the following way:

the term "drug shortage" or "shortage," with respect to a drug, means a period of time when the demand or projected demand for the drug, as reported by manufacturers, wholesale distributors, and health care practitioners, within the United States or a region of the United States exceeds the supply of the drug; and continues until six months starting on the day all manufacturers have stabilized market availability across the United States.

Enable Compounding Pharmacies to Help Earlier

Currently, under certain conditions, compounded drugs can be made and distributed by state-licensed compounding pharmacies when the drug appears on the FDA drug shortage list. These pharmacies are able to produce products when commercial manufacturers are not able to meet market demand. Because pharmacies compounding under 503A of the law oftentimes compound products for local patients, they are able to more quickly fill in gaps in availability, particularly if a shortage is identified regionally due to specific market demands. For example, if there is misaligned distribution of products across the U.S. because of concentrated cases of an infection, weather, or other acts of nature that surge demand in a region, or during the early or latter stages of a more widespread drug shortage. Unfortunately, current law does not support the ability of 503A pharmacies to fill these gaps. By modifying the definition of "drug shortage," as noted above, the FDA drug shortage list will reflect the dynamics in the marketplace and trigger the ability of 503A pharmacies to compound to prevent or mitigate a shortage.

Reform PBM Business Practices That Contribute to Drug Shortages

Another cause of drug shortages is the impact and influence of rebates and pharmacy benefit managers (PBMs). PBMs negotiate with manufacturers to get their drugs on formulary. In doing so, the manufacturers raise prices and provide the PBMs with large rebates, which are kept by the PBMs. This cycle of rebates continues even after a drug loses its patent protection and generics are approved for marketing. By keeping the higher-priced brand version on a plan formulary, the PBM can continue to get rebates, blocking out generic versions from getting on formularies. This disincentivizes generic manufacturers from producing their version, leading to fewer options and creating a greater risk of shortage if there is a problem meeting market demand.

Accordingly, APhA strongly supports the Committee's recently passed PBM reform legislation to reign in PBM practices, however, more must be done to mitigate the influence that PBM economic antics contribute to drug shortages by shifting preferences away from lower-cost generic drugs.

DEA/FDA Collaborative Forecasting and Surveillance

APhA appreciates that the FDA and DEA continue to work closely with hospitals, pharmacists, Congress, and others to prevent or reduce the impact of drug shortages.

For example, on August 1, 2023, the FDA and DEA released a rare joint public letter⁴ to provide an update on the recent attention deficit hyperactivity disorder (ADHD) drug shortage. The two agencies announced they are working with multiple manufacturers, agencies, and others in the supply chain to reduce the impact of these shortages and asked drug manufacturers to increase production. FDA is also taking steps to support alternative treatment options while there is a shortage and recommends the use of non-stimulant medications. FDA and DEA also stated that some drug manufacturers have allotted production quota they have not fully used and are on track to fall one billion doses below their allocated quota. Both agencies are asking for unused product quota to be reallocated to manufacturers who could produce these drugs.

On November 1, 2023, the DEA announced⁵ changes to its quota allocation process to be more flexible and resilient in allocation management. DEA reduced the amount that manufacturers must keep in inventory to make it easier to relinquish their quota allotments in case they are not able to produce a drug. DEA also took steps to increase manufacturer transparency and receive better real-time data on the status of drug production going forward.

It is essential that FDA and DEA continue with close communication and collaboration in exchanging forecasting and market surveillance data to be nimbler in addressing or mitigating drug shortages. We appreciate that DEA will be moving to a quarterly allocation system, however, by the time quotas are redistributed, it may be too late since manufacturers may not be able to ramp up production fast enough to prevent a shortage.

APhA Recommendations to Assist in Addressing Drug Shortages

APhA makes the following recommendations to the Committee to assist in addressing drug shortages, including:

- Amend the FDCA definition of “drug shortage” and what goes on the drug shortage list. to enable faster and broader prevention and mitigation response.
- Enable compounding pharmacies to help earlier.
- Reform PBM business practices that are contributing to drug shortages.
- Increasing transparency and accountability in drug manufacturing and oversight to help prevent and mitigate shortages and help purchasers make appropriate decisions based on the quality and reliable availability of drugs.
- Increase incentives to domestically manufacture generic drugs. Congress would also need to provide the FDA with additional funding to increase inspection coverage and review of new manufacturing facilities (*e.g.*, hiring more FDA staff to conduct these inspections and assess compliance and quality of drugs produced in these facilities, as well as the ability for personnel working on drug shortage prevention and mitigation to quickly address potential shortages).

APhA appreciates the opportunity to provide this Statement for the Record for the recent hearing to address drug shortages. Pharmacists play a critical role in helping to manage drug shortages for their patients. APhA encourages members of the Committee to leverage the expertise of our nation’s pharmacists as you consider solutions for addressing drug shortages for our patients in the United States. Please contact Doug Huynh, JD, APhA Director of Congressional Affairs, at dhuynh@aphanet.org if you have any additional questions or need additional information.

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December 6, 2023

My name is Girish Malhotra. I am President of EPCOT International, a consulting company.

Members are PBMs subsidiaries. None of the panel members or the legislators know about the manufacturing technologies, *e.g.*, continuous manufacturing or ad-

⁴ <https://www.dea.gov/sites/default/files/2023-08/DEA%20and%20FDA%20Issue%20Joint%20Letter%20to%20the%20Public.pdf>.

⁵ <https://www.dea.gov/sites/default/files/2023-11/Quota-Shortages%20Letter.pdf>.

vanced manufacturing practices. PBMs should be held accountable of distributing less than quality products. They are not.

It is ironic that three Executive Orders have been not implemented.

1. Executive Order 13588 Reducing Prescription Drug Shortages (<https://obamawhitehouse.archives.gov/the-press-office/2011/10/31/executive-order-13588-reducing-prescription-drug-shortages>), October 31, 2011, Accessed August 31, 2020
2. Executive Order 13944 (<https://www.govinfo.gov/content/pkg/FR-2020-08-14/pdf/2020-18012.pdf>), Accessed April 26, 2022
3. Executive Order on America's Supply Chains (<https://www.whitehouse.gov/briefing-room/presidential-actions/2021/02/24/executive-order-on-americas-supply-chains/>), Feb. 21, 2021 Accessed May 30, 2022

USA has held such hearings over and over again but then nothing meaningful has happened.

November 25, 2023

USA's Annual Ritual of Drug Sourcing/Pricing and Shortages:

In fourth quarter of every year in USA, there is a euphoria of finding the right prescription drug sourcing⁽¹⁾ plan. With number of players offering their plans one has to be careful to pick the right plan for their needs. It is interesting to note that we are given a filled price for the drug. Generally there is no breakdown of the components that make the payment to be made.

It is generally accepted that the drugs will be available or shipped from the selected pharmacy and all will be good. It is worth noting that about 90% of the drugs dispensed are generic drugs^(1,2) and sourced through various suppliers under Medicare healthcare plans. According to US Census Bureau about 92.1% of the US population has healthcare coverage.⁽³⁾ The numbers suggest that majority of the US population has access to generic drugs. However, issues of shortages and unaffordability prevails. Brand drug prices are not part of the discussion. Due to lack of any immediate competition they set their own sale prices.

Pathway of the generic drug to the patient and pricing needs some explaining. PBMs (pharmacy benefit managers and their partners) purchase the drugs from manufacturers and distribute them. Their mission is maximize profits.

Prescribers generally do not know the breakdown of the monies they pay, *i.e.*, cost of the drug, handling and shipping etc. Patient pays the price their drug provider charges. Table 1 reviews the price breakdown for two drugs.

One of the age old trading practices is to pressure the manufacturer to lower their selling price. If the manufacturer does not make their desired profit, they will not sell the drug to PBMs and this will result in shortages. Patients will experience these. For PBMs drug becomes an "ITEM" of trade rather than a person's life depends on it. To them profits are more important than the life of the patient/customer.

Generally a cost breakdown of any drug is not in public domain. Their discussion is healthy as many ambiguities can be cleared. A cost breakdown and comparison with and without insurance⁽⁴⁾ gives us the landscape. *CostPlusdrugs.com*⁽⁵⁾ drug price breakdown is reviewed here. Prices of *GoodRx.com*⁽⁶⁾ can be used for comparison. A review clears any misconception one could have. Perspective here reviews the cost of the generic drugs from the factory floor to the patient. Similar but different scale of numbers apply for the brand drugs. I am not influenced by any for or non-profit entity. Observations presented are my own.

With such a large population being covered by various healthcare drug programs it is my belief that number of patients going outside their healthcare system to purchase drugs is going to be minimal. For patient going out of the network would be an anomaly. It would be same as an impulse purchase. It is well known fact that such purchases are high priced.⁽⁴⁾ Thus listing of "retail prices" on respective sites^(5,6) seems more like a scare tactic than a reality as very limited number will purchase drugs at retail prices.

Lately drug shortages are increasing in the news. Has anyone analyzed why? Most likely no. They have a simple explanation. It is the profit at manufacturer level. Table 1 in the referred post⁽⁴⁾ and this post clearly show the drug price component of each drug sell price.

Even if manufacturing companies make a concerted effort to lower their manufacturing costs by using better processing technologies that can significantly lower their current environmental emission impact and are able to improve profits at their level, landscape will not change much. US will continue to see generic drug shortages⁽⁷⁾ as PBMs will continue to pressure manufacturers to lower their selling prices.

An analysis of adventure by Amazon, Berkshire Hathaway and J.P. Morgan⁽⁶⁾ was bound to fail from the onset as they had no comprehensive and rational plan. “Out of the box thinking” was needed but not considered.^(9,10) Only viable alternate is that drug manufacturers take over the distribution and compete.⁽⁷⁾ Competition will lower overall drug prices and will be an overall win for the country. Generally it is.

Table 1 is a comparison of factory drug prices and what a customer would pay if they bought the drugs from Costplus Drug Company⁽⁵⁾ and/or Amazon. Amazon does provide medications at discounted prices but details are not available unless one signs up.⁽¹¹⁾

It is interesting to note that the drug component even after manufacturer making 200% profit are a small percentage of the drug selling price after including handling and shipping. These charges can be as much as 700+% above the drug manufacturer's selling price. My conjecture is that such markups apply across the generic drug sale landscape. Better API and formulation manufacturing technologies⁽¹²⁾ and shipping and handling technology combination present an opportunity to improve profits and lower prices of drug manufacturers and their distributors.

There are two notable features of Costplus Drug and GoodRx companies. Unlike other drug plans patients do not have to become their subscriber.

Two Selected Drug Formulation Cost & Sell Prices

	Metformin			Lipitor		
	Percent of formula	Cost \$/kg	\$/kilo	Percent of formula	Cost \$/kg	\$/kilo
API (active pharma ingredient)	10	4.00	0.40	10	206.00	20.6
Inert (includes packaging)	90	4.00	3.60	90	100.00	90
Total	100		4.00	100		110.6
Service & Expense *	Cost % of total API + inerts	40%	1.60	60%	40%	44.24
Packaged cost per kilo			5.60			154.84
Factory Profit % Packaged cost**		200%	11.20		200%	309.68
Drug Bulk price \$/kg.			16.80			464.52
*Service & Expense include Hourly labor, Salaried labor, Utilities, Maintenance, Depreciation & Corporate overhead. If service & expense is more than 40% of the factory cost, it is an indication that the process is not optimum.						
**Extra profit of 200% is included.						
One kilo of drug produces ONE million tablets of One milligram						
Milligrams/tablet				500		20
Number of tablets per kilo				2,000		50,000

Factory sell price is based on the illustrated calculations above		
Factory sell price/finished tablet, \$	0.008	0.009

Where does difference between factory sale price to patient price go?

# of Tablets	Metformin			Lipitor		
	Appr. Selling Metformin MFG. price, \$	Costplus MFG. ⁽⁵⁾ price, \$	Costplus ⁽⁵⁾ customer price, \$***	Appr. Selling Lipitor MFG. price, \$	Costplus ⁽⁵⁾ MFG. price, \$	Costplus ⁽⁵⁾ customer price, \$***
30	0.25	0.30	5.60	0.28	0.60	5.90
60	0.50	0.60	6.20	0.56	1.20	6.80
90	0.76	0.90	6.80	0.84	1.80	7.70

***This price DOES NOT include \$5.00 shipping cost per order which is added when the order is placed. This increases out of pocket cost and would need to be compared against other seller prices.

GoodRx (5) prices are variable for drug at each participating drug store and are generally higher than Costplus prices.

Amazon Pharmacy prices⁽¹¹⁾

Metformin, 500 mg tablets		Lipitor, 20 mg tablets	
Days	price \$	Days	price \$
30	2.25	30	9.00
90	5.23	90	14.00

Table 1: Price comparisons

US healthcare system has serious issues. My conjecture is that US Legislators and policymakers have no real knowledge and/or grasp of the landscape. If they have any knowledge, it has been ignored. Drastic re-think is need. However, due to political and vested influence of many, an “ALL HANDS” re-think effort to handle the drug pricing, shortages and bring manufacturing home⁽⁷⁾ would be needed. Patient to have the best pricing has to have knowledge of all offerings to make the best decision for themselves. This is not an easy task. Question is “Do we have what it takes to address the issues and simplify drug purchases?” or policy makers, bureaucrats will just talk about it and succumb to political pressures and do nothing?

Girish Malhotra, PE
President

1. Editorial Board Bloomberg: Are Generics Too Cheap for Their Own Good? November 16, 2023, <https://www.bloomberg.com/opinion/articles/2023-11-16/drug-shortages-are-generics-too-cheap-for-their-own-good>
2. <https://www.fda.gov/drugs/generic-drugs/office-generic-drugs-2021-annual-report>
3. <https://www.census.gov/library/publications/2023/demo/p60-281.html>
4. Malhotra, Girish: Systematic Demystification of Drug Price Mystique and the Needed Creative Destruction, Profitability through Simplicity, October 2, 2019 <https://pharmaceuticalscoatings.blogspot.com/2019/10/systematic-demystification-of-drug.html>
5. Costplus Drug Company <https://costplusdrugs.com/>
6. GoodRx <https://www.goodrx.com/>
7. Malhotra, Girish: Roadmap to Reduce Drug Shortages and Bring Pharma Manufacturing Home (US), Profitability through Simplicity, October 30, 2023

generics, FDA's approval time is generally over FIVE years. Same would have happened for COVID-19 test kits and vaccines but Executive Branch had to intervene for faster approval.

Bottom line: Current systems are antiquated and suffer from "red-tap" bureaucracy. FDA has made no effort to review the current system and shorten the "filing and approval" process and time. If improved, it can reduce shortages. This is discussed later.

Filing and approval process for the Generic drugs, since their brands are already approved, needs to be reviewed. No one will admit and/or agree but the current process can still take 3-5+ years. I do not believe any effort has been made to fix the issues, *i.e.*, reduce the filing and approval time. This along with direct sale could reduce shortages. I am afraid that no one at FDA can as a person or a small team can file the necessary paperwork needed for approvals. They do not understand the impact their decisions have. Templates that detail as to what is need for fast approval could minimize the commercialization of generics. This process has significant advantages. Companies would know how much time would be expended and they can invest in appropriate processes and plants.

FDA has another issue. It keeps suggesting the kinds of technologies companies should use when they do not understand their applicability for various products. They have no experience in development, design and commercialization of the suggested technologies.

Basically FDA wants to tell companies what they should do for manufacturing and other technologies when they do not understand their value. They have not made any attempt to modernize their application filing and approval processes.

To top it off it issues non-compliance citations and suggests manufacturing companies to use consultants, who happen to be its ex-employees. Who like FDA's current employees have no process development, design and manufacturing experience. Irony is that same sites are cited again for non-compliance.

Over the years FDA has talked about drug shortages (congressional testimonies) and proposed nothing meaningful to simplify the processes so that companies would invest in USA to produce drugs. Testimonies in front of Congress are just smoke and mirrors.

Our Legislators:

Our legislators hold hearings about drug shortages. They are meaningless as nothing meaningful results. Lobbyists have their ears and their constituents die as they have no drugs to live on. Legislators need to rein in PBMs but there is no effort. Collusion of lobbyists with Legislators is detrimental to health of constituents.

Manufacturing companies:

World learnt US's insatiable demand for generic drugs. Companies overseas due to lower costs could do make and sell at profits. PBMs jumped on the opportunity for higher profits. That has resulted in better than 70% of Generic drugs coming from overseas. Lower environmental regulations helped the exodus from US. Companies rather than invest in better processes/technologies and keep the manufacturing home shut down facilities in US. All this along with long approval times to get adequate ROI speeded up exodus from US. No one is going to invest in processes and equipment due to long regulatory approval times.

Pharma companies have relied on "mortar and pestle" technologies to produce drugs. These technologies are labor intensive. Companies have never invested in better manufacturing technologies. All this has helped and allowed PBMs to flourish unabated. PBMs make the top FIVE of the top TEN Fortune 500 companies.

Remedies:

All said and done we in USA need to review and change the landscape. PBMS, FDA and Legislators have to be corralled in the same room and make better policies and pathways for generations to come. If we do not with increasingly worsening global political situation day of reckoning is speeding up when US may have to beg its adversaries for the survival of its population.

There are pathways to bring pharmaceutical, especially generic, home. Concerted effort and meticulous thinking uninfluenced by vested interests would be needed.

1. <http://bit.ly/34RYypH> (2019) This establishes 90 approvals of ANDAs. FDA is going to balk on this when they have been talking of improving things. This also holds PBMs and allies responsible for distributing less than quality drugs.

They are not held accountable for distributing less than quality drugs but take all the profits of selling less than quality drugs. Manufacturing companies after two strikes are barred from supplying drugs from supplying to US. Only FINANCIAL hurt will fix quality issues.

2. <https://bit.ly/3KbTSzP> (2022) This refers to establishing a FOUR STATE Model like we had in Puerto Rico. This will establish manufacturing in USA.
3. <https://bit.ly/39jBQdd> (2018) This discusses direct sale to patients. This will bring competition which brings bring better manufacturing technologies, quality lowers costs and improves profits to the companies and bypasses the middle men. PBMs, FDA and our politicians will detest this.
4. <https://bit.ly/3nxOIz> (2020) Lays out a ROAD MAP to bring pharma manufacturing home.
5. <https://bit.ly/3NUxhsP> (2022) Reviews NAS (National Academy of Science) report which is a disaster as it suggest US should have foreign country supply alliances.

For success independent technocrats and bureaucrats are needed. US science and engineering talent is unsurpassable and can accomplish the most arduous task if politicians and career regulators do not intervene.

Please ask questions. Thank you.

Warm regards,

Girish Malhotra, PE

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The Federation of American Hospitals (FAH) submits the following Statement for the Record in response to the Senate Finance Committee's (Committee's) full committee hearing "Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective." We appreciate the Committee's commitment to tackling this issue and agree that action should be taken to address the care delays and challenges caused by drug shortages.

The FAH is the national representative of more than 1,000 tax-paying community hospitals and health systems throughout the United States. FAH members provide patients and communities with access to high-quality, affordable care in both urban and rural areas across 46 states, plus Washington, DC, and Puerto Rico. Our members include teaching, acute, inpatient rehabilitation, behavioral health, and long-term care hospitals and provide a wide range of inpatient, ambulatory, post-acute, emergency, children's, and cancer services.

The healthcare supply chain is complex, with many active participants involved in ensuring adequate access to drugs used to provide hospital care. Hospitals aggregate drug sourcing and contracting through group purchasing organizations (GPOs) and don't typically contract directly with manufacturers. In turn, GPOs provide various services for their hospital members, including creating long-term contracts with generic drug manufacturers to achieve a sustainable and resilient supply chain. GPOs must partner with manufacturers that offer a robust pedigree channel that allows for redundancy when possible. To alleviate shortages, incentives are needed to bolster production and improve transparency and collaboration with manufacturers and distributors to support a robust supply of products. We encourage the Committee to extensively assess the drug supply chain and look for ways to strengthen the process to ensure that any proposed policies address drug shortages and safety without creating unintended, harmful consequences.

We look forward to working with the Committee on these critical issues. If you have any questions or would like to discuss these comments further, please do not hesitate to contact Ryann Hill, Vice President of Government Relations, at RHill@FAH.Org or (202) 624-1514.

Sincerely,

Ryann D. Hill, MPH
Vice President, Government Relations

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December 18, 2023

The Honorable Ron Wyden
 Chair
 Senate Finance Committee
 Washington, DC 20510

The Honorable Mike Crapo
 Ranking Member
 Senate Finance Committee
 Washington, DC 20510

Dear Chair Wyden and Ranking Member Crapo,

The Healthcare Leadership Council (HLC) thanks you for holding a hearing on, “Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective” on December 5, 2023.

HLC is a coalition of chief executives from all disciplines within American healthcare. It is the exclusive forum for the nation’s healthcare leaders to jointly develop policies, plans, and programs to achieve their vision of a 21st century healthcare system that makes affordable high-quality care accessible to all Americans. Members of HLC—hospitals, academic health centers, health plans, pharmaceutical companies, medical device manufacturers, laboratories, biotech firms, health product distributors, post-acute care providers, homecare providers, group purchasing organizations, and information technology companies—advocate for measures to increase the quality and efficiency of healthcare through a patient-centered approach.

Access to the appropriate medications when a patient needs them is critical to the best patient outcome and a central element in the U.S. healthcare delivery system. HLC and our member companies are united in our commitment to work with the public sector to ensure a resilient supply chain.

The U.S. is facing a nearly 10-year peak in drug shortages. In spring 2023, medications in shortage surpassed 300 for the first time since 2014.¹ There are concerning shortages across clinical care, including oncology treatments, local anesthetics and basic hospital drugs, asthma medications, ophthalmic medication, attention deficit hyperactivity disorder (ADHD) treatments, and others.

Generic drugs comprise the majority of drug shortages, with generic sterile injectables (GSIs)—including older platinum oncology drugs in current shortage—accounting for the lion’s share of generic shortages. The Food and Drug Administration (FDA) reports that generics comprise 70 percent of drug shortages, and 62 percent of the drugs on the FDA shortage list in January 2023 GSIs.²

The current drug shortages are most acute in the GSI market, which is experiencing a confluence of drivers in the persistent shortage. Chief among them is the low profit margins in GSI markets, which limits supply chain resilience. Moreover, production of GSIs requires robust quality control measures. Lack of supply chain resilience results in manufacturers pausing production for long periods of time or exiting the market. Additional factors contributing to shortages include workforce shortages and lingering supply chain disruptions from the COVID-19 pandemic.

As the shortages continue, providers are making difficult decisions, including providing alternative treatments and rationing, with potential adverse outcomes for patients. Hospitals regularly experience drug shortages. A 2019 Vizient survey found that all hospitals experienced shortages in 2018, with two-thirds experiencing 20 or more shortages at a given time.³ Hospitals routinely work with prescribers to offer therapeutically equivalent alternatives; however, these alternatives may be less familiar to the provider or have unfamiliar side effects for the patient. In more extreme circumstances, when faced with a shortage of oncology medications in particular, hospitals engage their ethics departments to make difficult allocation deci-

¹Drug Shortages Statistics, American Society of Health System Pharmacists (ASHP), (accessed December 4, 2023), <https://www.ashp.org/drug-shortages/shortage-resources/drug-shortages-statistics>.

²Drug Shortages: Root Causes and Potential Solutions, U.S. Food and Drug Administration (2019), www.fda.gov/media/131130/download and Federal Policies to Address Persistent Generic Drug Shortages, Brookings’ Hamilton Project (June 2023), www.brookings.edu/wp-content/uploads/2023/06/20230621_ES_THP_GSI_Report_Final.pdf.

³New Study Shows Drug Shortages Have a Large Impact on Hospitals, Pharmacy Times (July 2, 2019), <https://www.pharmacytimes.com/view/new-study-shows-drug-shortages-have-a-large-impact-on-hospitals>.

sions. Evidence of efficacy and tolerability are considered in tandem with ethical principles including beneficence, non-maleficence, transparency, fairness, distributive justice, responsible stewardship, and others. Allocation decisions prioritize patients with potential for cure over those receiving the drug for palliation. These devastating decisions may hasten the end of life—potentially by many months—or, in some cases, years for palliative patients who may achieve unexpected benefits with the drug.

The likely substantial impact the current shortage of chemotherapy drugs is having on patients is yet to be measured. For example, a 2009 shortage of mechlorethamine which led providers to use cyclophosphamide as an alternative in treating Hodgkin's lymphoma in children, was associated with a decrease of the 2-year survival rate from 88 percent to 75 percent.⁴

While direct patient treatment is the most critical consequence of drug shortages, research, and development (R&D) and healthcare costs are also impacted. Clinical trials take years to meticulously develop. The results of a clinical trial may be affected if researchers must substitute the drug or otherwise alter the design of the clinical trial at the onset or during the course of the study period in response to a drug shortage. Shortages are costly both for manufacturers working to increase supply and for hospitals that must purchase alternative medications and otherwise compensate for drugs in scarcity. Shortages increase pharmaceutical spending for hospitals by 6 percent on average.

As Congress explores mechanisms to increase drug supply resiliency, please consider the following policy solutions:

Invest in a Robust Government Stockpile and a Targeted Buffer Inventory

HLC took a leadership role on disaster readiness even before the pandemic. HLC worked with the Duke-Margolis Health Policy Center and a broad array of organizations to develop recommendations focused on three key areas: improving data and evidence generation, strengthening innovation and supply chain readiness, and innovating care delivery approaches. This initial report (https://www.ndhi.org/files/1816/1281/7553/disaster_preparedness_report_FINAL.pdf) was released in February 2021. Many of these recommendations have been implemented through legislative or administrative action. As Congress considered reauthorization of the Pandemic and All Hazards Preparedness Act (PAHPA), we once again partnered with the Duke-Margolis Center for Health Policy and other organizations to release updated recommendations (<https://www.hlc.org/wp-content/uploads/2023/04/Final-HLC-Duke-Report.pdf>) in May 2023 specific to PAHPA reauthorization. One key recommendation we make is to substantially and consistently fund the Strategic National Stockpile (SNS). It is also critical to engage manufacturers in longer-term committed contracts with frequent, scheduled ordering rather than occasional bulk purchases. Guaranteeing a reliable market of a certain level for goods that may have more episodic demand in commercial or other markets ensures ready availability of drugs and medical goods that are certainly needed sometimes, though otherwise too seldom to justify steady production.

We strongly urge Congress to reauthorize PAHPA before the end of the calendar year in the same bipartisan fashion it has been supported since the original authorization 17 years ago.

HLC also supports the government funding a targeted buffer inventory. A June 2023 Brookings report proposing federal solutions to the GSI shortage recommends the Department of Health and Human Services purchase GSI products and hold a buffer inventory.⁵ Unlike an emergency stockpile, the buffer inventory would be held by a wholesaler and immediately disbursed when production is disrupted. Criteria to hold a drug in the buffer inventory would include lack of substitutes, unavailability would lead to immediate and significant adverse health outcomes, and vulnerable supply chains. Oncology GSIs meet each criterion. As a first step, we support an essential medicines stockpile pilot program which would cross reference with FDA's Essential Medicines list. HLC recommends transparency and close coordination with the private sector.

⁴The Impact of Drug Shortages on Children with Cancer—The Example of Mechlorethamine, *New England Journal of Medicine* (December 27, 2012), <https://www.nejm.org/doi/10.1056/NEJMp1212468>.

⁵Federal Policies to Address Persistent Generic Drug Shortages, Brookings' Hamilton Project (June 2023), www.brookings.edu/wp-content/uploads/2023/06/20230621_ES_THP_GSI_Report_Final.pdf.

Review and Enhance FDA Supply Chain Resilience Efforts

HLC supports the following policy solutions for Congress to bolster FDA supply chain resiliency efforts:

- **Build on recent FDA supply chain resiliency efforts.** Before creating new reporting requirements, we urge Congress to review and build upon recent efforts undertaken by the FDA. Recent measures include expedited reviews of new drug and biologics applications, expedited requests to facilitate expanded manufacturing capacity, and exercising regulatory flexibility and discretion to increase supplies of critically needed medications.⁶ Congress should expand these efforts by allowing the FDA to fast-track abbreviated new drug applications (ANDAs) and expedite manufacturing inspections and approvals for drugs facing a critical shortage.
- **Update the FDA Essential Medicines list.** HLC supports more transparency from the FDA regarding the process and data sources used to develop the FDA's Essential Medicines list. We urge the FDA to work with stakeholders, including group purchasing organizations (GPOs) and distributors, to update the Essential Medicines list and make use of other lists in shortage prevention efforts.
- **Fund incentives for generic manufacturers to meet quality management maturity (QMM).** We urge Congress to provide funding for the FDA to develop incentives for generic/biosimilar drug manufacturers to achieve QMM. These incentives should be developed with industry stakeholder input. Congress should also allow the FDA to share generic manufacturers' QMM-related information with various entities in the supply chain, including GPOs, distributors, and hospitals, to help inform purchasing and contracting decisions.

Support a Resilient Global Supply Chain

Global, diversified supply chains are important to enable a consistent response to external stressors, including natural disasters, health emergencies, or supplier disruptions. HLC supports the following three policy approaches to streamline global supply chain collaboration:

- (1) The free flow of goods to support robust business continuity processes, strong partnerships, and the ability to actively monitor end-to-end supply chain using digital tools;
- (2) Improved country-to-country global cooperation within supply chains to enhance resiliency and flexibility and reduce over-reliance on any one market for any aspect of manufacturing or supply; and
- (3) Accelerated adoption of Fourth Industrial Revolution technologies to digitalize supply chains, allowing for better information sharing and enabling better signals of disruption.

Provide Reimbursement Incentives

HLC suggests that Congress and the Centers for Medicare and Medicaid Services consider payment adjustments (*i.e.*, N95-like policy and/or add-on payments) for generic essential medications frequently in shortage, such as GSIs, where the manufacturer agrees to certain supply chain mitigation and resiliency requirements.

Thank you for your efforts to increase the drug supply chain resiliency. In the coming months, HLC plans to work with our diverse membership to continue to offer solutions on this important topic. We look forward to working with you on our shared priorities. If you have any questions, please do not hesitate to contact Debbie Witchey at (202) 449-3435 or dwitchey@hlc.org.

Sincerely,

Mary R. Grealy
President

⁶*Ibid.*

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December 19, 2023

The Honorable Ron Wyden
 Chairman
 Committee on Finance
 United States Senate
 Washington, DC 20510

The Honorable Mike Crapo
 Ranking Member
 Committee on Finance
 United States Senate
 Washington, DC 20510

Re: Statement for the Record on the Senate Finance Committee’s “Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective” Hearing on December 5, 2023

Dear Chairman Wyden and Ranking Member Crapo:

On behalf of the Healthcare Supply Chain Association (HSCA), which represents the nation’s leading healthcare group purchasing organizations (GPOs), we appreciate the opportunity to provide a statement for the record regarding the December 5, 2023, hearing on examining supply challenges, impacts, and policy solutions for drug shortages. HSCA supports your continued efforts to address this pressing problem, and we look forward to continuing to work with you to determine long-term solutions to prevent and mitigate drug shortages and preserve access to high-quality care.

Healthcare providers initially formed GPOs in the early 1900s as an efficient means to aggregate purchasing volume, drive competition among suppliers, and reduce healthcare costs. Today, traditional healthcare GPOs serve as the sourcing and contracting partners to hospitals, long-term care facilities, surgery centers, clinics, and other healthcare providers across the country. GPOs secure high-quality medical products at fair prices for the benefit of patients, providers, Medicare, Medicaid, and taxpayers. Both independent and industry funded studies (<https://www.supplychainassociation.org/wp-content/uploads/2019/05/HSCA-Group-Purchasing-Organizations-Report-FINAL.pdf>) confirm the effectiveness and tremendous value of GPOs, finding that GPOs deliver annual cost savings of 12–18%.^{1,2} GPOs allow smaller providers to obtain critical supplies at the same value as large providers while allowing all healthcare providers to focus on their core mission: providing first-class patient care.

The GPO Business Model and Value Proposition.

The GPO business model is voluntary, flexible, and clinically driven. We work in close collaboration with our member hospitals and healthcare providers to develop sourcing policies and contract award decisions. GPOs take a comprehensive approach to sourcing and contracting that not only accounts for the competitive price offered, but also the quality, reliability, and stability of supply. We recognize that market conditions change, and when they do, GPOs work with suppliers to adjust contracts. GPOs work diligently to ensure member hospitals and providers can select the products they need to care for their communities and patients most efficiently and provide clinical resources across their network of providers.

American hospitals are continuing to operate at razor thin margins and face an increasing number of closures, particularly among small and rural hospitals. GPOs allow these small and rural healthcare providers—who often lack the negotiating power to access competitive pricing for essential supplies—to take advantage of the same efficiencies and discounts as large providers, enabling them to focus on providing necessary care to their communities.

Health systems and independent physician offices often depend on GPOs for much more than their ability to collectively aggregate purchasing power. GPOs provide a range of services, including broad clinical feedback and providing supply chain ana-

¹Burns, Lawton R, and J Andrew Lee. “Hospital purchasing alliances: utilization, services, and performance.” *Health care management review* vol. 33, no. 3, 2008, pp. 203–15 2008: 203–15. doi:10.1097/01.HMR.0000324906.04025.33.

²Dobson, Allen, and Joan DaVanzo, “A 2018 Update of Cost Savings and Marketplace Analysis of the Health Care Group Purchasing Industry,” Dobson DaVanzo & Associates, LLC, Apr. 2019.

lytics, which are especially important in rural and underserved areas. Individual practices and community hospitals do not have the resources, scale, and expertise to perform themselves.

The Scope and Impact of Drug Shortages.

Drug shortages place significant strain on hospitals, health systems, healthcare providers, and their patients. In 2022, the University of Utah Drug Information Service (UUDIS) identified a total of 160 national drug shortages. This figure is likely an underestimate, however, as many shortages go unreported and may occur in smaller geographic areas. A survey of manufacturers by UUDIS offered insight into the causes of drug shortages. More than half of those surveyed (56%) either did not know the cause of the shortage or would not provide this information. Those manufacturers that did respond cited supply/demand (19%), manufacturing (18%), business decisions (5%), regulatory issues (1%), and raw material issues (1%) as reasons behind shortages.

The U.S. Food and Drug Administration (FDA) identifies manufacturing quality control issues as the primary cause of drug shortages, along with production delays, lack of raw materials, and manufacturer business decisions to discontinue products. HSCA and its member GPOs are committed to collaborating with healthcare providers and suppliers to bolster the resiliency of the healthcare supply chain and to ensure that patients and providers have consistent access to the drugs, products, and devices they need.

GPOs Take Steps to Prevent and Mitigate Drug Shortages.

Despite some limitations on existing data, GPOs track all available data on shortages and raw materials, including active pharmaceutical ingredients (API). GPOs track this data on a global scale to anticipate possible supply disruptions and to provide suppliers with notice to plan for production capability. GPOs also identify and help bring to market additional manufacturers of at-risk drugs, ensuring that there are auxiliary suppliers of essential medications and products.

GPOs routinely evaluate drug suppliers on the consistency of product availability, fill rates, recall frequency and management, disaster preparedness, secondary supply lines, and manufacturing transparency. GPOs recognize and reward quality while encouraging a healthy market, and when shortages do occur, GPOs identify and support alternative sources and clinically appropriate substitutes.

GPOs recognize the cost and impact of drug shortages on their member hospitals and the patients they serve, and we are leaders in working to prevent and mitigate drug shortages. Every HSCA member GPO has innovative programs that are operating effectively to prevent and minimize the impact of shortages. The GPO business model creates a vigorously competitive and healthy market among GPOs and suppliers, and competition among GPOs is essential to preventing drug shortages. Shortages are antithetical to the GPO model, as without sufficient products, suppliers, or competition, GPOs are unable to provide their services.

Given our unique line of sight into the healthcare supply chain, HSCA and its member GPOs respectfully offer the following recommendations and comments to the Committee:

Re: Proposed policy solutions to prevent and mitigate drug shortages.

We understand that solving the ongoing drug shortage crisis is a complex task. HSCA proposes the following recommendations to help prevent and mitigate drug shortages, several of which build on existing congressional authorities:

Investing in quality and building secondary supply lines. HSCA recommends incentivizing not just production, but also investment in quality and capacity, including the addition of secondary supply lines and having alternate or backup sources of API, to support long-term access to generic medications.

Creating incentives to increase domestic manufacturing. HSCA recommends that if Congress elects to create incentives related to domestic manufacturing that the incentives be tied to quality and the amount of product sold in the U.S. For incentives to tangibly impact pricing dynamics, they must align with the quality products being made and sold in the U.S.

Refine authority related to the Strategic National Stockpile's (SNS) ability to enter into vendor contracts. HSCA encourages congress to refine the authority pertaining to the Fiscal year Consolidated Appropriations Act (Pub. L. 117-328), which authorized the Strategic National Stockpile (SNS) to enter into contracts to

assist with the rotation of soon-to-be expired products so supply chain stakeholders can work collaboratively with agency officials to help identify when and where product should be released.

Maintain and/or require buffer inventory. To increase critical access to drugs, HSCA recommends that the federal government, through the Administration for Strategic Preparedness and Response (ASPR) and SNS, create, maintain, and/or require buffer inventory for critical medications and devices.

Increasing transparency. HSCA recommends transparency regarding buffer inventories and that input from GPOs and other private industry stakeholders be used to determine which drugs, and if possible, which products, should be considered for buffer inventory.

Fund and implement FDA's Quality Management Maturity (QMM) program. HSCA recommends that Congress fully fund FDA's quality management maturity (QMM) program and require manufacturer participation and implementation as soon as possible. HSCA further recommends that FDA share its QMM ratings with appropriate supply chain stakeholders, including GPOs, to best inform purchasing decisions.

Increase ongoing visibility into manufacturing locations and API sources. HSCA recommends that manufacturers be required to include on their package inserts and boxes the finished product manufacturing location, including for contract manufacturers, and API source(s) on all products.

Increasing facility inspections. HSCA recommends that Congress increase funding for and encourage the FDA to increase the number of inspections. HSCA further recommends that Congress encourage FDA to begin unannounced foreign inspections for API supplies and drug product manufacturers.

Re: Consolidation among Group Purchasing Organizations (GPOs).

It is important to recognize that traditional healthcare GPOs are distinct entities from pharmacy benefit managers (PBMs), PBM rebate aggregators, and large retail buying groups such as wholesalers/distributors. Traditional provider-aligned healthcare GPOs serve healthcare providers, are fully transparent with their healthcare provider members, do not take title to product, do not participate in the Medicare Part D prescription drug program, and are net-price driven. GPOs negotiate point-of-sale price reductions, and any rebates members earn on their purchases are passed entirely through to them. Flexibility for providers and suppliers is integral to the GPO business model, and actual purchases are made by GPO member providers, not GPOs.

The interests of GPOs are completely aligned with their healthcare provider members, and some GPOs are owned by providers. Pharmacy benefit managers work primarily in the retail prescription market with health insurance and plan sponsors, and PBM-operated "GPOs" aggregate rebates. Pharmaceutical wholesalers/distributors—known as "buying groups"—also aggregate purchasing and compete in the drug supply market, but they do purchase and take possession of products and are not subject to the transparency requirements of traditional provider-aligned healthcare GPOs. GPOs operate in a vigorously competitive market and competition among GPOs is essential to preventing and mitigating drug shortages.

Additionally, it is worth noting that the statistic about GPO market share that Dr. Hernandez referenced in her written testimony is inaccurate and is sourced incorrectly.^{3,4} We believe the original source for this statistic actually refers to the market share of drug wholesalers, and not GPOs. There are hundreds of traditional healthcare GPOs in the United States. Definitive Healthcare reports data on 150 GPOs, which is likely a conservative estimate. Eighty of them are considered regional GPOs, or "regional purchasing coalitions," and 70 are national GPOs. The market share percentage of total spend through the contract portfolios of the seven largest GPOs in 2020 was between 54.1% and 60.5%, while the share of the three largest GPOs was 41.5%.

Many healthcare providers maintain membership with more than one GPO at a time and can shift their purchasing from one GPO contract portfolio to another.

³Bruhn, William E., et al. "Group Purchasing Organizations, Health Care Costs, and Drug Shortages." *JAMA*, vol. 320, no. 18, 13 Nov. 2018, p. 1859, <https://doi.org/10.1001/jama.2018.13604>.

⁴Drug Shortages Task Force. "Drug Shortages: Root Causes and Potential Solutions." U.S. Food and Drug Administration, Oct. 2019.

GPO contracts with healthcare providers are voluntary, and providers can shift to new areas, customers, or product focus, which helps maintain vigorous competition among GPOs. GPOs help create a fair, open, and competitive marketplace and compete for business on a variety of factors including, but not limited to, supplier product pricing, strength of supplier contract terms, breadth of contract portfolio, supply chain and clinical analytical assistance, and customer service.

We appreciate the opportunity to provide you with our comments and recommendations and appreciate the subcommittee's willingness to learn about the GPO industry, our role in the healthcare supply chain, and how we work to prevent and mitigate drug shortages. We look forward to continuing to serve as a resource to Congress and all stakeholders as we all work to continue improving the healthcare system.

Please do not hesitate to contact me directly if HSCA can be a resource on this issue moving forward. I can be reached at (202) 629-5833 and tebert@supplychainassociation.org.

Sincerely,
Todd Ebert, R. Ph.
President & CEO

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**Statement for the Record of Phillip L. Zweig, MBA,
Executive Director/Co-founder**

Senate Finance Committee Hearing: "Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective"

Thank you for the opportunity to comment on the cause, impact, and solution to the decades-long artificial shortages and inflated prices of essential generic drugs, mostly sterile injectables. These mainstay medications include lifesaving cancer drugs, antibiotics, anesthetics, nutritional IV fluids, even sterile saline (salt water) and dextrose solution (sugar water). My comments also apply to the deadly shortages of N95 masks, gowns, gloves and other personal protection equipment (PPE) and medical supplies during the pandemic. To put it bluntly, Congress created this travesty, and it's up to Congress to fix it. More on that later.

First, some background. I'm a financial journalist (former *American Banker*, *Wall Street Journal*, *Bloomberg*, *BusinessWeek* etc.) and national best-selling author turned patient advocate. In October 2012, I co-founded Physicians Against Drug Shortages Inc. (PADS), a pro bono patient advocacy group, with seven anesthesiologists who were outraged that they couldn't get propofol and other drugs that they needed to put their patients to sleep, but they didn't understand why. I did. Since then, I've served as unpaid executive director. Our mission is to expose and address the real root cause of the shortages: the exhaustively documented anticompetitive contracting and pricing practices, self-dealing, conflicts of interest, "legalized" kickbacks and "share backs" of giant hospital group purchasing organizations (GPOs).

My PADS colleagues and I have written numerous articles and have submitted countless comments on drug shortages and the misbegotten GPO anti-kickback safe harbor in response to requests by the FDA, the HHS Office of Inspector General (OIG), and the Federal Trade Commission (FTC) and congressional committees—obviously to little effect. We've also been quoted widely on this issue in health care publications. For an overview, read our op-eds in *The New York Times* of Sept. 3, 2013 ("How a Cabal Keeps Generics Scarce")¹ and *The Wall Street Journal* of May 8, 2018 ("Where Does the Law Against Kickbacks Not Apply? Your Hospital")². More recently, we worked closely with 60 Minutes³ on a May 22, 2022 segment examined how these predatory middlemen caused shortages of lifesaving chemo agents by demanding that suppliers pay them huge "fees" (aka kickbacks) in return for ac-

¹ <http://www.nytimes.com/2013/09/03/opinion/how-a-cabal-keeps-generics-scarce.html?module=Search&mabReward=relbias:r.%7B%221%22:%22R1:6%22%7D>.

² <https://nebula.wsimg.com/fe4916f65b3cd1d2e8052ee95960260a?AccessKeyId=62BC662C928C06F7384C&disposition=0&alloworigin=1>.

³ <https://www.youtube.com/watch?v=0VdEFWq1P0I&t=48s>.

cess to their member hospitals. PADS Chair Mitch Goldstein M.D. MBA was featured in the program, entitled “In Short Supply.” Three days later, in his testimony on the baby formula shortages before the House Energy and Commerce Committee, FDA Commissioner Robert Califf M.D. repeatedly urged members to watch it. He has testified that to end this crisis we must address the underlying economics. In recent speeches, he’s pointed the finger directly at GPOs.

On November 22, 2022, our coalition of nine advocacy groups, including the American Economic Liberties Project, PADS, and Public Citizen sent a letter to FTC Chair Lina Khan (<https://www.economicliberties.us/press-release/advocates-urge-the-ftc-to-investigate-gpos-impacts-on-drug-medical-equipment-shortages-and-rising-healthcare-costs/>) urging the agency to conduct an investigation into the role of GPOs in causing the shortages and inflating prices.

On October 31, 2011, when President Obama announced his executive order to the FDA to end the drug shortage crisis, I was unaware that there was one, but I knew what had caused it. As an editor at *BusinessWeek*, I had initiated and co-written the first article, entitled “Locked Out of the Hospital”⁴ (3/16/98) on how GPOs block entrepreneurial medical device companies that made innovative and often cheaper devices from marketing them to thousands of hospitals. About 18 months later, the CEO of the company that was Exhibit A in the article asked me if I would consider taking a sabbatical from journalism to try to reform this corrupt system. I agreed, and soon began working with 60 Minutes⁵ on a segment with legendary correspondent Mike Wallace, entitled “Needles,” on how these practices denied health care workers safer syringes and other “sharps” devices. Producer Walt Bogdanich, now a three-time Pulitzer Prize winner, then accepted a job as an investigative editor at *The New York Times* and launched a year-long series on GPO abuses that won a prestigious George Polk award. The entire series is posted on the “Media Reports” page of our website, www.physiciansagainstdrugshortages.com.

The media coverage focused primarily on anticompetitive GPO practices that undermine competition, innovation, and patient care in the entrepreneurial medical device sector. But one article in the *Times* of March 26, 2002, entitled “When a Buyer for Hospitals Has a Stake in the Drugs It Buys”⁶ foretold the destruction GPOs would wreak on the generic drug industry, patients, clinicians, and our healthcare system generally. It revealed how Premier Inc., now the second largest GPO, had begun to seize control of the generic drug business by co-founding American Pharmaceutical Partners and taking it public in late 2001. According to the *Times*, Premier transformed a \$100 investment in 1996 into shares valued at \$46 million, enabling at least two Premier executives with stock options to hit the jackpot. Sen. Herb Kohl (D-WI), then chairman of the Senate Antitrust Subcommittee, called this arrangement “scandalous” and forced Premier to divest its stake in APP.

This coverage resulted in four Senate Antitrust Subcommittee hearings on GPO abuses from 2002 to 2006; federal and state investigations, including a Justice Department criminal investigation of Novation (since renamed Vizient), which ended without charges; multiple successful antitrust lawsuits filed by medical device entrepreneurs against GPOs and/or their dominant supplier partners; independent research; a book by S. Prakash Sethi, a university distinguished professor at the Zicklin School of Business, Baruch College [“Group Purchasing Organizations: An Undisclosed Scandal in the U.S. Healthcare Industry,” Palgrave/MacMillan 2009], and even a barely fictionalized 2011 feature film, *PUNCTURE*, starring Captain America’s Chris Evans.

The original and sole purpose of GPOs was to save hospitals money by purchasing supplies in bulk. The first one was founded in 1910 when several New York City hospitals, including Bellevue, banded together to form a nonprofit co-op. Member hospitals paid dues to cover salaries, rent, and other administrative expenses. By all accounts, this worked fine for more than 80 years.

But Congress couldn’t allow a terrific idea like that to continue. In 1987, at the behest of hospital lobbyists, Congress enacted what became known as the Medicare anti-kickback “safe harbor,” which exempted GPOs from criminal prosecution for taking kickbacks from suppliers. Lobbyists claimed that GPOs would somehow save more money if suppliers paid the fees. What’s more, they argued that since sup-

⁴ <https://nebula.wsimg.com/81a188a2312890198579e3ce8a24332c?AccessKeyId=62BC662C928C06F7384C&disposition=0&alloworigin=1>.

⁵ <https://www.youtube.com/watch?v=E1fTC2djVmk>.

⁶ <https://www.nytimes.com/2002/03/26/business/when-a-buyer-for-hospitals-has-a-stake-in-drugs-it-buys.html>.

pliers were already paying illegal kickbacks, why not just “legalize” them? This amendment to the Social Security Act upended the entire supply chain, creating perverse incentives that led to higher, not lower, prices for hospital goods. That’s because GPO kickbacks are calculated based on price times volume purchased. Congress awarded GPOs a “Get Out of Jail Free Card,” becoming the only industry we know of that has received such a gift. It is no coincidence that the generic drug industry is also the only industry we’re aware of that has experienced debilitating chronic shortages in the post-WWII economy. Any freshman economics student knows that we’re simply not supposed to have shortages in what is otherwise a market economy. But the GPOs have turned our drug and health supply industries into a vestige of the disgraced ex-Soviet economy. They are the oligarchs of American health care.

The HHS OIG was designated to write and monitor the safe harbor rules, which it issued July 29, 1991. The rules called for a “soft cap” of 3% for “admin fees” and authorized the OIG to request data on fees that exceeded this amount. The GPOs, however, cleverly circumvented this cap by inventing other fees: advance, conversion, licensing, marketing fees, even fees to sit next to a GPO contracting officer at dinner. The unsafe “safe harbor” transformed the GPO business model from non-profit cooperatives that saved hospitals money to predatory middlemen that exist only to make money for top GPO insiders and executives of major GPO shareholder hospitals. They make their money by literally selling market share, in the form of sole-source contracts, for outrageous fees to the highest bidder. According to Novation “Excess Fee Reports,”⁷ which were obtained in discovery in a 2003 federal whistleblower lawsuit, these fees have often amounted to double digits and sometimes more than half of a company’s total revenue for a single drug. GPOs perform no medically, socially or financially useful function. They are nothing more than a sophisticated “pay-to-play” scheme—a “legalized” fraud.

The analysis is actually quite simple. GPO middlemen, who do nothing but award exclusionary contracts, are making all the money, while the companies that actually produce the drugs are closing shop. There is something terribly wrong with this picture. Compare, for example, the 2019 financial statements (SEC 10K) and seven-figure executive compensation of publicly-held Premier Inc. [PINC] with those of Akorn Pharmaceuticals, which filed for bankruptcy under Chapter 7 in February after more than 50 years manufacturing prescription ophthalmic drugs and other essential medications, exacerbating existing shortages.

One document that was obtained by plaintiffs in an ongoing antitrust lawsuit against Vizient tells the whole story. Incredibly, Vizient’s marketing material boasts that one of the services it offers contracted suppliers is “Protection from Competitive Threats and Rebidding!” [exclamation point added].

What’s more, there is virtually no disclosure, transparency, oversight or regulation of this powerful industry. Today, three giant companies—Vizient (formerly Novation), publicly-held Premier Inc., and HealthTrustPG—control purchasing for about 90% of an estimated \$300 billion in annual GPO contract volume. Nearly half of the amount is for drugs and supplies for patients covered by Medicare, Medicaid, and other government health care programs. The OIG is ostensibly responsible for overseeing the safe harbor. But it has proven to be a paper tiger. For example, it is authorized to request data on excess GPO “fees” from GPOs, but to the best of our knowledge, it has never done so. This was underscored in a March 30, 2012 GAO report entitled “Group Purchasing Organizations: Federal Oversight and Self-Regulation.”⁸

In 2005, Senators Kohl and Mike DeWine (R–OH), who presided over four hearings, from 2002 to 2006, on GPO abuses, drafted a bipartisan bill, called the “Ensuring Competition in Hospital Purchasing Act,”⁹ that would have restored free, fair and open competition to the supply chain by repealing the ill-conceived safe harbor. But it died in the Subcommittee because of fierce opposition by the GPO and hospital industries. We later learned why the American Hospital Association and state hospital associations opposed it: CEOs of certain major GPO shareholder facilities get a piece of the action, in the form of six to seven figure “share backs” or “equity dis-

⁷ <https://nebula.wsimg.com/c15ea9a527af70ceaaaf434f3cd3ce0e?AccessKeyId=62BC662C928C06F7384C&disposition=0&alloworigin=1>.

⁸ <https://www.gao.gov/products/gao-12-399r>.

⁹ <https://nebula.wsimg.com/a862289b485f16554cfb4f8d8567221a?AccessKeyId=62BC662C928C06F7384C&disposition=0&alloworigin=1>.

tributions.” I would be pleased to provide documentation, with names and dollar amounts, on request.

If the safe harbor had been repealed in 2005, the drug shortage crisis that triggered President Obama’s executive order would not have happened. Contrary to statements by GPO industry executives, repeal would not have eliminated GPOs. It would only have ended the perverse GPO “pay-to-play” system. With generic drug makers foundering or exiting the business at a rapid clip, it would make domestic production of generic drugs financially viable again. Tax breaks, government subsidies, low interest loans, various convoluted and unworkable quality rating systems, or a federal takeover of the generic drug business, as some members of Congress have proposed, are not the answer. They would be a total waste of taxpayers’ money.

Besides creating chronic shortages, GPOs have inflated prices of drugs and other hospital goods by at least 30%, or upwards of \$100 *billion* annually. While they and their cohorts claim that they save hospitals billions, the only documentation they can present are bogus “sponsored research studies” produced by ethically-challenged academics and consultants. Over the years, at least three government studies have found that there isn’t a single shred of independent evidence that they save hospitals a dime. They include:

- *GAO pilot study of April 30, 2002*¹⁰ that found that prices of certain devices purchased through GPO contracts were often up to 39% higher than when they were bought off-contract.
- *May 2, 2003 letter from Senators Kohl and DeWine*¹¹ to Secretary of Defense Donald Rumsfeld, advising him against hiring a GPO to purchase medical supplies for the military.
- *2010 Senate Finance Committee*¹² Minority Staff Report requested by Sen. Chuck Grassley.
- In 2021, I reviewed all of the available empirical and anecdotal evidence on GPO pricing over more than 20 years and concluded that they actually inflate prices of supplies by at least 30%, or roughly \$100 billion annually. My analysis is attached. Some well-informed supply chain practitioners have told me that my estimate is too low. Competition reduces prices. Cartels inflate them.

Since 2011, when drug shortages became page one news, the GPO industry and their proxies have disseminated various bogus explanations for the shortages, all of which have been thoroughly discredited by government or other independent researchers. Their basic mantra is that the causes are “complex and multifactorial,” or a “perfect storm.” This is absolute nonsense. There is a cause and a solution: repeal of the safe harbor. Other bogus GPO explanations appear below:

- **Alleged “price-gouging, gray market” drug distribution companies.** These are mostly small to mid-sized “mom and pop” firms that provide smaller quantities of essential drugs to physicians, hospitals and other medical facilities, often in emergencies or on weekends. They perform a perfectly legitimate market function. But they can’t compete on price with the “Big Three” GPO-authorized distributors, notably McKesson, Amerisource Bergen, and Cardinal, because they’re not permitted to get “chargebacks” from GPO contracted suppliers. Premier Inc. demonized them in a bogus August 2011 report. The FBI investigated and found no wrongdoing, as reported in the inaugural February 10, 2014 GAO report on drug shortages, which was mandated by the Food and Drug Administration Safety and Innovation Act of 2012. That report identified GPOs as a potential “underlying cause.” It concluded correctly that manufacturing and quality problems and other issues were secondary or intermediate causes. [For more on GPO pricing, read “Connecting the Dots”¹³ of January 4, 2012, a white paper by drug distribution consultant Pat Earl and me.]
- **340B Program and Medicaid Rebates.** Another red herring. In a normal market, suppliers would be able to incorporate regulatory requirements into

¹⁰ <https://www.gao.gov/products/gao-02-690t>.

¹¹ <https://nebula.usimg.com/2c05bf026ed6c9ae9cd03339d59efe78?AccessKeyId=62BC662C928C06F7384C&disposition=0&alloworigin=1>.

¹² <https://nebula.usimg.com/32ce499df16ad66aede1ee5b4ed7d2a0?AccessKeyId=62BC662C928C06F7384C&disposition=0&alloworigin=1>.

¹³ <https://nebula.usimg.com/fbedc9449e9b7c932054548798378f8a?AccessKeyId=62BC662C928C06F7384C&disposition=0&alloworigin=1>.

their prices. But the pharmaceutical and medical goods supply chain is a rigged market.

- **Overzealous FDA inspections.** I began to hear this in late 2011 around the time Bedford, OH-based Ben Venue Laboratories shuttered, causing acute shortages of methotrexate and other chemo drugs. The FDA inspection report suggests otherwise. Inspectors even found a 10 gallon bucket of urine near the production area. According to an expert in sterile drug production, this was a cost-saving measure that was intended to reduce the time workers needed to de-gown, do their business, re-gown, scrub back in and return to the production area. In a LinkedIn search, I located someone familiar with Ben Venue's collapse and the FDA inspection. Fearing retribution, this person initially declined to speak with me. I asked this individual to answer just one question: Were these allegations against the FDA true? This person, who requested anonymity, said, "Absolutely not. They were professionals. They did their job." Some of the cancer meds that had been manufactured for years by Ben Venue were later made by a troubled plant in China.
- **Change in the Medicare reimbursement formula from wholesale acquisition cost (WAC) to average sales price (ASP) plus 6%** under the Medicare Modernization Act of 2003. Former HHS Assistant Secretary Sherry Glied Ph.D., who had conducted a formal study on this issue, walked me through it in person after she left office. The Medicare reimbursement formula has nothing to do with drug shortages, she explained, because it doesn't affect monies received by suppliers. And contrary to popular belief, Medicare reimbursement prices weren't subject to price controls. She explained that in a December 23, 2014 letter to the editor of the *Journal of Oncology Practice*.
- **FDA backlog in approving generic drug applications.** Yes, there was a backlog in applications. But as a 2016 study by the Center for American Progress found, very few of those applications were for drugs in short supply. They were scarce because drug makers couldn't earn a reasonable profit and stopped making them.
- **Just-in-time inventory practices.** Totally false and illogical. A red herring. Just-in-time inventory works when supply is adequate and reliable, but no supplier would continue to use this practice for drugs in short supply.
- **Hurricane Maria.** When the hurricane devastated Puerto Rico in September 2017, Baxter's plants, which produced sterile saline and other critical drugs, were heavily damaged. So the GPOs blamed the shortages on Maria. However, for several years before Maria the U.S. Had been importing sterile saline from Spain, Germany and Norway. Afterwards, the U.S. had to import it from several additional countries. The real reason: sole-source contracts. In fact, in 2007 Baxter boasted in a press release about its sole-source Novation (now Vizient) contract, attached. For more on this, see the chapter on GPOs in *MONOPOLIZED*,¹⁴ a 2020 book by *American Prospect* editor in chief David Dayen.
- **COVID-19.** The pandemic gave GPOs a convenient alibi for shortages of many drugs and supplies, including N95 masks. To be sure, COVID exacerbated drug shortages. But the GPOs caused the shortages of N95 masks and other PPE. In a remarkably prescient October 4, 2008 article in *Infection Control Today*,¹⁵ Mike Bowen, EVP of Prestige Ameritech, a small Texas mask maker, was quoted as saying that the U.S. wouldn't be prepared for a future pandemic because of the GPO "chokehold" on the medical supplies industry.
- **"Race to the Bottom"** in pricing. This is a catchy but misleading buzz phrase. It suggests that the "low prices" received by drug makers are real prices. They're rigged prices. Real prices adjust according to the law of supply and demand. But the GPOs have undermined this immutable principle. In fact, the outrageous kickbacks GPOs have extorted from generic drug makers have made this business a money-losing proposition.

I should add here that while the number of big GPOs has consolidated from more than six in the late 1990s to the "Big Three," the primary problem is the corrupt "pay-to-play" business model. I'm all in favor of breaking up the "Big Three," but that would have to be accompanied by repeal of the safe harbor.

¹⁴ <https://prospect.org/culture/books/monopolies-are-why-salt-and-water-in-a-bag-became-scarce-dayen-monopolized-book/>.

¹⁵ <https://www.infectioncontroltoday.com/view/us-pandemic-could-severely-strain-face-mask-other-ppe-supply-pipeline>.

The GPO industry exists only because of its highly aggressive lobbying and PR activities. They have literally bought the silence or active support of medical “thought leaders,” former top federal officials, academics, even medical societies and prominent media personalities. They include former FDA Commissioner Scott Gottlieb M.D. In 2018, he told the Associated Press of July 12 2018,¹⁶ that GPOs had caused the shortages. Then after he left office, he went silent on the GPO issue. He also became a speaker, presumably well-compensated, at an elaborate Vizient conference. For the details, see “Buckraking”¹⁷ by Matt Stoller, research director of the American Economic Liberties Project, a respected anti-monopoly think tank.

By far the most visible GPO hired gun is so-called “drug shortage expert” Erin Fox, D.Pharm, who collects data on shortages as director of the University of Utah Drug Information Service (UUDIS). I was well-aware of her conflicts of interest with the GPO industry, notably Vizient. In October 2017, we had a conference call with FTC staff who were organizing a November 8 conference on drug market competition. They denied our request to participate as panelists, saying that the speakers had already been selected. They declined to name names, but they did tell us the occupations that would be represented, including a pharmacist. “Erin Fox?” I asked. There was stone silence at the other end of the line. I then enumerated her conflicts of interest. She’s a lobbyist, PR spokesperson, and consultant to Vizient, and an employee of the University of Utah Medical Center, a major Vizient shareholder facility. She has persistently denied, at least in interviews and public forums that GPOs have anything at all to do with drug shortages, when in fact they have everything to do with drug shortages. FTC staff apparently prevailed on her to disclose these conflicts at the conference. Here’s my recent LinkedIn post on her conflicts: <https://www.linkedin.com/in/phillip-l-zweig-491ba83/recent-activity/all/>.

So we were appalled when she appeared as the lead witness in the March 22, 2023 Senate Homeland Security and Governmental Affairs hearing on the national security implications of drug shortages.

Those they can’t buy, including PADS, they’ve harassed and even threatened. In 2018, someone presumably affiliated with the GPO industry hired a bogus “investigative” outfit called “Checks and Balances” to try to intimidate me and certain physician members. His targets were mostly PADS doctors who practiced at academic medical centers and had written negative articles about GPOs. Its principal, Scott Peterson, a former Wall Street PR rep, sent letters to the heads of their schools or hospitals falsely alleging egregious conflicts of interest. Nothing came of the resulting “investigations,” but our members wasted precious clinical and research time responding to these unfounded charges.

In late 2018, after the November 27, 2018 FDA conference on drug shortages, Peterson posted this item about my actions at the all-day meeting: <https://checksandbalancesproject.org/philip-zweig-disrupts-health-policy-forum/>. He accused me of disrupting the meeting with my persistent commentary on GPOs from the floor during the Q&A. To that I plead guilty.

Everyone who works in the health care supply chain knows that it is broken, and they know why it’s broken and who broke it: Predatory GPO middlemen. So do members of Congress, including members of the Senate Finance Committee. Some of the same committee members who attended the December 5, 2023 hearing were present at the first one on December 7, 2011, almost *exactly 12 years earlier*. It’s high time that members of Congress worked up a fit of courage and ended the kick-backs (aka bribes, payola etc) and “share backs” (dividends, patronage fees, rebates) by repealing the unsafe safe harbor.

Please feel free to contact me if you have any questions or would like to discuss this urgent issue further.

FULL DISCLOSURE: PADS and I have no financial conflicts of interest. We have no budget and cover expenses out of our own pockets.

¹⁶ <https://apnews.com/998a244e3ac849b787bcd3c893eb6806>.

¹⁷ https://mattstoller.substack.com/p/buckraking-did-a-medical-monopolist?utm_source=substack&utm_medium=email&utm_content=share.

SOCIETY OF GYNECOLOGIC ONCOLOGY

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The Society of Gynecologic Oncology (SGO) applauds the Senate Committee on Finance for holding the recent legislative hearing, *Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Perspective*. Our members and their patients have been profoundly affected by the recent chemotherapy shortages, and SGO has been actively engaged in finding policy solutions to prevent future shortages and welcome the opportunity to work with the committee to address this issue.

SGO is the premier medical specialty society for healthcare professionals trained in the comprehensive management of gynecologic cancers. Our more than 2,800 members include physicians, advanced practice providers, nurses, and patient advocates who collaborate with the Foundation for Women's Cancer to increase public awareness of gynecologic cancers and improve the care of those diagnosed with gynecologic cancers. Our primary mission focuses on supporting research, disseminating knowledge, raising the standards of practice in the prevention and treatment of gynecologic malignancies, and collaborating with other organizations dedicated to gynecologic cancers and related fields, all with the ultimate vision of eradicating gynecologic cancers.

Scope of the Problem

As you know, this year we faced one of the worst chemotherapy drug shortages in the country's history, with 15 indispensable chemotherapy drugs in short supply simultaneously. Carboplatin and cisplatin, which are both generic, sterile injectable drugs and have been in shortage since mid-February 2023, are first-line therapies for ovarian, endometrial, and cervical cancers. Carboplatin serves as a backbone drug for most gynecologic cancer therapies. At the peak of the shortages earlier this year, SGO estimated that over 500,000 patients were affected by chemotherapy drug shortages. Moreover, although the data is not yet available, we believe that individuals in marginalized communities and rural areas have likely borne the brunt of the impact caused by drug shortages, and we are currently evaluating if the chemotherapy shortages have negatively affected survival outcomes for people with gynecologic cancers. The bottom line is that patients deserve better than having to wonder whether they will have access to standard of care cancer treatments.

Legislative Solutions

Since the onset of the shortages, SGO has been working with policymakers and other stakeholders to mitigate the current shortages and prevent future shortages. Over a decade ago, we witnessed a similar shortage of generic chemotherapies. Patients with cancer deserve better and must not be subjected to the unnecessary uncertainty regarding the availability of standard of care therapies. Therefore, we recommend that a comprehensive legislative solution be developed to avoid future shortages and include the following components.

Provide incentives to realign hospital purchasing practices to promote the purchase of high-quality generic drugs:

Currently, hospitals purchase drugs from group purchasing organizations (GPOs), pharmacy benefit managers (PBMs), and entities that provide the lowest prices because there are no incentives for purchasing drugs from more reliable manufacturers at higher prices. The information from Quality Management Maturity (QMM) and Risk Management Programs (RMPs) programs discussed below could be used to inform standards and best practices for contracts with GPOs and PBMs and allow the Centers for Medicare & Medicaid Services (CMS) to establish a voluntary reporting system that would include financial rewards for purchasing drugs from manufacturers with more resilient supply chains. Dr. Marta Wosińska from the Brookings Institution discussed this concept in detail at the recent hearing as well as in the recent article titled "Federal Policies to Address Drug Shortages."¹ We believe this policy would empower hospitals to be informed consumers of essential medicines, providing a concrete benefit to the patients they treat.

Additionally, authorized tax incentives, grants, and loans will encourage the manufacturing of generic drugs and required active pharmaceutical ingredients as part

¹ <https://www.brookings.edu/articles/federal-policies-to-address-persistent-generic-drug-shortages/>

of more resilient supply chains. The increased funds will allow generic manufacturers to invest in new facilities and expand existing operations, adopt newer innovations, and ultimately improve the redundancy in their manufacturing processes; the lack of investment in generic drug manufacturing and the supply chain are key drivers of the current shortage. As drug shortages are often caused by quality issues at manufacturing facilities, these incentives should be conditioned upon achievement of quality and supply chain resilience metrics such as Food and Drug Administration's (FDA) QMM program.

Authorize and appropriate funding for the FDA's quality management maturity (QMM) program:

SGO believes that a robust QMM program, regulated by the FDA's Center for Drug Evaluation and Research, is critical to supporting resilient supply chains and preventing future drug shortages, particularly for generic chemotherapies. QMM is the state attained when drug manufacturers have consistent, reliable, and robust business processes to achieve quality objectives and promote continual improvement; through a QMM program, assessments would be conducted to support manufacturers' achieving higher levels of QMM by integrating high quality practices and technological advancements to optimize manufacturing process performance and product quality, enhance supply chain reliability, and foster proactive continual improvement. We agree with the FDA that the root cause for many drug shortages is the absence of incentives for manufacturers to strive for more than simply meeting current good manufacturing practice regulations and to develop mature quality management systems.

The QMM rating system will help incentivize manufacturers to attain higher levels of QMM at their facilities and address many issues we faced during the most recent chemotherapy shortage. Currently, the only information available to purchasers is the price of drugs. Absent any additional information, purchasers do not have a rationale to purchase a drug with a higher price if the same drug is available elsewhere at a lower price. A voluntary QMM program would provide purchasers with helpful additional information with which to guide their purchasing decisions. A purchaser could, for example, justify paying more for a drug if the manufacturer is part of a QMM program instead of paying less for a drug whose manufacturer is not part of a QMM program with the expectation that the product from the QMM manufacturer would be less likely to go into shortage or have history of contamination or recall.

Additionally, a QMM program would emphasize the importance of high-quality drug production and quality control measures, which would minimize the risk of shortages caused by operational inefficiencies or lapses in quality control. We believe that this is particularly important for the manufacture of generic drugs. Lack of transparency related to drug shortages also would be addressed by the QMM program. The FDA, hospitals, and providers would be able to better anticipate shortages and develop rapid guidelines to optimize drug supply, including strategies such as dose reduction, identification of alternative therapies with similar efficacy, and the initiation of pharmacy drug preservation protocols. This enhanced transparency would ensure a more agile response to potential shortages, mitigating the impact on patients.

Establish a Drug Supply Chain Reliability (DSCR) Program

Once a QMM program is established, the SGO recommends piloting a product-level DSCR program, which should be established and led by an independent third party. This pilot should be overseen by the Department of Health and Human Services Supply Chain Resilience and Shortage Coordinator and other federal agencies. This program would include drug shortage prevention factors like backup raw material suppliers, manufacturing flexibilities and redundancies, inventory buffers, domestic and nearshore manufacturing capabilities, and risk management plans. This information would enable product-specific assessments that would help prevent shortages and inform drug purchasers.

Support and appropriate funding for inspection of RMPs for high-priority essential generic medicines, including rating the strength of the RMP, like the FDA assigns a site status after site inspections:

The FDA already has guidance on RMPs, which are designed to prevent drug shortages, but a more robust RMP would provide drug purchasers with meaningful evaluations of manufacturers' practices so they could purchase drugs from companies that invest in their supply chains. This, in turn, would encourage manufacturers to invest in and prioritize improvements of their supply chain practices. Given the

shortages stemming from issues with generic manufacturers, an enhanced program should focus on these manufacturers. This attention would involve more rigorous inspections, ensuring that these manufacturers adhere to the highest standards of quality control and supply chain management.

Additional Recommendations

Establishing and Maintaining a Stockpile of Chemotherapies

The SGO supports the establishment of a government funded stockpile that is strategically maintained by the Administration for Strategic Preparedness and Response to address potential disruptions in the supply chain of chemotherapies and other essential medicines. However, if Congress mandates this, it is crucial that there is an allocation mechanism in place to ensure that small and rural community hospitals that may be least equipped to navigate the market during shortages are able to treat their patients without forcing them to travel to larger hospitals and academic medical centers. During the current chemotherapy shortages, we have witnessed that some institutions have been more capable of maintaining supply than others placing additional burden on patients.

Additionally, it is important to note that chemotherapies are currently missing from most essential medicines lists. Prior to acquiring a stockpile of essential medicines, these lists must be updated by closely determining which drugs are most essential and vulnerable to shortage. Additionally, SGO recommends that if a stockpile of chemotherapy drugs or other essential medicines were to be established, it should not be implemented until the current shortages are resolved completely.

Thank you again for the opportunity to submit this statement and for your commitment to addressing this issue. SGO looks forward to working with you to develop a comprehensive, bipartisan solution to this complex issue to ensure patients have timely access to the required medications.

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December 6, 2023

Senate Committee on Finance
219 Dirksen Senate Office Building
Washington, DC 20510

Written Testimony for Hearing: “Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective,” December 5, 2023

Dear Chairman Wyden and Ranking Member Crapo:

Thank you for holding a hearing on the important and timely issue of drug shortages. STAG Pharma is an experienced 503B Pharmaceutical Outsourcing Facility, leading a new generation of sterile-injectable medical preparations. Based in Colorado and Ohio, our facilities have been built from the ground up to comply specifically with the rigorous Current Good Manufacturing Practices set by the Food and Drug Administration. Our goal is to anticipate the needs for and develop injectable medical treatments to avoid severe domestic drug shortages. We have already contributed to the critical shortage in the production of Albuterol for children in respiratory distress, concentrated Electrolytes to provide life sustaining nutrition in newborns and infants, and lifesaving medication for hemophilia patients through our work with the National Hemophilia Foundation. STAG will be looking to expand our product offering next year to meet the ongoing shortages in life-saving oncology treatments. For many pediatric and adult hospital systems, STAG Pharma is the only solution for shortage medications. Our facilities are built to be flexible and offer a readily available manufacturing capacity on domestic soil that can address drug shortages. We are currently expanding our Columbus OH facility which will create an additional 125,000 sq. ft. of manufacturing space to address drug shortages here in the U.S.

We were heartened to learn about President Biden’s November 27th Executive Order, which invokes the Defense Production Act to make more essential medicines in America and mitigate drug shortages. It also emphasizes the importance of do-

mestic manufacturing of essential treatments, broadening the authority and available funding within the U.S. Department of Health and Human Services (HHS). We view these as critical steps forward in the effort to ensure a strengthened supply chain to advance public health. The Committee should continue to encourage the Administration to fund public-private partnerships with the goal of eliminating domestic drug shortages, particularly within ASPR–BARDA and ARPA–H.

As you know, drug shortages of any kind can significantly impact patient care and public health. According to a recent report¹ by the Senate Committee on Homeland Security and Governmental Affairs, drug shortages increased by almost 30% between 2021 and 2022, reaching a 5-year high with 295 active shortages at the end of 2022. Currently, STAQ Pharma produces 15 sterile injectable treatments on the FDA Drug Shortage list, filling a critical role in the nation’s healthcare infrastructure and meeting the needs of major hospital systems across the country in order to best treat their patients.

As a recent white paper² issued by the Duke University affiliated Margolis Center for Health Policy points out, Congress should consider authorizing a multi-agency coordinated effort, appropriately funded by Congress, to solve the drug shortage problems our country will face in the coming years. This will require a stronger synergy amongst federal agencies, in particular the FDA (which has oversight on cGMP standards), DOD, and other divisions of HHS.

On behalf of STAQ Pharma, thank you for your attention to this important issue and your commitment to improving health care and quality. We look forward to making our presence known in Washington DC and hope to meet with Committee staff in 2024.

Sincerely,

Joe Bagan
Chief Executive Officer

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The United States Pharmacopeia (USP) is pleased to submit the following statement for the record on the hearing “Drug Shortages: Examining Supply Challenges, Impacts, and Policy Solutions from a Federal Health Program Perspective.”

USP is an independent, scientific, global non-profit organization founded in 1820 when 11 physicians took action to protect patients from poor-quality medicines. Convening in the old U.S. Senate Chamber, they published the first-of-its-kind, national, uniform set of guidelines for medicines and formed the organization now known as USP. Our organization is governed by more than 500 entities, including scientific, healthcare practitioner, consumer, and industry organizations, as well as dozens of government agencies, who together comprise the USP Convention.¹ A core pillar of USP’s work is to help strengthen the global supply chain so that the medicines that people rely on for their health are available when needed and meet USP’s quality standards as expected and/or required.

The Federal Food, Drug, and Cosmetic Act of 1938 created the statutory requirement that medicines sold in the United States generally must adhere to USP’s public quality standards to help ensure the quality of medicines and the safety of patients. Currently, USP standards are developed by nearly 800 scientific and healthcare experts who volunteer their time on USP’s standard-setting committees, which also include more than 200 U.S. Food and Drug Administration (FDA) government liaisons. In these and other ways, USP works closely with the FDA, other government agencies and across health and science communities to develop USP standards (more than 6,000 today) that are enforced by the FDA.

¹<https://www.hsgac.senate.gov/hearings/drug-shortage-health-and-national-security-risks-underlying-causes-and-needed-reforms/>.

²<https://healthpolicy.duke.edu/publications/advancing-federal-coordination-address-drug-shortages>.

¹USP’s governing bodies, in addition to the Council of the Convention, include its Board of Trustees and Council of Experts.

Drug shortages continue to pose a significant threat to our nation's patients and public health. Mitigating and preventing drug shortages requires the identification of vulnerabilities in the pharmaceutical supply chain to pinpoint the investments and policy and payment system reforms required to make measurable progress against the continued proliferation of shortages. As policy makers consider solutions to drug shortages, it is imperative to take steps to foster a more resilient supply chain to effectively reduce shortages over the long term. A more resilient medicines supply chain will enhance our national security, improve our ability to respond to medical and public health crisis, and most importantly, will help ensure that patients have access to the quality medicines that are essential for both critical and routine patient care. Now is the time to act.

Understanding Factors Driving Medicine Supply Chain Vulnerabilities

Over the past year, there have been more 300 drugs experiencing ongoing shortages, the highest in a decade. The impact on patients has been significant, causing treatment delays or the use of less effective treatments, often with suboptimal outcomes. Using the *Medicine Supply Map*,² USP found four risk categories to be correlated with drug shortages, which singularly or in combination can increase a medication's risk for shortage:

1. **Low prices:** Drug products with low prices (most commonly older drug products which are usually generics) have a higher risk of drug shortage.
2. **Manufacturing complexity:** Drugs with more manufacturing complexity, such as sterile injectables, have an increased vulnerability to shortage. Examples of manufacturing complexity include product categories that require dedicated manufacturing facilities (*e.g.*, certain antibiotics) and complex chemical synthesis of the active ingredient.
3. **Geographic concentration:** Drugs with greater geographic concentration of sourcing of active pharmaceutical ingredient (API) and/or finished dose manufacturing are more susceptible to shortages.
4. **Quality concerns:** Quality failures, accounted for in the *Medicine Supply Map* as outcomes of FDA inspections and a history of recalls, predict increased vulnerability to drug shortages.

These four risk factors are often interrelated, and, in combination, can exacerbate economic challenges for manufacturers of low-margin drug products and impact business decisions about whether to continue manufacturing some drug products. For example, manufacturing complexity increases the cost to manufacture a medicine, which, when combined with low prices of certain drug products, can yield a margin that is unsustainable. To improve margins, industry has sought to reduce manufacturing costs by concentrating production in lower-cost geographies. This concentration creates a range of vulnerabilities. Moreover, the low price/low margin dynamic impedes industry's ability to invest in increased manufacturing capacity and may lead to underinvestment in quality management systems. To increase resiliency, it is essential to account for these dynamics.

Lower-priced drugs

Lower-priced drugs have a higher likelihood of being in shortage. The association between pricing and drug shortages is well documented. For instance, Root Cause 1 in the 2019 FDA report "Drug Shortages: Root Causes and Potential Solutions" was the "lack of incentives for manufacturers to produce less profitable drugs" which included "unfavorable pricing dynamics" among other market conditions that could limit profitability. In that same report, FDA analyzed 163 drugs regulated by the Center for Drug Evaluation and Research (CDER) that went into shortage between 2013 and 2017, and found that "[w]hen compared with all marketed drugs with the same dosage form during the same period, including both generics and brands, the prices of the shortage drugs were at the 36th percentile of prices, while the prices of injectables that were in shortage were at the 33rd percentile and oral

² In determining the four primary factors contributing to drug shortages, the *Medicine Supply Map* used multiple sources of information to identify worldwide sites of pharmaceutical ingredient and finished dose medicine manufacturing. More than 40 datasets from USP, U.S. Food and Drug Administration (FDA), the Centers for Medicare & Medicaid Services, European Medicines Agency, World Health Organization, and private sector sources are utilized by the *Medicine Supply Map* platform. These data are enriched with information about risk drivers such as price and ingredients and cover 92 percent of FDA-approved generic prescription drugs. The *Medicine Supply Map* includes over 250 million aggregated datapoints to evaluate indicators of drug shortage risk, including geographic concentration, manufacturing complexity, price, and quality. The model is also informed by insights on the use of USP quality standards in over 80 percent of FDA-registered finished dose and API manufacturing facilities.

products in shortage were at the 46th percentile.”³ Lower price and margin drug products offer limited incentives for manufacturers to stay in or enter the market. The fact that lower-priced drugs have more availability issues should be evaluated within the context of quality and supply chain vulnerability.

For instance, USP *Medicine Supply Map* analysis shows low price is a significant risk factor for antimicrobial shortages, the impacts of which we recently experienced. During the winter of 2022–2023, with multiple respiratory viruses circulating, drug shortages were experienced among certain antimicrobial drug products. Previously, in the summer of 2022, USP’s *Medicine Supply Map* found that antibacterial drug products were 42 percent more likely to be in shortage than the average drug product. Out of the 128 antibacterial drug products approved in the United States, 20 were in shortage (15.6 percent compared to 10.9 percent for all drug products).⁴

Manufacturing complexity

There are numerous ways to assess the complexity of pharmaceutical manufacturing, including the type and variation of dosage forms, the number of underlying ingredients and key starting materials, the expertise needed to synthesize the molecule, storage requirements, and the size and molecular structure of the active pharmaceutical ingredient. A USP *Medicine Supply Map* analysis shows that the injectable dosage form and certain specifics of the manufacturing and API synthesis processes are predictive of drug shortages. Injectables are particularly vulnerable to supply chain disruptions when compared to solid oral dose medications. Injectable medicines often undergo a manufacturing process called lyophilization, which is expensive and complex, and therefore medicines made with this process have lower supply chain resilience. The complexity of the chemical synthesis of the API was also found to be correlated to drug shortages.

As an example, while not currently in shortage, vincristine sulfate injection, which is used for the treatment of cancer, has been in shortage in previous years and remains highly vulnerable to shortage. This drug requires plant-based starting materials that can be difficult and expensive to obtain. Moreover, its cytotoxic active ingredient is hazardous, expensive to manufacture, and requires dedicated facilities?. Manufacturers of vincristine sulfate injection also cannot take advantage of economies of scale due to the low dose/strength of the drug and the low total API needed.

Geographic concentration

USP’s *Medicine Supply Map* data show that geographic concentration anywhere—including within the United States—increases the risk of drug shortage. While the globalization of the supply chain has generally facilitated access to medicines at a lower cost, it poses the risk of unreliable supply following sudden or unexpected shocks in specific locations, followed by a lack of understanding of what might be impacted because the mapping of where products are made is complex and incomplete. Geographic concentration of the medicines supply chain is generally an outcome of specialization and pricing pressure and can result in drug shortages when a variety of issues occur, including natural disasters (e.g., earthquakes, hurricanes), trade wars, domestic or geopolitical strife, or pandemics such as COVID–19.

In March 2021, nearly three-quarters of FDA-registered API manufacturing facilities and approximately half of all FDA-registered finished dosage form (FDF) manufacturing facilities were located outside of the United States. Within the generic drug market, 87 percent of FDA-registered API facilities and 63 percent of FDA-registered FDF facilities were located outside of the United States. While instructive, these figures do not account for the volume produced within these facilities.⁵

USP used the *Medicine Supply Map* to assess U.S. dependence on foreign API. USP leveraged machine learning techniques, including Natural Language Processing, on data from FDA, information from non-U.S. regulatory agencies and its own proprietary insights to map manufacturing locations associated with approximately 90 percent of active API Drug Master Files (DMFs) around the world. DMFs are submitted to FDA by companies when they intend to supply drug ingredients to an-

³FDA. 2019. Drug Shortages: Root Causes and Potential Solutions. Available at: <https://www.fda.gov/media/131130/download>.

⁴Supply chain vulnerabilities exist for antimicrobial medicines: USP *Medicine Supply Map* analysis | Quality Matters | U.S. Pharmacopeia Blog.

⁵The White House. Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth: 100-Day Reviews under Executive Order 14017 2021 [cited 2021 August 20]. Available from: <https://www.whitehouse.gov/wp-content/uploads/2021/06/100-day-supply-chain-review-report.pdf>.

other company without disclosing proprietary information. FDA publishes the names of companies filing the DMFs. While DMFs are commonly utilized in the generics industry, some manufacturers may choose to make their own API or not use a DMF. Nevertheless, this mapping provided a picture of U.S. reliance on foreign API sources at the end of 2021. The USP *Medicine Supply Map* analysis counted the number of active API DMFs by location:

- India: 48%
- Europe: 22%
- China: 13%
- United States: 10%
- Other: 7%

USP *Medicine Supply Map* insights also show how U.S. reliance on foreign API sources has changed over time. In 2021, India contributed 62 percent of active API DMFs filed that year, up from 20 percent of currently active DMFs that were filed in 2000. This increase is consistent with India's well-publicized national ambition to enhance API manufacturing capabilities. Meanwhile, Europe's contribution declined from 49 percent of active API DMFs filed in 2000 to 7 percent filed in 2021. The United States likewise contributed a lower percentage in 2021: 4 percent. China contributed 23 percent of new API DMFs filed in 2021. USP data suggest that China produces a wide variety of APIs for medicines marketed in the United States.

Understanding these data could give leaders an opportunity to prepare for a potential disruption caused by a shock event, such as an emerging public health, political, or trade crisis. Questions remain from the current analysis, however, when thinking about facets of U.S. reliance on foreign API manufacturers. For example, USP's analysis does not take volume into account, and it is not clear if certain DMF holders are responsible for larger volumes of drugs compared to competitors. Importantly, we also do not understand U.S. reliance on other countries for key ingredients that are used in the manufacture of API.

Quality concerns

USP underscores that medicines supply chain resilience and medicines quality are inextricably linked; issues with medicines quality can threaten medicines supply chain resilience, and medicines supply chain failures, vulnerabilities and disruptions can lead to medicines quality issues, increasing the risk of substandard and falsified medicines. It is well documented that quality issues remain a primary contributor to drug and medical product shortages.

USP *Medicine Supply Map* analysis found that poor FDA inspection outcomes at a facility and products with a history of recalls were correlated with a higher likelihood of shortage. This is consistent with FDA's findings: for example, of the 163 drugs that went into shortage between 2013 and 2017, the FDA found that 62 percent went into shortage due to quality issues.⁶ Root Cause 2 outlined in FDA's 2019 drug shortages report suggested that the market does not recognize and reward manufacturers for mature quality management systems.

USP Policy Recommendations

A fundamental shift in the market for lower-priced drugs is needed to align supply and demand forces to create a predictable, sustainable, and quality supply chain that can reliably provide critical drugs to patients. Policymakers and public and private drug purchasers must value quality and resilience through sustainable prices of drugs that demonstrate these characteristics. While the programs and policies to achieve this are being developed and implemented, it is imperative in the near term to utilize and expand tools to assess supply chain vulnerabilities and shortage risks, and to use these insights to proactively intervene in a coordinated manner. USP urges policymakers, regulators, and industry to take further action to identify and respond to risks and vulnerabilities and reduce medicine supply disruptions. While we recognize that drug shortages span various Congressional Committees due to both public health and national security concerns, we urge the Committee to work across committee jurisdictions to ensure that meaningful reforms are enacted and implemented.

1. Promote sustainable prices for generic medicines by valuing supply chain resiliency

The leading and root cause of most drug shortages is unsustainably low prices. Lower margins undermine initiatives to ensure supply chain resiliency by limiting

⁶*Ibid.*

the ability of manufacturers to reinvest in manufacturing facility maintenance and manufacturing updates and quality assurance and management, causing manufacturers to seek lower-cost geographies for their sourcing and manufacturing. USP understands the necessity for a fundamental shift in the market for lower-priced drugs to guarantee more certainty and predictability of both demand and supply and to increasingly value a drug's supply chain resiliency in addition to its price. As such, USP:

- Supports the development of initiatives to assess manufacturer supply chain resiliency, sustainability, and reliability. Such initiatives will provide information that can support purchasing and contracting decisions that financially recognize and reward manufacturer supply chain capacity and resiliency efforts.
- Encourages policymakers and public and private drug purchasers to explore:
 - The establishment and utilization of payment and purchasing models that value and incentivize supply chain resilience and reliability.
 - The authorization and use of longer-term guaranteed-volume contracts, in which prices are assured for a defined, guaranteed volume. Such long-term, guaranteed-volume contracts could include provisions to help ensure supply chain resiliency and reliability, including requirements for manufacturing capacity that accounts for potential disruptions and diversification of suppliers.

2. Advance broader geographic diversification of the manufacturing base including incentives to advance more U.S.-based medicine production

USP supports reforms to foster more resilience in the manufacturing base for U.S. drug products—especially for medicines or ingredients that are most vulnerable to supply disruptions—and to reduce the risk to patients of potential disruptions and shortages that result from the concentration of drug manufacturing in limited geographies. USP supports:

- Economic or other incentive measures that will encourage multiple suppliers for key drugs, geographic diversification of manufacturing facilities, and broader component supply.
- Economic incentives to encourage increased domestic manufacturing of APIs and finished drug products in the United States, prioritizing specific medicines or ingredients that are most vulnerable to supply disruptions.
- Market-based and pricing incentives that encourage utilization of excess domestic manufacturing capacity: up to 50 percent of manufacturing capacity in the United States has been identified as unutilized.
- Financial incentives to provide manufacturers with the necessary support to build facilities supporting advanced manufacturing technologies (AMTs) on U.S. soil: manufacturers of low-margin drug products that have a higher likelihood of shortage have insufficient profitability to invest in AMTs.
- The development of tools and standards to help reduce the technical barriers to wider adoption of AMTs and support medicine quality.

3. Utilize existing early warning capabilities and invest to fill gaps in the supply chain map

Both government and non-governmental stakeholders should utilize the full range of early warning capabilities developed for the U.S. drug supply chain. In particular, the U.S. Government should further leverage information platforms that provide actionable data-based insights into medicines supply chain vulnerabilities, while also funding additional initiatives to fill information gaps on a broad range of vulnerabilities including for key starting materials and critical excipients. These capabilities can be housed in a funded Early Warning System and Research Coordinating Center and would enable the U.S. Government and private sector pharmaceutical supply chain stakeholders to adopt a more proactive and informed approach to preventing shortages and mitigating the impact of those that do occur. Early warning capabilities would also help the U.S. Government increase the return on its investments in strengthening the nation's medicine supply by targeting investments and resources to the particular vulnerabilities of specific medicines.

U.S. Government entities and the private sector stakeholders responsible for getting medical products to patients—including manufacturers, wholesalers, and hospitals—need actionable insights that can assist in anticipating and predicting supply chain vulnerabilities and their causes before they result in a drug shortage. Moreover, a need exists to integrate already existing data—such as unit volume, supply chain

structure, facility quality management maturity, company financial health, epidemiology, and other demand drivers—to prevent drug shortages or mitigate their impact.

In the case of recent shortages in oncology drugs, alerts issued by an early warning system could have enabled distributors and manufacturers to act, including by communicating with hospitals and putting carboplatin and cisplatin on allocation or quota until actions could be taken to increase supply. In the case of methotrexate, its market has shown signals of supply vulnerability for more than 4 years, according to the *Medicine Supply Map*, since long before the most recent shortage. The methotrexate market has experienced significant price declines, market consolidation leading to a concentration of risk, and persistent shortages. These patterns could have been flagged proactively as a concern, potentially guiding preventive actions and policy responses.

Identifying, characterizing, and quantifying risks and vulnerabilities throughout the medicines supply chain—from raw materials and APIs to distribution and administration of drug products to patients—can yield meaningful and timely insights, inform impactful decisions and solutions to avert shortages, and support effective responses to shortages when they do happen. For example, a comprehensive simulated model of the medical product supply chain can enable tactical and training exercises that will help our nation better prepare for the next public health emergency or geopolitical shock by identifying nodes of vulnerability, especially overreliance on one foreign country or any single geographic area. When a shortage does happen, the data and lessons learned can be used to tailor a response and minimize the impact based on an understanding of the shortage’s potential duration and magnitude, supported by insights into root cause(s), market share, and potential alternative suppliers.

4. Utilize a vulnerable medicines list to guide policy interventions and investments

A vulnerable medicines list that highlights medicines that are vulnerable to shortage based on a range of indicators would provide both government and non-government stakeholders with insights to inform policy and purchasing decisions. Factors that would inform a vulnerable medicines list could include the number of suppliers, geographic concentration of manufacturers and API, excipient, and KSM suppliers, political and geopolitical risks, climate change susceptibilities, manufacturing complexity, price, and other information.

5. Coordinate supply chain resilience and reliability efforts

USP supports efforts to coordinate medicines supply chain resilience and reliability activities among federal agencies and non-governmental stakeholders. We encourage the coordination of multi-disciplinary efforts, defining measurable outcome metrics for implementation efforts, and strategic planning activities to maximize the utility of new programs and increase the impact of existing initiatives. Additionally, necessary authorities and sufficient funding should be allocated to lead these cross-functional efforts to improve drug supply chain resilience and reliability.

Conclusion

USP thanks the Committee for considering USP’s recommendations and for the thoughtful, bipartisan attention to the underlying causes of drug shortages and to the policy and payment system reforms required to improve medicine supply chain resilience. We look forward to working with the Committee and Congress to seek solutions to drug shortages that will help ensure that patients have access to the quality medicines they need.

