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EXAMINING CHRONIC DRUG SHORTAGES IN THE UNITED STATES

HEARING

BEFORE THE

COMMITTEE ON WAYS AND MEANS HOUSE OF REPRESENTATIVES

ONE HUNDRED EIGHTEENTH CONGRESS

SECOND SESSION

FEBRUARY 6, 2024

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United States House Committee on
Ways & Means
CHAIRMAN JASON SMITH

FOR IMMEDIATE RELEASE
January 30, 2024
No. FC-19

CONTACT: 202-225-3625

Chairman Smith Announces Hearing on Examining Chronic Drug Shortages in the United States

House Committee on Ways and Means Chairman Jason Smith (MO-08) announced today that the Committee will hold a hearing to examine the pervasive problem of drug shortages and its harmful impact on patient access to care. The hearing will take place on **Tuesday, February 6, 2024, at 10:00 AM in 1100 Longworth House Office Building.**

In view of the limited time available to hear the witnesses, oral testimony at this hearing will be from invited witnesses only. However, any individual or organization not scheduled for an oral appearance may submit a written statement for consideration by the Committee and for inclusion in the printed record of the hearing.

DETAILS FOR SUBMISSION OF WRITTEN COMMENTS:

Please Note: Any person(s) and/or organization(s) wishing to submit written comments for the hearing record can do so here: WMSubmission@mail.house.gov.

Please ATTACH your submission as a Microsoft Word document in compliance with the formatting requirements listed below, **by the close of business on Tuesday, February 20, 2024**. For questions, or if you encounter technical problems, please call (202) 225-3625.

FORMATTING REQUIREMENTS:

The Committee relies on electronic submissions for printing the official hearing record. As always, submissions will be included in the record according to the discretion of the Committee. The Committee will not alter the content of your submission but reserves the right to format it according to guidelines. Any submission provided to the Committee by a witness, any materials submitted for the printed record, and any written comments in response to a request for written comments must conform to the guidelines listed below. Any submission not in compliance with

these guidelines will not be printed but will be maintained in the Committee files for review and use by the Committee.

All submissions and supplementary materials must be submitted in a single document via email, provided in Word format and must not exceed a total of 10 pages. Please indicate the title of the hearing as the subject line in your submission. Witnesses and submitters are advised that the Committee relies on electronic submissions for printing the official hearing record. All submissions must include a list of all clients, persons and/or organizations on whose behalf the witness appears. The name, company, address, telephone, and fax numbers of each witness must be included in the body of the email. Please exclude any personal identifiable information in the attached submission.

Failure to follow the formatting requirements may result in the exclusion of a submission. All submissions for the record are final.

ACCOMMODATIONS:

The Committee seeks to make its facilities accessible to persons with disabilities. If you require accommodations, please call 202-225-3625 or request via email to WMSubmission@mail.house.gov in advance of the event (four business days' notice is requested). Questions regarding accommodation needs in general (including availability of Committee materials in alternative formats) may be directed to the Committee as noted above.

Note: All Committee advisories and news releases are available on the Committee website at http://www.waysandmeans.house.gov/.

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EXAMINING CHRONIC DRUG SHORTAGES IN THE UNITED STATES

TUESDAY, FEBRUARY 6, 2024

HOUSE OF REPRESENTATIVES,
COMMITTEE ON WAYS AND MEANS,
Washington, DC.

The committee met, pursuant to call, at 10:04 a.m., in Room 1100, Longworth House Office Building, Hon. Jason T. Smith [chairman of the committee] presiding.

Chairman SMITH. The committee will come to order.

Before we begin, I would like to first recognize a member who is returning to the Ways and Means Committee, Mr. Jimmy Gomez.

I am sure that, in your time away, you have been reinforced of how this is the best committee in Congress, and so we are glad to have you back.

[Applause.]

Chairman SMITH. Today in the United States, there are over 250 medicines in short supply. These drugs treat everything from blood clots to asthma. Especially worrisome, some of these medications include those needed to treat and beat multiple kinds of cancer. Most of these are low-cost generics that make a real difference for patients struggling to pay for both medication and other health care expenses. Active drug shortages are at the highest levels since 2014. Over half of the medicines currently in short supply have been limited in availability for at least two years.

Patients are living in fear that they may be unable to get the treatments they need when they need them. When a patient's drug is out of stock, they don't just worry about access, they also worry about how they will afford their medicine. It is simple supply and demand that drives up prices. If you can get medication in shortage, you pay, on average, 15 percent more. Patients forced to switch to alternative therapies may be paying as much as three times more than their original medication.

While some temporary shortages might be caused by natural disasters or sharp demand increases, poor manufacturing quality is the leading driver of chronic shortages, and it is the most preventable. Government policies and consolidation in the supply chain forced manufacturers to close drug production because they can't make the math work.

Medicare's reimbursement system ensures affordability and access for seniors but should be reexamined to avoid making the situation worse. Everyone—drug manufacturers, wholesalers, group purchasing organizations, and medical providers—should be working together to ensure ready access and availability of medicine.

We aim to learn more today about how these actors can prevent shortages and whether our Federal regulations support that goal.

Another concern of our supply chain is that many of the medications available to Americans are sourced from countries outside America. Over 80 percent of the essential ingredients used in medications taken by Americans are made in a foreign country.

China in particular is a major supplier of pharmaceuticals and drug ingredients to the United States. In 2021, China was the leading source of imported pharmaceutical products by weight to the United States. This, as with other aspects of our medical supply chain, can pose a serious risk to the American people if access to quality medications is subject to the whims of a hostile foreign power. Americans should not have to rely on adversarial nations to stock their medicine cabinets.

Fortunately, there are some innovative examples of private sector and local government solutions. One of our witnesses represents a private business who uses long-term contracts to support quality manufacturing. My good friend and former Ways and Means Committee member, Governor Kristi Noem, invested state funds in buffer stocks for South Dakota. But there is not a one-size-fits-all solution, and many small rural hospitals and communities may have a harder time procuring this medication for their patients or investing in long-term solutions.

Washington has tried and failed to address drug shortages before. It is clear to me that we need to incentivize the development of higher-quality drugs and improve purchasing dynamics without relying on mandates from Washington. Our solutions should balance affordability with accessibility. We should be using health care, tax, and trade policy to make more medicine and their ingredients here in the United States. Congress should support access to the lifesaving therapies we do have and ensure America realizes the promise of innovative future cures to come.

I hope today's hearing can help us zero in on bipartisan solutions that will get more and better medications into the hands of the patients who need them.

Chairman SMITH. I am pleased to recognize the ranking member, Mr. Neal, for his opening statement.

Mr. NEAL. Thank you, Mr. Chairman. First, as you did, I want to welcome back Congressman Jim Gomez to the Committee on Ways and Means, a valued member in the past as we know he will be in the future. And he answered the appropriate question during the interviewing process, as you raised it: What is the best committee in Congress?

He quickly said, "Ways and Means."

And we said, "You are going on the committee." [Laughter.]

Mr. NEAL. It is good to have him back on this most storied dais in Congress, fighting for workers and their families.

Today's hearing comes on the heels of major milestones in health care, thanks to the Democrats. More Americans have health insurance today than ever before: 21 million people signed up during the latest open enrollment, with four out of five people being able to access high-quality plans for less than $10 a month. This committee was responsible for that.

Our historic Inflation Reduction Act is starting to take hold, saving the American people money and delivering more breathing room. Last week, Medicare made its first fair price offers on 10 of the most common costly drugs used by Americans. We are talking about delivering savings of up to 25 percent, and yet our Republican colleagues are still making efforts to block the law, siding with interests beyond our imagination as they keep costs higher for the nation's seniors.

Our progress is important, but our work is far from finished. We also must address access issues that come from drug shortages of phenomena like high drug prices that have become all too common. Quality challenges in the manufacturing of generic drugs have led to shortages, disrupting patient care and creating ripple effects that intensify the challenges that vulnerable groups already face.

Meanwhile, supply chain dynamics can worsen shortages through short-term contracting prices with exclusivity with one manufacturer instead of engaging with many who could fill the gaps in case of the challenge, or by squeezing manufacturers in a race to the bottom.

The path forward is clear: Congress must act in a multifaceted, bipartisan way to reward quality, reliable manufacturing, and incentivize improvements in the process. Joe Biden has already taken unprecedented steps to combat these shortages by bolstering authorities under the Defense Production Act and investing in domestic production of key materials.

While supply chain issues and shortages are extremely troubling, it is only half the issue. This committee must also be concerned about the millions of Americans who can't access lifesaving prescriptions because of costs.

We had no Republican help when we gave Medicare the power to negotiate lower drug prices for the first time in our nation's history. At a time when the American people are forced to pay three times more for their prescription drugs than some counterparts across the world, not a single one of our colleagues from the other side helped us out and sided with those below the poverty lines. Luckily, we didn't need their votes. We took action to put an end to pharma's price gouging, capped out-of-pocket costs at $2,000 and insulin at $35 a month for seniors.

Our work brings people the peace of mind they deserve. It is fundamentally challenging and a changing health care opportunity for America. At the same time, we will all attempt to give families some breathing room with lower drug prices. There is certainly more to do, and, in a bipartisan manner, we certainly are capable of doing it in this committee when we are ready and willing to act.

Mr. NEAL. And, with that, I yield back, Mr. Chairman.

Chairman SMITH. Thank you, Mr. Neal. I will now introduce our witnesses.

Dr. Stephen Schleicher is chief medical officer of Tennessee Oncology.

We have Gene Cavacini, a senior vice president and chief operating officer of McKesson Pharmaceutical Solutions and Services.

And Allan Coukell is senior vice president for public policy of Civica Rx.

Dr. Stephen Schondelmeyer is director of the PRIME Institute at the University of Minnesota's College of Pharmacy.

Dr. Julie Gralow is chief medical officer and executive vice president of ASCO.

And Dr. Jeromie Ballreich, an associate research professor at Johns Hopkins Bloomberg School of Public Health.

Thank you all for joining us today. Your written statements will be made part of the hearing record, and you each have five minutes to deliver remarks.

Dr. Schleicher, you may begin when you are ready.

STATEMENT OF DR. STEPHEN SCHLEICHER, MD, MBA, CHIEF MEDICAL OFFICER, TENNESSEE ONCOLOGY

Dr. SCHLEICHER. Chairman Smith, Ranking Member Neal, and members of the Committee on Ways and Means, I want to thank you for the opportunity to appear here today to discuss severe chemotherapy drug shortages.

I am a medical oncologist at Tennessee Oncology, the largest provider of cancer care in Tennessee, where I also serve as chief medical officer. I am also a board member of the Community Oncology Alliance and a member of the American Society of Clinical Oncology.

Last year presented a significant challenge to our patients due to drug shortages of older but essential generic injectable chemotherapies. The two drugs I want to discuss today are carboplatin, first approved in 1989; and cisplatin, approved in 1978. These very inexpensive generic chemotherapy agents continue to serve as the preferred backbone of many important curative and palliative cancer treatments.

So how bad was the shortage at Tennessee Oncology? For carboplatin, at our peak shortage, we were unable to treat 90 percent of patients as scheduled who should have received the drug. For cisplatin, we were unable to treat over 50 percent of patients who needed it. We went a full 10 days without a single shipment of either drug, and, at the time, there was no end in sight.

What was the impact of these shortages? As oncologists, we were suddenly faced with the near-impossible task of determining which of our patients could receive our very limited drug supply. These are patients who are facing cancer, perhaps the scariest word in medicine, and are trusting us to guide them through their journey during one of the most vulnerable times of their lives. In a country that offers the most advanced, cutting-edge cancer therapies, we were put in a situation that a decade of medical training did not prepare us for: the moral dilemma of how to ration our limited supply of these chemotherapies.

As chief medical officer, I had to send an email to all of our providers on June 18 last summer that communicated we had only enough cisplatin to be used in patients with testicular or bladder cancer, and only enough carboplatin to be used for chemo, radiation, and lung cancer. What that meant is that we were not—we did not have enough to allow any use in patients with breast, metastatic lung, endometrial, cervical, or many other cancers.

The most significant impact, of course, was on the patients themselves, who required carboplatin or cisplatin but were unable to get

them. Imagine being a patient with a hope for cure or wanting to live longer with family suddenly being told that you don't have the optimal treatment anymore. There are hundreds of examples at Tennessee Oncology alone, but for interest of time I want to share two.

Last summer, I was treating a very sweet, 52-year-old female with aggressive, triple-negative breast cancer who had one shot at cure with a regimen that included carboplatin. Unfortunately, halfway through, in the middle of her four-month treatment, we ran out of the drug and I was unable to give her carboplatin for three consecutive doses. Already paralyzed with fear by her diagnosis, her first question to me was whether not getting carboplatin would affect her chance of cure. I had to tell her I hope not, but I honestly don't know.

A colleague of mine was treating a 61-year-old female who had stage four lung cancer. The goal of her treatment, which also included carboplatin, was to try to extend her life and extend her quality of life for as long as possible. Unfortunately, after needing to stop carboplatin because we ran out of supply, her condition deteriorated rapidly, and she died soon after. Whether she could have lived an additional several months or longer to spend cherished time with family, we—and most importantly, the family—will never know.

Now, I practice at a large oncology group with significant purchasing power, but we were still faced with severe shortages. It is virtually impossible to predict an inventory enough supply in advance of drugs that may have shortages in the future. And that is us. I can't even imagine how a small, say, one-physician practice in rural America would ever be able to navigate these shortages.

Finally, I want to mention that even if cisplatin and carboplatin are improved right now, we are still dealing with drug shortages. An example is methotrexate, another older generic chemotherapy used to treat CNS lymphoma; and vinblastine, a generic chemotherapy used to treat curable Hodgkin's lymphoma. The problem of drug shortages is not over yet.

In summary, I testify today as a practicing oncologist representing my patients, as well as the thousands of cancer patients around the country and their treating oncologists. I am not an economist or policymaker, but common sense tells me that these shortages of inexpensive, generic drugs must be tied to the lack of incentives for manufacturers to produce these.

We are all concerned with the financial toxicity of expensive cancer drugs, but we also need to be equally concerned about the chronic shortages of inexpensive but essential generic drugs. I implore Congress to act to stop these drug shortages, and thank you for the opportunity to testify today.

[The statement of Dr. Schleicher follows:]

Written Testimony on Hearing:

Examining Chronic Drug Shortages in the United States

February 6, 2024

United States House of Representatives

Committee on Ways & Means

Stephen Schleicher, MD

Practicing Oncologist and Chief Medical Officer

TENNESSEE ONCOLOGY

Submitted February 3, 2024

Chairman Smith, Ranking Member Neal, and members of the Committee on Ways and Means, I appreciate the opportunity to submit this written testimony and to appear as a witness at this extremely important hearing on drug shortages, especially in cancer treatment. I frame this written testimony, opening statement, and answers to questions from the perspective of both a medical oncologist and Chief Medical Officer of a large independent community oncology practice.

I implore Congress to take meaningful action to prevent further shortages of vital life-saving cancer drugs and therapies needed to treat this life-threatening disease. These drug shortages, as I will describe in this testimony, seriously interfere with our ability to treat our patients

By way of background, I currently practice as a medical oncologist at Tennessee Oncology, the largest provider of cancer care in the state of Tennessee. Our practice has over 200 providers who practice in 35 clinics in both urban and rural settings across the state. Our mission at Tennessee Oncology is simple: to provide the highest quality, most affordable and comprehensive cancer care close to home, in the communities where our patients live. Last year, we provided care to almost 100,000 patients, and that number continues to grow. Personally, I see patients two days a week in Lebanon, a rural town in Wilson County, TN. I also serve as Chief Medical Officer of our practice. I am extremely proud to say that at Tennessee Oncology we take care of every patient who walks in our doors, regardless of their insurance status or ability to pay.

In addition to my responsibilities at Tennessee Oncology, I serve as an officer and Board member of the Community Oncology Alliance, a non-profit organization dedicated to serving cancer patients in their communities and supporting practices like ours across the country. I am also a member of the American Society of Clinical Oncology.

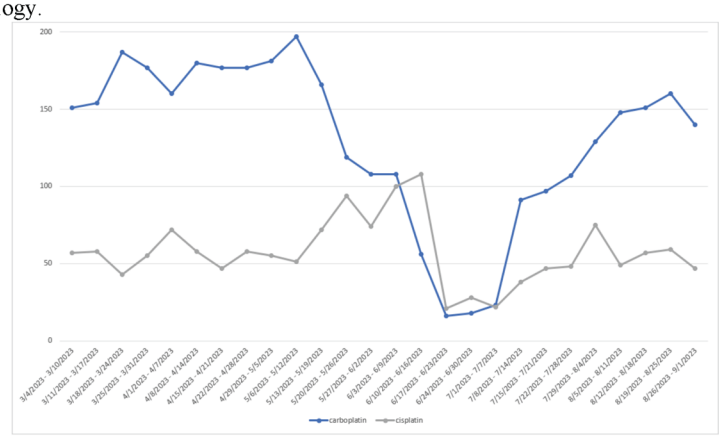
As physicians, we are trained to adhere to evidence-based guidelines based on rigorous scientific and clinical research in order to provide our patients with the best possible treatment, whether it be for a cure to their cancer, whenever possible, or for the preservation of their quality-of-life and to extend their life living with cancer, when a cure is not possible. We develop bonds with our patients during some of the scariest times in their lives. Not to minimize any other physician-patient relationship at all, but the oncologist-patient relationship is a special one that makes this profession more than just a job.

As you may be aware, last year presented a significant challenge for oncologists and our patients due to drug shortages. These shortages were not with new cutting-edge treatments like immunotherapies and other therapies commonly referred to as precision "targeted" therapies, but with generic injectable chemotherapies that have been in use for decades. These generic chemotherapy drugs often serve as the backbone of important cancer treatments for both curative and palliative intent.

In particular, I want to focus on two generic injectable chemotherapies: cisplatin, which was first FDA approved in 1978 and carboplatin, which was first FDA approved in 1989. It is true that we have come a long way with cancer treatment since both of these drugs were first approved, with dozens of new FDA approvals in oncology each year[1]. However, these older, now generic drugs still serve as a vital foundation for many important cancer treatment regimens, especially in the curative setting for breast, lung, ovarian, cervical, endometrial, and testicular and bladder cancers, to name just a few. These older but vital generic drugs are not just *options* for treating patients with these diseases, but are often part of the *only* preferred treatment regimen for these cancers.

So how bad was the shortage of these drugs at Tennessee Oncology? Under normal circumstances, when the supply is sufficient to meet demand, we usually administer treatment to approximately 170 patients using carboplatin and 50 patients using cisplatin *per week*. In contrast, as show in **Table 1 (below)**, during mid-June of last year there was a one-two week period where we were only able to treat 16 patients with carboplatin and 21 patients with cisplatin. Described another way, we were **unable to treat 90 percent of patients who required carboplatin and over 50 percent of patients who required cisplatin during that time**. Although the peak of the shortage for our large practice was only several weeks, there was an interval of over 10 days during which we did not receive any shipments of these medications, and without any indication of when the supply would resume. Please keep in mind that we are one of the largest cancer treatment facilities in the country, including both independent practices and large hospital health systems, with significant purchasing power. Just imagine what smaller cancer treatment facilities, particularly those in rural America, must have faced.

Table 1: Doses of carboplatin (blue) and cisplatin (gray) delivered per week at Tennessee Oncology.



[1] New FDA-Approved Oncology Drugs (2021-2022), The ASCO Post, 2022.

How do these shortages impact our patients? The majority of patients whose recommended evidence-based treatments called for the inclusion of carboplatin or cisplatin were unable to receive these medications as part of their treatment for a period of time. Their providers had to ration the use of chemotherapies. Imagine being a patient already dealing with the many difficulties that come with a cancer diagnosis, only to discover that you must also navigate the added obstacle of not receiving the best or only treatment available. Imagine how difficult it was for patients to hear they were not going to receive the optimal treatments.

As oncologists, we suddenly had the near impossible task of determining which patients could receive our very limited allotment of these drugs. The best training in the world and access to all evidence-based guidelines did not prepare us for the moral dilemma we now faced: how to ration our limited supply of these chemotherapies. Was it based on chance at cure? Options for a substitution drug? Number of patients affected? As the Chief Medical Officer, I had to the send the following email to our providers and teams on June 18, 2023:

Please be on the lookout for regular updates on drug shortage treatment recommendations:

- *Current indications where cis/carbo can be used:*
  - *Cisplatin use: we only have enough for **Testicular Cancer** and **Neoadjuvant Bladder**.*
  - *Carboplatin use: we have been completely out but got a small shipment on Friday. For now, due to a lack of good alternatives to platinum agents, we are limiting use to **chemoradiation for curative intent in NSCLC**. As indicated last week, it could take several months to have this fully replete. We will update regularly whenever small shipments come in since recs might change accordingly.*
- *Unfortunately, we do not have enough supply of cis/carbo for any other indications at this time and need to use alternatives instead.*

For patients where there was not an acceptable substitution to the drugs in short supply, they simply did not get the complete evidence-based regimen. For example, two very important and commonly used curative regimens[2,3] in breast cancer require the use of carboplatin.

To share some actual experiences from my practice, last summer I had the privilege of treating a remarkably kind 52-year-old female who was undergoing treatment with a

[2] Schmid P, Cortes J, Pusztai L, et al. Pembrolizumab for early triple-negative breast cancer. NEJM, 2020.
[3] Von Minchwitz G, Procter M, de Azambuja E, et al. Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. NEJM, 2017.

combination of chemotherapy and immunotherapy[4] for aggressive triple-negative breast cancer. Her cancer had metastasized to several lymph nodes but was still potentially curable with this aggressive regimen, of which carboplatin was a critical component. Unfortunately, halfway through her four-month treatment course, we experienced the shortage of carboplatin, resulting in the omission of this drug from her regimen for three consecutive doses. From the outset of her diagnosis, she was overwhelmed with fear, and the news that we could not procure the necessary chemotherapy added to her distress. Her immediate concern was whether this shortage would compromise the efficacy of her treatment, a question for which we unfortunately lack data to provide concrete numbers. Should her cancer recur in the future in an incurable manner, I am troubled by the thought that she might forever question whether the outcome could have been different had she received her complete chemotherapy regimen.

Even for patients without curable cancers, these drug shortages had a profound impact. For example, one of my colleagues was treating a 61-year-old female in Chattanooga who had incurable lung cancer with the goal to control her cancer as effectively as possibly, thereby enhancing her quality of life and prolonging her lifespan to the greatest extent possible. Unfortunately, following the depletion of our carboplatin supply – a key component of her therapeutic regimen – her condition deteriorated rapidly, and she quickly died. Whether she could have lived an additional several months or longer to spend cherished time with family, we will never know. And as my colleague said, *"The family still believes this was the main reason which led to her cancer progressing and ultimately her death. This will probably be on their minds every time they think about her."*

Thankfully, as I have stated previously, I practice at a large oncology group that additionally has many ties to other community and academic oncology practices. The 200 oncology providers in Tennessee Oncology were able to email and call each other asking *"How would you treat this cancer given we have no drug available?"* We were able to lean on each other as a team going through this together and ask each other for help. In addition, we have analytics to help us monitor drug inventory and are large enough to absorb any financial burden of "overstocking" as much as possible once we see supply of a certain drug starting to decrease. And despite these benefits of being large, we still faced huge challenges during this time that negatively impacted our patients.

With that said, I cannot even imagine what it would have been like to be part of a mid-size or even smaller physician group, especially in rural America where a provider may not have colleagues to discuss cases with or the resources to manage complicated drug inventory. I can only think that their situations were even worse than ours – for the oncologists, their staff, and most importantly their patients.

To put the complexity of inventory management into perspective, at Tennessee Oncology we purchase and deliver over 200 unique drug formations each year to our patients. To add

[4] Schmid P, Cortes J, Pusztai L, et al. Pembrolizumab for early triple-negative breast cancer. NEJM, 2020.

to this complexity, the influx of biosimilars has made it such that in some situations, a parent drug like trastuzumab now has 5 different biosimilars. This would potentially be manageable if we could select one preferred biosimilar to use for all appropriate patients. However, we are often forced to carry every single biosimilar since each payer often requires a specific biosimilar based on their own economics. Balancing the plethora of drugs needed to deliver high quality care plus the payer mandates that require their own preferred biosimilar is nearly impossible!

Thus, with the number of drugs we must inventory, it is virtually impossible to have enough drug in inventory to avert a shortage. Furthermore, if cancer treatment practices and hospitals were to inventory large quantities of drugs prone to shortages this could actually amplify shortages and worsen disparities in care (those with supply versus those without).

While the shortages of carboplatin and cisplatin have now improved, we continue to face risks of shortages with similar older generic chemotherapies. This includes methotrexate, which is a common part of treatment regimens for hematologic malignancies. For example, at Tennessee Oncology I know of several patients who had treatments delayed for the cure of CNS lymphoma. We will never know the impact these delays had on their outcomes. Additionally, we have also been close to facing a crisis with vinblastine, part of the treatment regimen[5] for highly curable Hodgkin's Lymphoma.

I am not here to tell you with absolute certainty that these shortages have led to increased patient deaths. However, I can state unequivocally that there were too many patients – in fact, hundreds just at Tennessee Oncology– that were unable to get the optimal cancer treatments they needed and should have received. The clinical and psychologic consequences from these drug shortages are all too real and need to be addressed.

My goal in this testimony as an oncologist is to share this story on behalf of my patients, as well as the thousands of cancer patients around the country and their oncologists who care for them. I am not an economist or policy maker, and therefore ask for your guidance and help solving this problem. However, if you ask my view on what is causing these shortages and how to fix them, it is clear that manufacturers have decreasing financial incentives to make these very inexpensive but critical generic injectable drugs, thereby jeopardizing the stability of their supply chains. While we are all concerned about the financial toxicity patients face with increasingly expensive cancer drugs and other therapies, we must also be equally concerned about the challenges patients face when they cannot get access to less expensive mainstay generic drugs.

[5] Canellos GP, Anderson JR, Propert KJ, et al. Chemotherapy for advanced Hodgkin's Disease with MOPP, ABVD, or MOPP alternating with ABVD. NEJM, 1992.

The Community Oncology Alliance, with which I am affiliated, has identified probable causes for these shortages and proposed several detailed, targeted solutions. I call the Ways & Means Committee's attention to the following documents:

- Witness testimony to the Energy & Commerce Committee on Drug Shortages
- Response to Energy & Commerce RFI on Drug Shortages
- Comments to the Senate Finance Committee that Ranking Member Crapo Submitted for the Record

I appreciate the opportunity to provide this testimony.

Stephen Schleicher, MD
Tennessee Oncology

Chairman SMITH. Thank you very much.
Mr. Cavacini, you are now recognized.

STATEMENT OF EUGENE CAVACINI, SENIOR VICE PRESIDENT AND CHIEF OPERATING OFFICER, MCKESSON PHARMACEUTICAL SOLUTIONS AND SERVICES (PSAS)

Mr. CAVACINI. Thank you. Good morning, Chairman Smith, Ranking Member Neal, and esteemed members of the committee. My name is Gene Cavacini, and I am the senior vice president and chief operating officer for McKesson's drug distribution businesses. In that role, I oversee distribution, sales, and customer service for our operations in the United States.

McKesson applauds this committee's efforts to mitigate drug shortages and shares your goal of strengthening an already strong global supply chain. I am grateful for the opportunity to be here today to share McKesson's perspective and to offer some recommendations.

McKesson is a diversified health care services company founded nearly two centuries ago. We play a critical role in health care delivery, making medications and supplies available to health care providers and patients across North America. In fact, about one-third of the nation's pharmaceutical products flow through our facilities each and every day. We are passionate about our mission to improve care in every setting one product, one partner, and one patient at a time. If you visit one of our more than 30 distribution centers, you will walk under a banner that reads, "It is not just a package, it is the patient." McKesson constantly evaluates our processes to help surety of supply to help identify and mitigate potential problems.

When sourcing products, we prioritize three pillars: the first is consistent supply and supply chain quality; second, clinical importance and therapeutic options; and third, of cost or price. These pillars are fundamental to our business model and responsible sourcing practices. For vulnerable drug categories, we also examine clinical and patient need to ensure access to alternative therapies.

While drug shortages affect only one percent of all prescriptions, we know that even that small percentage can have significant impact on health care providers, caregivers, and most importantly, patients.

To address drug shortages, we must agree on a common definition, and distinguish whether the occasional disconnect between supply and demand represents true supply limitations, or just temporary gaps in access. Our view is that most drug shortages fall within three categories: market-wide supply disruptions, product-specific issues, and then reimbursement and market access limitations.

Common causes include sourcing or manufacture problems, natural disasters, market economics, changes in prescribing or demand patterns, and product discontinuations. The key drugs and classes making headlines demonstrate the range of root causes and also highlight the need for unique solutions.

A robust, competitive market is one that naturally buffers against drug shortages. Government intervention should correct the market to its natural, competitive state, but be careful not to

create misaligned incentives that could add to shortages. Policymakers should focus on products most at risk of shortage, like generic, sterile injectables and particularly those products for cancer patients.

As for root causes, we offer the following recommendations.

We must strengthen access to Active Pharmaceutical Ingredients, or APIs, as well as fully manufactured products. This will require more than just increasing domestic capacity. Preservation programs must be coordinated with all stakeholders, including manufacturers, distributors, providers, and the national stockpile to be careful that we don't stress all very—already vulnerable products or trap precious inventory where it might not be accessible. We must provide equitable access to all settings of care and all patient populations.

And second, we must examine reimbursement with market incentives necessary to revitalize investment in manufacturing, especially for drugs with low margins and a limited number of manufacturers. This could include temporary relief from rebate requirements and inflationary penalties contingent upon building manufacturer capacity and investing in quality programs.

And third, we must improve transparency across the supply chain. This requires the sharing of insights both up and down the supply chain, with safeguards to protect competitive, sensitive information.

McKesson believes strongly that solving drug shortages requires the collaboration of all stakeholders in the supply chain, and we are committed to doing our part. By addressing the variable root causes, bolstering supply preservation efforts, and improving communication between stakeholders we can make meaningful progress in protecting the health of our nation.

Thank you, and I look forward to your questions.

[The statement of Mr. Cavacini follows:]

Statement for the Record – McKesson Corporation

Good morning, Chairman Smith, Ranking Member Neal, and esteemed members of the committee. My name is Gene Cavacini. I serve as the Senior Vice President and Chief Operating Officer for McKesson's drug distribution business. In this role I oversee sales, distribution, and customer service operations in the United States.

McKesson applauds the Committee's focused efforts to mitigate drug shortages and shares your goal of bolstering the resiliency of our global pharmaceutical supply chain. I am grateful for the opportunity to be here today to share McKesson's perspective and to offer recommendations for your consideration.

McKesson is a diversified healthcare services company founded nearly two centuries ago. We play a critical role in healthcare delivery, making medications and supplies available to healthcare providers and patients across North America. About one third of all North American pharmaceutical products flow through our facilities every day. We're passionate about our mission to improve care in every setting, one product, one partner and one patient at a time. If you visit one of our more than 30 distribution centers you will probably walk under a banner that reads "It's not a package, it's a patient".

Understanding Drug Shortages

While the U.S. supply chain is part of a global system which is fragmented and complex, it has proven to be resilient in times of crisis. Today, distributors connect approximately 1,400 manufacturers to over 330,000 sites of care, and safely and securely deliver approximately 11 million products daily.

While drug shortages affect only 1% of all prescriptions, we know even that small percentage can have a significant impact on caregivers, healthcare providers, and most importantly, patients.

Drug shortages occur when commercially available supply of a drug does not meet demand. It is important to distinguish whether the occasional disconnect between supply and demand reflects true supply limitations, or temporary gaps in access.

Our view is that most drug shortages fall within three key categories: market-wide supply constraints, product-specific issues, and reimbursement and market access limitations.

Common causes within those categories include sourcing or manufacturing limitations, natural disasters, market economics, changes in prescribing or patient demand patterns, and product discontinuation. Key drugs and classes making headlines demonstrate the range of root causes, but also highlight the need for unique solutions.

While each drug shortage is unique, together, we can strengthen supply chain resiliency by understanding the root causes and deploying targeted solutions. McKesson's primary commitment is to get critical medications to our providers and the patients they serve. That commitment is foundational to our reliable and sustainable sourcing initiatives.

Predicting & Managing Drug Shortages

At McKesson, we are continually improving our processes, building redundancy and contingency-planning to proactively predict, identify, and mitigate drug shortages. A few examples include:

- Data Driven Solutions: Use real-time insights, predictive analytics, and AI capabilities to align our evolving supply and demand needs, anticipate shortages, and provide insights for channel participants about how to manage their inventories.

- Critical Care Drug Task Force: Multidisciplinary team of clinicians and supply chain experts that monitor, communicate, and respond to supply chain trends and needs; engage targeted customers as needed for feedback and assess cost sensitivity.
- Supply Optimization: Optimize inventory despite constraints, secure backup product and alternatives where available, and obtain supply from multiple manufacturers, when possible.
- Diversify Supplier / Manufacturer Partners: Open contracting and formulary model allows us to diversify partners and bring on new market entrants at all times.
- New Market Entrants: We support emerging and diversified suppliers with new product launches to bring greater supply to market.
- Equitable Allocation: When supply constraints occur, we work diligently to ensure equitable distribution of available supply across all our customers based on their ordering history.

As part of our proactive approach, we deploy a supply chain risk assessment. First, we examine risk across three key domains: clinical & patient need, supply vulnerability, and manufacturer resilience. Clinical and patient needs are paramount. We examine the drug's indication and impact on clinical regimen – meaning is it curative, is it foundational to common treatments, are there clinical alternatives? We also examine relevant operational differences between products, like refrigeration or special handling requirements. We evaluate supply vulnerability by determining the number of manufacturers in the market, the number of active pharmaceutical ingredient (API) sources, any history of disruptions, potential impactful regulatory actions, or geopolitical considerations.

Finally, we assess manufacturer/supplier resiliency. We examine their size, capacity, service lines, growth potential, regulatory actions, performance history and business health. We rely on our experience with them – past performance is often an indicator of future performance. We are limited, however, in utilizing data that is publicly available or willingly shared by the manufacturer or supplier.

For those drugs with the greatest clinical impact on patients, such as curative cancer treatments, we prioritize:

- Diversifying our suppliers
- Diversifying manufacturing sites and/or API sources
- Increasing monitoring or check-ins
- Long-term contracts
- Securing supply
- Supporting new market entrants
- Diversifying and bolstering access to GSI products

McKesson Public Policy Recommendations

A robust, competitive market is one that naturally buffers against drug shortages.[1] Government interventions should correct the market to its natural competitive state and be careful not to create misaligned incentives that could further exacerbate shortages. Policymakers should focus on products most at risk of shortage like generic sterile injectables, particularly those for cancer patients.

We also note that supply-side shortages are often the result of upstream supply chain issues. Distributors have limited insight and even less control over these problems. We defer to manufacturers on what specific investments should be made to address those issues.

On other root causes, we offer the following recommendations:

Reimbursement and Market Access Incentives

The right incentives could make it financially appealing for new market entrants or existing manufacturers to invest in the necessary redundancies and quality programs to guard against supply disruptions. This will require significant investments to bolster the market and economic opportunity for historically competitive, low margin drug classes and those which rely on a limited number of global manufacturers (e.g., two or less). Determining drugs eligible for such programs and the duration of such efforts is imperative. Initiatives must not generate misaligned incentives to create or maintain a drug shortage.

Programs must have clear guardrails and metrics to ensure market correction and program exploitation are prioritized. Efforts must be led through public-private partnerships between federal agencies (e.g., FDA, CMS) and key stakeholders across the supply chain, including but not limited to manufacturers, distributors, patient advocacy organizations, and impacted physician specialty organizations. We outline key opportunities below:

- **Enhance Medicare Access and Reimbursement:** Mandatory equitable or favorable formulary placement under Medicare Part D could fuel greater competition, especially for biosimilars and competitive drugs classes. Formulary exclusivity contracts can make it difficult for new market entrants to secure enough patient volumes to make manufacturing investments. Mandatory coverage could level the playing field and address some access barriers. Additionally, enhanced reimbursement for drugs across therapeutic classes with a history of shortages or risk of shortage within Medicare programs can create economic favorability to support investment or reinvestment in manufacturing capabilities.
- **Limit Federal Program Rebate and Pricing Requirements:** We should consider modifying current policies and contemplate when it is best to allow manufacturers to 'reset' prices[2] to reflect the current cost of producing goods, or at minimum buffer against additional penalties that make necessary price increases disadvantageous.
    - *Inflation Reduction Act (IRA) Inflationary Rebate Penalties:* The IRA[3] does contain some level of safeguards to protect eligible inflationary rebatable Medicare Part D and B drugs that may be susceptible to shortage. However, this discretion is left to the Health & Human Services (HHS) Secretary and does not define the parameters for a drug becoming "eligible" for exemption, the market data/criteria needed to make such assessments, or the duration of a drug being excluded. We recommend codifying exclusions more clearly to create better economic safeguards for drugs in shortage and those at risk of shortage.
    - *Medicaid Drug Rebate Program (MDRP) Average Manufacturer Price (AMP) Cap Penalties:* Manufacturers of brand and generic covered outpatient drugs must pay each state Medicaid program a statutory rebate to participate in the program. The Medicaid Rebate is currently capped at AMP. Starting January 1, 2024, drugs facing Medicaid rebates higher than AMP will no longer by capped at 100% of the drug's AMP. This is likely to create considerable market constraints and may further drive manufacturers out of the market. We recommend suspending all MDRP rebate requirements for an established period of time to allow manufacturers to invest in the production of drugs in or at risk of shortage. We recognize the magnitude of impact will depend heavily on which drugs are eligible for such a safe harbor, and therefore recommend that at a minimum, penalties remain capped at 100%.

        - *Inclusion of inflationary penalties on generic drugs in the MDRP*: As a result of these penalties, when generic manufacturers pull their drugs from the marketplace due to pricing economics, the remaining manufacturers have no flexibility to raise prices when they are adversely impacted by the MDRP inflation rebates. We recommend suspending inflation penalties on generic drugs that are in shortage.
    - *Modify the 340B Program:* Federal pricing programs, such as a 340B ceiling price, can deter market entry of new generic manufacturers. We recommend temporarily excluding certain drugs (e.g., low-cost generics, critical drugs in or at risk of shortage) from the program or limiting the ceiling pricing to avoid "penny pricing" challenges (e.g., make ceiling price equal to AMP). This exclusion should accompany specific quality and production goals for manufacturers.
- **Quality-Based Incentives:** Ensuring quality of medicines, including manufacturer and supplier resiliency, is paramount to a safe and stable drug supply chain. In addition to product quality requirements, rewarding manufacturers that adopt quality best practices is a sensible and worthy pursuit. Integrating quality within drug manufacturing is not a new concept. For years, FDA has contemplated the need for a Quality Management Maturity (QMM) program for greater manufacturer transparency and is currently soliciting public comments on how to create a voluntary program[4]. Integrating business and manufacturing incentives is foundational to building global supply chain resiliency. As such, quality-based incentives such as accelerated approvals, vouchers, and enhanced payments for manufacturers demonstrating exceptional quality practices are appropriate. We support incentivizing a culture of quality, and whether done through FDA or industry-prescribed metrics, believe that improving global quality will favorably impact drug shortages. It is important to note that direct purchaser organizations conduct their own quality due diligence during sourcing. Such diligence may include a review of prior FDA inspections, product recalls, site inspections, and other quality assurance assessments.

Supply Preservation Programs

Improving access and preservation of API bolsters global supply chain resiliency. This requires creating and aligning incentives across the supply chain that go beyond on- or near-shoring manufacturing capabilities. For maximum benefit, all efforts must be contemplated in coordination with federal and state Strategic National Stockpile (SNS) efforts.

- **Incentives for Buffer Stock Programs:** If implemented with the appropriate safeguards, creating incentives for manufacturers to maintain a 3 to 6-month reserve capacity of critical medicines could be another solution for drug shortages in certain therapeutic categories. Manufacturers should further be encouraged to maintain reserve capacity of APIs and other necessary ingredients for emergency production, if needed.

In order to prevent against inadvertently aggravating a drug shortage, these programs should be made available to both hospital and community providers. While we support CMS's overall goal of creating a buffer stock incentivization program for hospitals as early as CY 2024, we believe that the current proposal could further exacerbate access gaps if additional sites of care are not included. As the recent cancer drug shortage has demonstrated, creating safeguards in only one part of the care delivery ecosystem disproportionally disrupted access for patients unable to seek care in hospitals or Cancer Centers of Excellence. Buffer stock programs should include core capabilities to support the safe and efficient storage, management (e.g., staffing, record keeping), and rotation of supply (e.g., virtual vendor managed inventory). Additionally, since demand can fluctuate regionally and by individual customers, the

ability to seamlessly pass product both regionally and nationally should be a key attribute for entities facilitating buffer stock programs.

Most providers and manufacturers may not have the infrastructure and core capabilities necessary to operationalize buffer stock programs. Distributors are ideally positioned to serve in this role and should be recognized as preferred partners to entities working on behalf of providers or manufacturers. Should CMS elect to move forward with permitting a buffer stock program(s), it is important that the agency has methods for evaluating impact to the supply chain, and tactics ready to deploy should unintended consequences be observed.

Supply Chain Visibility

Enhancing the integrity of our global supply chain necessitates greater visibility and insight into the original source of excipients (inactive substances that serve as the vehicle or medium for a drug or other active substance), APIs, and finished dosage products. We continue to support efforts to improve data collection from manufacturers to improve our understanding of potential supply chain vulnerabilities. The ongoing collaboration between distributors and FDA and Administration for Strategic Preparedness and Response (ASPR) continues to provide valuable insights.

Where FDA and ASPR may see market softness across distributors, early warning signals should be shared with distributors to optimize our ability to respond. For example, while distributors continue to diversify our supply sources, lack of "origin" insights prohibit us from ensuring our efforts are truly creating safeguards or simply new sourcing routes to the same "origin" source. Additionally, while distributors conduct their own partner evaluations to ensure suppliers meet core quality metrics, these may not uncover the same vulnerabilities as identified in FDA evaluations.

We recommend the private sector and federal agencies maintain an open dialogue - one that encourages sharing data and insights while protecting commercial interests. The focus should be on the exchange of required information, rather than onerous reporting requirements. We must continue to build trust across public-private partnerships in order to effectively identify early warning signs that a shortage may be on the horizon.

To avoid unnecessary burdens, there should be clarity on the criteria for inclusion of APIs or finished product(s) on the critical medication shortage list. Similarly, when that drug is no longer on the shortage list and there is evidence that market supply has stabilized, then reporting requirements should be rescinded.

McKesson believes solving drug shortages requires the collaboration of all the stakeholders in the supply chain, and we are committed to doing our part. By addressing the highly variable root causes, bolstering supply preservation efforts, and improving communication between stakeholders, we can make meaningful progress in protecting the health of our nation.

For more information on McKesson's pragmatic, solutions-oriented approach to mitigating drug shortages, please visit www.mckesson.com/drugshortages.

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[1] Experience with the Generating Antibiotic Incentives Now (GAIN), passed in 2012, demonstrates that without the appropriate reimbursement and market access incentives, manufacturers are reticent to invest in the development and marketing of drugs when presented with incentives focused on expedited FDA reviews and extended exclusivity

alone. Source: https://www.fda.gov/news-events/fda-brief/fda-brief-fda-reports-its-progress-advancing-policies-developing-next-generation-antibiotics

[2] "Resetting" price in this context means allowing a manufacturer to establish a once in a lifetime "new" price for a drug for the purposes of Federal drug reporting programs, such as 340B and the MDRP. As such, 340B ceiling price and MDRP Average Manufacturer Price (AMP) calculations would start anew and not be subject to the restrictions of predecessor market dynamics.

[3] U.S. Congress. HR 5376 Inflation Reduction Act of 2022.

[4] Food and Drug Administration. Quality Management Maturity Program for Drug Manufacturing Establishments; Request for Comment. Sept 15, 2023.

Chairman SMITH. Thank you.
Mr. Coukell, you are now recognized.

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

Mr. COUKELL. Thank you, Chairman Smith, Ranking Member Neal, and members of the committee. I appreciate the opportunity to speak with you today about drug shortages, their causes, and policies to prevent them. 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 more than a decade of chronic drug shortages, realized that the market is not self-correcting and that a different approach is required. They created Civica as a non-profit with a mission to deliver a safe, stable, and affordable supply of medicines to U.S. patients.

In our first five years of operation, our hospital membership has grown to 1,500 hospitals. We supply more than 80 drugs today, with more than 150 million vials delivered to date. And, with U.S. government support, we have built a state-of-the-art manufacturing facility in Petersburg, Virginia.

Civica chooses drugs not for their return on investment. In fact, they are chosen by hospitals because they are in shortage or at risk of shortage. They tend to be old and low-cost products, but absolutely essential to patient care and used in every hospital every day.

Because of our mission, Civica takes a different approach 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 six-month buffer inventory of every drug to ensure continuity of supply. We also emphasize U.S. sourcing whenever possible, with Canada and the EU as our next preference. We don't source from China unless there is no other option. And, to reduce the risk of a failure to supply, we perform an intensive quality audit of our potential suppliers with ongoing data, metrics, and quality reviews. And every drug is sold at the same price to any purchaser.

The success of this approach has been proven. In fact, 20 of our top 25 drugs are currently a national shortage, and yet we are supplying our member hospitals without interruption. When a tornado hit a manufacturing plant in North Carolina a few months back, Civica let our member hospitals know that we could supply double their committed volume for all of the drugs we supplied that overlapped with those from that facility. And recently a top—a study in a top medical journal showed that supply through Civica was both more reliable than conventional sources, but also produced net cost savings to the health care system.

So the resilience of this model points to steps the 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 the 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 this equation, but there is more to be done. Without changes, shortages will get worse, not better.

The immediate cause of most shortages of injectable drugs is a quality problem with the manufacture of the finished dosage form. But the root cause is widely acknowledged to be low prices. And it is remarkable when you think about it. An injectable prescription drug that requires extensive testing, development, has a complex supply chain, exacting manufacturing, and regulatory approval required then sells for less than a bottle of water from the corner store. These low prices reduce the incentive and ability of manufacturers to invest in quality or in newer facilities. That pushes production offshore to low-wage markets, where quality problems proliferate and the FDA presence is inconsistent.

So policy responses to shortages need to change the market, including measures to incentivize or encourage providers to contract for adequate buffer inventory, evaluate manufacturer quality on an ongoing basis, and choose ones that are less likely to have supply 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. At a modest cost of about $4 million per drug, Congress can ensure that we have a backup domestic manufacturing capacity ready to go when a shortage starts. If the United States had made this investment in cancer drugs five years ago, we would have been prepared for the shortages that we are experiencing today. We have the opportunity now to make a targeted investment to protect the drug supply in the future.

Thank you again for your attention, and I welcome your questions.

[The statement of Mr. Coukell follows:]

Testimony of

Allan Coukell, BSc (Pharm.)

SVP Public Policy, Civica Inc. (Civica Rx) & President, Civica Foundation

Presented before the United States House of Representatives

Ways & Means Committee

Hearing on:

"Examining Chronic Drug Shortages in the United States"

06 February 2024

Summary of Testimony:

- Civica is a non-profit generic drug company created by US health systems and philanthropies to address drug shortages.
- Civica currently delivers 80+ drugs, all chosen by US hospitals because they are at risk of shortage, with more than 150 million containers delivered over five years.
- The "Civica model" is designed to ensure a resilient supply and relies on:
    - Long-term purchase and supply contracts that add stability to the market. Civica contracts directly with hospitals, rather than through middlemen that may contribute to price and supply instability.
    - Maintaining approximately 6-month buffer inventory of every drug
    - US sourcing whenever possible, with the EU and Canda as a second choice. We don't source finished drugs or API from China unless there is no other source.
    - Intensive quality oversight of suppliers.
    - A single cost-plus price, available to every purchaser.
- A peer-reviewed study shows that the Civica model is both a more reliable supply than the conventional wholesaler model and produces net cost savings.
- Using its authority over providers, the Committee should incentivize or encourage systemic changes that lead to generic injectable drug purchasing strategies that include:
    - Measures to ensure adequate buffer inventory.
    - Measures to ensure that generic sterile injectable drugs are priced sustainably; and
    - Measures to create market demand from manufacturers that are less likely to have quality failures.
- In addition, Congress can, at a modest one-time cost, create an "insurance policy" so that quality U.S. manufacturers are ready to produce priority drugs when a shortage starts.

Full Testimony

Chairman Smith, Ranking Member Neal, 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 non-profit 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 several manufacturers have experienced quality problems, causing them to permanently or temporarily leave the market. Cancer drugs are among the products of highest current concern, but shortages affect all 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 are a non-profit, non-stock organization founded 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 to deliver a safe, stable, and affordable supply of essential medicines to U.S. patients.

In its five years of existence, Civica's hospital membership has grown to 55 health systems, accounting for one-third of licensed beds in the United States. Participating hospitals are large and small, urban and rural, non-profit and for profit.

To date, we have supplied 155 million containers of generic sterile injectable drugs – currently 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, Virginia.

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 particpating hospitals.

These drugs 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 US system. In particular:

- Civica enters long-term purchase and supply contracts that add stability to the market. Civica contracts directly with hospitals, rather than through middlemen that may contribute to price and supply instability.

- 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 Canda 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, Virginia, 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, North Carolina, 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]

Causes of shortages

[1] ASHP Drug Shortage list as of 28 NOV 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

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]

Policy responses

Therefore, policy responses should focus on changing the current system that causes shortages because it favors acquisition at the lowest possible price over resiliency of supply. While Civica 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

[3] For example, see FDA "Drug Shortages: Root Causes and Potential Solutions," 2019; Brookings "Federal Policies to Address Persistent Generic Drug Shortages," 2023; Duke Margolis, "Advancing Federal Coordination to Address Drug Shortages" 2023.

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. Holding buffer inventory "upstream" of the provider also reduces the risk of hoarding during a shortage.

The Centers for Medicare & 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:

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

- 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;
- 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

It is possible to predict with high accuracy which drugs will go into shortage in the future. (Largely because the strongest predictor of a future shortage is a past shortage.) If it chooses to do so, Congress can ensure that quality U.S. manufacturers are ready to manufacture drugs that are at high risk of shortage – a kind of "insurance policy" against future shortages that can be accomplished at modest cost.

Current low market prices – often below $4 for a vial – make it financially infeasible for US manufacturers to develop many of these products and find commercial sales at today's prices. However, it takes a manufacturer roughly two 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 (that is, 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. This could be done at the cost of a one-time investment of $3 million to $4 million per drug.

Conclusion

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

Chairman SMITH. Thank you.
Dr. Schondelmeyer, you are now recognized.

STATEMENT OF STEPHEN SCHONDELMEYER, PHARMD, PHD, DIRECTOR OF THE PRIME INSTITUTE, UNIVERSITY OF MINNESOTA'S COLLEGE OF PHARMACY

Mr. SCHONDELMEYER. Thank you, Mr. Chairman, and thank you, Ranking Member Neal and committee. I am Stephen Schondelmeyer, I am a professor of pharmaceutical economics and management at the University of Minnesota, and I also direct a resilient drug supply project.

Over my 50-year career, I have studied virtually every drug product that is on the market in the U.S. I have databases with information on those drugs and their prices and their availability and issues over time, and I have used that database to learn and understand the market.

First, let me point out that the relatively recent COVID–19 pandemic isn't the primary reason for drug shortages. It has had a bump in drug shortages and increased it a bit, but really, COVID–19 has exposed vulnerabilities that we didn't realize previously, and we have some new emerging vulnerabilities that are coming out in this market, and those are the things I will address.

I agree with my colleagues. I agree with the chairman and ranking member and their comments about the patient harm and critical nature of shortages, but I am going to address geopolitical risk, quality of production issues, and potential trade barriers and their impact on drug shortages.

Basically, geopolitical risk is a term that we are using more and more these days to talk about vulnerabilities that may be related to the geographic location of where something happens, may be related to the political orientation of where something happens, or both. And, in pharmaceuticals, we have situations where geopolitical risk is both locational and political in terms of affecting availability of drugs or potentially affecting them.

Among the things that are important in pharmaceuticals and geopolitical risk are where active pharmaceutical ingredients are made and their key starting materials, and where finished dosage forms are made. And I would remind you, when I go to the grocery store or the clothing store, I can look at the label and see where the product was made. In pharmaceuticals, that isn't always the case. And, even if it does say where the product was made, you don't know if that is where somebody put it in the box and called it being made in that country, or where they actually made the capsule or tablet, or where they actually made the chemicals that go into the drug. And all three of those are important in drug supply chains, and yet the market is very opaque with respect to where products come from.

A stable drug supply relies on complex interdependencies in international relations, both politically and commercially. The United States is heavily dependent on foreign manufactures for active ingredients and finished dosage forms. We get—about 45 percent of our finished dosage forms and as much as 60 percent of our active ingredients that are in products that people take every day in America come from either China or India. So we are heavily de-

pendent on these two countries. That is not necessarily bad. It is not to say that their products aren't good all of the time, but there are issues with that.

I would point out from our research at Minnesota that about 80 percent of all U.S. doses taken every day by Americans come from foreign sources. China and India, as I said, are responsible for 45 and 60 percent, respectively, of those. There are about 100 drug products that the only place the active ingredient is made in the world is China. It is not made in the U.S., it is not made anywhere else. And so, if China chose to develop trade policies that prohibited export of those drugs, we wouldn't have any in the U.S.

Now, we have companies that could begin to make those, but it may take one, two, three years to come on the market. So I believe in markets, and I believe markets do self-correct over time, but that—the catch is in over time, and the U.S. market, and particularly with pharmaceuticals, we can't begin making a product as quickly as you could make a clothing item or other goods. So we have to take into account the timelines in pharmaceuticals.

I would point out some trade barriers. During the COVID pandemic, India put an embargo on or an export ban on about 25 products and was going to ban shipping them because they wanted to make sure they had enough product for their own country. They later reversed that. But, if every country in the world took this protectionist approach, only the producing companies would have product and the non-producers wouldn't. And I remind you of the generics we have in the U.S. market: 80 percent aren't produced in the U.S. So what is going to happen if everybody else starts protecting where they produce the drug? We won't have generics.

One final comment on what could happen is you might have recently heard that Florida was approved by the FDA to start a reimportation program, a very important concept. And I have worked with and advocated consideration of such policy over time. As soon as Canada heard that that was approved and it might actually happen, Canada passed a law prohibiting export of drug if it resulted in a shortage in Canada. So we are going to have to have the U.S. administration and the trade representative and Department of Commerce and others work together with Canada if that is ever going to work.

My final point is the upstream drug supply in the U.S. needs to be mapped comprehensively and continuously to identify vulnerabilities and help us prepare with coordinated responses.

[The statement of Mr. Schondelmeyer follows:]

Statement on

A Resilient U.S. Drug Supply: Current & Emerging Vulnerabilities

at the House Hearing on

Chronic Drug Shortages in the United States

Statement before the

Committee on Ways & Means
United States House
Congress of the United States
Tuesday, February 6, 2024, at 10:00 a.m.
1100 Longworth House Office Building.

Statement of

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94-0419A

Thank you Chairman Smith, Ranking Member Neal, and other members of the House Committee on Ways & Means for this opportunity to address "A Resilient U.S. Drug Supply: Current & Emerging Risks."

I am Stephen W. Schondelmeyer, a Professor of Pharmaceutical Management & Economics at the University of Minnesota where I serve as Co-Principal Investigator for the Resilient Drug Supply Project (RDSP). In addition, I am Director of the *PRIME* Institute which focuses on research and policy issues related to the pharmaceutical market and its impact on society. These remarks are my own views based upon my research and experience in studying the pharmaceutical marketplace for the past fifty years. During my career, I have had the opportunity to interact with many federal entities that shape and influence our nation's healthcare system including the Department of Health and Human Services (DHHS), many of its divisions such as FDA, CMS, ASPE, ASPR, BARDA, as well as other federal agencies such as the FTC, DOJ, GAO, and OMB.

This hearing on chronic drug shortages in the United States will explore reasons for the long-term presence of drug shortages and the impact they have had on patients and the U.S. healthcare system. My remarks will address those issues as well as emerging vulnerabilities in the market infrastructure that are challenging the resilience of the U.S. drug supply.

First, let me point out that the relatively recent COVID-19 pandemic is not responsible for the chronic presence of drug shortages in the U.S., although COVID-19 has exposed and highlighted several new and emerging vulnerabilities including geopolitical risk, quality of production issues, and potential trade barriers.

The Nature of Chronic Drug Shortages and Why They Matter?
A reliable U.S. drug supply is an issue of public health, national security, and economic importance. Americans depend on a safe, accessible, and affordable drug supply for both personal and public health. When needed drugs are inaccessible for any reason, Americans suffer consequences such as lost days of work, disease progression and complications, increased emergency room visits, hospitalizations, and even premature death. *A robust drug supply chain is critical infrastructure for the health and well-being of the entire country, as well as the world.*

Life-threatening, critical drug shortages can, and do, occur in the U.S. market. For decades, the U.S. market has experienced substantial shortages of critical pharmaceuticals that can mean life or death for patients. Market forces alone have proven insufficient to resolve these challenges and have failed to provide a consistent drug supply chain. The COVID-19 pandemic did make issues in our upstream drug supply chain more visible. During the pandemic, there has been an increase in demand for many pharmaceuticals paired with numerous disruptions in supply chains. This has

further exposed systemic vulnerabilities in the pharmaceutical supply chain in the United States and around the globe. Even as we begin to emerge from the COVID-19 pandemic, the number of drug shortages has not abated. In fact, a recent Senate hearing (March 2023) reported that "Drug shortages are increasing, lasting longer, and impacting patient care."[1] Between 2021 and 2022, new drug shortages increased by nearly 30 percent. By the fourth quarter of 2023 the ASHP reports a total of 301 current drug shortages, near an all-time high for active drug shortages in the U.S.[2]

In the United States we have tracked drug shortages for nearly three decades and the literature has reported on specific drug shortages well before our tracking systems were initiated.[3] Over the past decade, there have been 170 to more than 300 national active drug shortages at any point in time. In the fourth quarter of 2023, the American Society of Health-System Pharmacists (ASHP) reported 301 active drug shortages.[4] This level of drug shortages and consequences for Americans is clearly not acceptable.

When a patient does not get a critical acute drug in a timely manner (i.e., minutes to hours to days) the consequence can be serious leading to emergency room visits, hospitalization, or even premature death. In addition to the clinical impact on patients, there are economic costs for patients, providers, health systems, distributors, and other stakeholders. Health systems have been estimated to incur extra costs due to shortages for purchasing alternate products, adding staff, and notification and training of healthcare personnel.[5] These added costs may be as high as $230 million[6] to $359 million per year or more.[7]

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[1] Chairman Gary Peters, United States Senate Committee on Homeland Security & Governmental Affairs, HSGAC Majority Staff Report, Short Supply, The Health and National Security Risks of Drug Shortages, March 2023, p. 5.
[2] Fox, E, National Drug Shortages, Active Shortages by Quarter – 10 Year Trend, University of Utah Drug Information Service, American Society of Health-System Pharmacists, found on February 3, 2024 at: https://www.ashp.org/drug-shortages/shortage-resources/drug-shortages-statistics.
[3] Fox, E, Tyler L, Managing drug shortages: Seven years' experience at on health system, Am J Health-Syst Pharm, Vol. 60, Feb. 1, 2003, pp. 245-253.
[4] Fox, E, National Drug Shortages, Active Shortages by Quarter – 10 Year Trend, University of Utah Drug Information Service, American Society of Health-System Pharmacists, found on February 3, 2024 at: https://www.ashp.org/drug-shortages/shortage-resources/drug-shortages-statistics; see, also: Fox, E, National Drug Shortages, New Shortages by Year, January 2001 to December 2023, % Injectable, University of Utah Drug Information Service, American Society of Health-System Pharmacists, found on February 3, 2024 at: https://www.ashp.org/drug-shortages/shortage-resources/drug-shortages-statistics.
[5] Shukar S, Zahoor F, Hayat K, Saeed A, et al., Drug Shortage: Causes, Impact, and Mitigation Strategies, Frontiers in Pharmacology, Vol. 12, July 2021, found at: https://www.frontiersin.org/articles/10.3389/fphar.2021.693426/full.
[6] Rapaport L, Drug shortages may add $230 million to annual U.S. drug costs, Reuters Health, Sept. 10, 2018, found at: https://www.reuters.com/article/us-health-drug-shortages-pricing/drug-shortages-may-add-230-million-to-annual-u-s-drug-costs-idUSKCN1M12LC/.
[7] Gu A, Wertheimer AI, Brown B, Shaya FT. Drug Shortages in the US–Causes, Impact, and Strategies. (2011). Inov Pharm. Vol 2, p. 6.

Virtually everyone in America has used, or needed, prescription drugs at some point in their lifetime. In 2021, Americans took about 189 billion daily doses of prescription drugs and 90.7% of those doses were generic products vulnerable to drug shortages.[8] Most, but not all, drug shortages involve generic drug products which account for only 19% of invoice-level spending on prescription drugs while branded drug products account for 81% of invoice-level spending on prescription drugs, but only 9.3% of prescriptions by volume.[9] For this reason, assessments of the impact of drug shortages should be based on the volume of daily doses affected and the number of Americans impacted. Additionally, drug shortages tend to be found most often in drug products that are generics (84%), injectables (67%), and highly-concentrated markets with few suppliers.[10]

Chronic drug shortages continued even during the COVID-19 pandemic, and several emerging changes in the structure of the pharmaceutical market were exposed and highlighted new vulnerabilities in the upstream U.S. drug supply chain. I will briefly describe each of these vulnerabilities including geopolitical risk, quality of production issues, and potential trade barriers.

Geopolitical Risk & Drug Supply Resilience

Geopolitical risk is a term that encompasses vulnerabilities in the upstream drug supply chain due to geographic location, political orientation, or both for the country where key stages of pharmaceutical production are performed. Among these key stages are production of key starting materials, manufacture of active pharmaceutical ingredients (API), and manufacture of finished dosage forms (FDF).

A stable drug supply relies on complex interdependencies in international relations, both commercially and politically. The United States is heavily dependent on foreign manufacturers for its active pharmaceutical ingredients and finished products, particularly China and India. About 45% of finished dose form units and about 60% the active pharmaceutical ingredients (API) in drug products consumed in the U.S. market come from India and/or China. This level of concentration of drug production in specific geographic areas poses significant problems in the face of natural disasters or pandemics, accidental or intentional adulteration, and trade relations and geopolitical risk. Geopolitical conflict and degradation of international trade relations could prove

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[8] Aitken M, Kleinrock M, Drug Shortages in the U.S. 2023, The Use of Medicines in the U.S., Spending and Usage Trends and Outlook to 2025, IQVIA Institute, p. 25, May 2021, found at: https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/the-use-of-medicines-in-the-us-2023/the-use-of-medicines-in-the-us-2023.pdf.

[9] Aitken M, Kleinrock M, Drug Shortages in the U.S. 2023, The Use of Medicines in the U.S., Spending and Usage Trends and Outlook to 2025, IQVIA Institute, p. 49, May 2021, found at: https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/the-use-of-medicines-in-the-us-2023/the-use-of-medicines-in-the-us-2023.pdf.

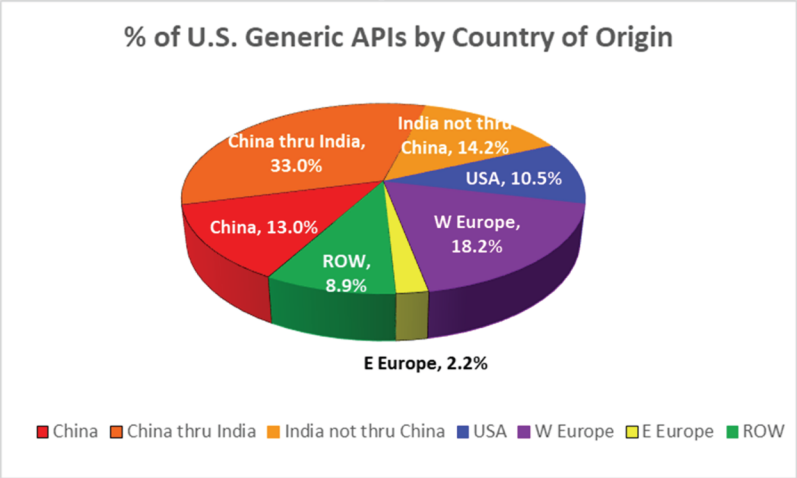
[10] Aitken M, Kleinrock M, Pritchett J, Drug Shortages in the U.S. 2023, A Closer Look at Volume and Price Dynamics, IQVIA Institute, p. 2, November 2023; found at: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/drug-shortages-in-the-us-2023.

catastrophic for the health and national security of all Americans including our military personnel. With drug shortages near an all-time high in the U.S., both the U.S. civilian population and military personnel are vulnerable to adverse health consequences from these critical drug shortages. Continued disruptions, either intentional or unintentional, in the upstream U.S. drug supply threaten the public health and national security of Americans.

Based on research at the Resilient Drug Supply Project (RDSP) using data from CGI Cortellis, FDA, and other sources, the following conditions in the upstream market create geopolitical vulnerability for the U.S.:

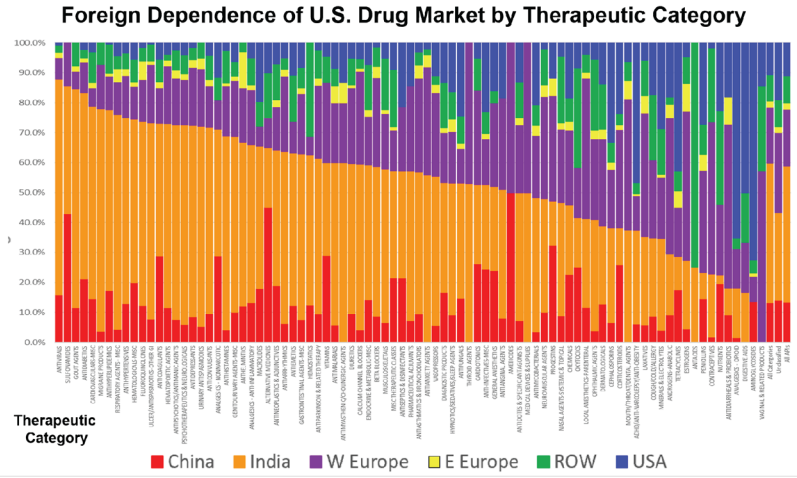
- The U.S. drug supply is heavily dependent on foreign sources with most generics coming from India and China and most patented brands coming from Europe.
- >60% of all U.S. daily drug doses have API or finished product from China or India.
- India is dependent upon China for about 70% of its API sources,
- India alone & India through China accounts for 47.2% of API facilities (Fig.1).
- China alone & China through India account for 46% of API facilities (Fig.1)..
- The U.S. accounts for only about 10.5% of the API facilities (Fig.1).
- Greater than 80% of the world's fermentation antibiotics are made in China.
- There are about 100 important APIs made only in China and nowhere else.
- There are about 229 important APIs made only in India and nowhere else.
- There are about 680 important APIs made only outside of the U.S.
- In the past decade, U.S. API facilities have dropped from 3,198 to 1,247 (-61%).
- In the past decade, India's API facilities have grown from 1,433 to 5,109 (254%).
- In the past decade, China's API facilities have grown from 962 to 1,494 (55%).
- In the past decade, Taiwan's API facilities have grown from 58 to 247 (326%).
- In the past decade, Israel's API facilities have grown from 108 to 250 (131%).
- The four countries with the fastest growing API capacity are geopolitical hot spots.
- Most therapeutic categories depend on India or China for >50% of their API facilities (Fig.2)..

Figure 1.



Source: Analysis by Resilient Drug Supply Project, University of Minnesota, based on data from CGI Cortellis and other sources, 2022.

Figure 2.



Source: Analysis by Resilient Drug Supply Project, University of Minnesota, based on data from CGI Cortellis and other sources, 2022.

Drug manufacturing has undergone a shift from in-house production to production through Contract Manufacturing Organizations (CMOs) and Contract Development & Manufacturing Organizations (CDMOs). Essentially the pharmaceutical manufacturer has become like the general contract for home builders—one firm coordinates all of the contributors who are building the house, but the general contractor does not actually 'make' the house. Also, it is not clear whether the FDA has the same degree of oversight for CMOs and CDMOs and their role in manufacturing drug products for the U.S. market.

Another shift in the drug manufacturing process for APIs and FDFs has been the move from U.S.-based facilities to facilities in Asian countries, especially India and China. Over the past two to three decades, many firms in the West looked to Asian countries for production of API and FDF because of lower cost of labor, lower cost of production, fewer environmental regulations, and economy of scale in production and other factors.[11] Asian countries usually have a 40% to 60% lower cost structure than Western nations when it comes to pharmaceutical production. As noted earlier, in just the last decade the number of U.S. API production facilities has decreased more than 60%. With strong cost reduction pressures, it will be difficult to move production of API and FDFs back to the West without substantial incentives.

The pharmaceutical market needs to move toward API production that has built-in redundancy of production sites. Dual sourcing, when possible, should be the minimum best practice with additional locations of production when the market is large enough to support them.

The U.S. and other countries should move toward regional markets with re-shoring and friend-shoring of redundant API production facilities. The U.S. can encourage some re-shoring of API production in the U.S., but it is also important to diversify the location of redundant API production facilities. For example, if two API facilities were built in Puerto Rico, a single hurricane could disable both of the redundant facilities. As a result of Hurricane Maria in 2017, a major share of the U.S. large volume parenteral solutions market was disrupted and hospitals throughout the U.S. had to find alternative products.[12]

The U.S. needs to have visibility into the market-wide upstream supply chain for API and FDF facilities and which products each one makes. This upstream drug supply map can then be used to target incentives to the products most needed and most likely to

[11] Bumpas J, Betsch E, Exploratory Study on Active Pharmaceutical Ingredient Manufacturing for Essential Medicines, Health, Nutrition and Population, The World Bank, September 2009, p.12.
[12] McGinley L, Hospitals scramble to avert saline shortage in wake of Puerto Rico disaster, Washington Post, Oct. 9, 2017, found at: https://www.washingtonpost.com/news/to-your-health/wp/2017/10/09/hospitals-scramble-to-avert-saline-shortage-in-wake-of-puerto-rico-disaster/.

experience drug shortages. Drug molecules with only one source of API production in the world are vulnerable, and especially if they are located in a country that is geopolitically sensitive. Also, even if there are two or three API production facilities, but they are located in the same country, there is more risk than if they are located in different countries.

Quality of Production Issues

The quality of drug products is of the utmost importance in the pharmaceutical market. The U.S. FDA has specific authorities and appropriations from the U.S. Congress with respect to the quality of production processes used by pharmaceutical manufacturers. Within the scope of their authorities, FDA has issued detailed guidelines for Good Manufacturing Practices that are to be voluntarily followed by pharmaceutical firms.

There have been concerns over the FDA's ability to assure quality with limited foreign inspection capabilities. Both the number of inspections done and the ability to engage in unannounced inspections, limit FDA's opportunity for meaningful inspections overseas. In recent years there have been a growing number of recalls and product withdrawals because of quality problems. Since 2015 companies have recalled products of more than ten drug molecules due to NDMA (or other potential carcinogen) contamination levels. FDA has also recalled batches of eye drops and baby formula because of bacterial contamination that led to patient harm and in some cases, deaths. While improved and increased frequency of inspections may be helpful in minimizing these quality issues, a broader approach to quality assurance is also needed.

In 1990, the U.S. FDA was a founding member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). There are now 13 countries who are regulatory members of the ICH who agree to participate and implement harmonized drug regulations. In addition to the United States, other countries participating as members of the ICH include Canada, Mexico, the European Union, Japan, China, and others. Notably, India is not a member of the ICH. Recall that India is the single largest producer of drug products for use in the United States, yet the country does not participate in the ICH.

Not only does India not harmonize with other countries on drug production and regulation, but the Indian regulatory scheme for pharmaceutical production is delegated to each of the 38 state entities within India. India's drug manufacturing and regulatory scheme is "a fragmented system spanning 38 drug regulators."[13] There is lack of coordination even within India. One observer noted that if one state finds a violation, the violation is not likely to be shared with other states or federal regulators.

[13] Kaul R, Govt plans common drugs standards for all state regulators, Hindustan Times, March 17, 2023, found at: https://www.hindustantimes.com/india-news/govt-plans-common-drugs-standards-for-all-state-regulators-101678990617259.html.

This situation needs to be addressed by the FDA, the U.S. Trade Representative, the Department of Commerce and other sources for exerting leverage on India to participate in the ICH for harmonization of drug regulation with the U.S. and other major world partners.

Emerging Trade Opportunities & Barriers

The U.S. needs like-minded trading partners to secure its drug supply chain. Re-shoring the manufacturing of both APIs and finished drug products can be part of the solution for a more resilient drug supply. However, it is not feasible for the United States to manufacture all, or even most, of its needed pharmaceuticals. Near-shoring to markets, such as Canada and Mexico or other places in the Americas, will allow for cost-effective production while affording improved geographic access and opportunities for strengthened trade partnerships. While drug firms in Mexico, and other countries in the Americas, have expressed interest in developing or increasing the production of APIs for export to the U.S., they would require significant policy support and subsidization to be competitive in the market with countries like China and India.

The U.S. should pursue trade partnerships with other countries in the Americas as alternative sources of pharmaceutical production. The COVID-19 pandemic has challenged global supply chains, in general, and, in particular, it has sensitized the United States to the heavy dependence it has on Asian countries and especially China and India. Currently, *U.S. policymakers are looking for alternative supply channels to decrease the U.S. dependence on China and India for critical and essential pharmaceuticals.* One solution is encouragement of re-shoring to the U.S. of pharmaceutical manufacturing for critical active pharmaceutical ingredients (API) and finished dose forms (FDF). In addition to increased U.S. production of pharmaceuticals, there is a need to develop geographically diverse supply chains that address environmental, economic, and geopolitical challenges.

Geographic diversity of supply sources is needed in the Americas. Mexico, Canada and other nearby countries can provide near-shoring of pharmaceutical production that can decrease the U.S. dependence on more distant Asian sources such as China or India. Near-shoring in Mexico, Canada or other countries in the Americas is a means to minimize over-concentration of production in Puerto Rico or the mainland of the United States.

Near-shoring can improve logistics and transportation. *Mexico, Canada and other nearby countries are geographically juxtaposed to the U.S. and offer more efficient shipping and logistical access.* For example, Mexico is strategically located at the southern edge of the United States where it shares a border with four states (i.e., Texas, New Mexico, Arizona and California). Mexico's proximity and physical border with the U.S. enable transportation and shipping routes by rail and road that are entirely

over land. This means that shipping of pharmaceuticals from Mexico can avoid more expensive and congested sea and air transport.

There may be a lower cost of production through near-shoring. *Mexico can produce pharmaceuticals at a cost that is 14.4% less than in the U.S.* By comparison, Canada can produce pharmaceuticals at a cost that is 4.6% less than the U.S. and in Italy, costs are about 1.9% less than in the U.S.[14]

Near-shoring can improve inspection access. Pharmaceutical production in Mexico would allow FDA to have improved access to manufacturing facilities for inspection and oversight. The FDA does have an office and staff based in Mexico, which would facilitate more frequent and efficient inspections for quality and Good Manufacturing Practices than can be achieved in Asian countries.

The COVID pandemic, however, precipitated some new trade issues with respect to pharmaceuticals. India, for example, imposed export curbs on 13 APIs and 13 drug product formulations.[15] These export bans were to ensure that India would have enough drug product to treat the Indian population. Under pressure India reversed the ban in one day. China imposed bans on masks and ventilators. Other countries instituted limited bans on exportation of drugs and medical supplies. Policy experts worried that if every country turned protectionist in the time of a pandemic, only producing countries would have supplies and others would be without needed drugs and medical supplies. One article recommended that "The world needs to change how it trades drugs."[16] The trade disputes were not over intellectual property rights, but rather access to exports of certain drug products used to treat pandemic-related conditions. China threatened to embargo trade of certain drugs which would have left the U.S. vulnerable or without those certain critical drug products.

One final trade issue with respect to prescription drugs is the importation of drugs from Canada under a program proposed by the State of Florida. On January 5, 2024, the FDA authorized Florida's drug importation program.[17] The Florida program is limited to providing drugs under certain state-run health programs through the Department of Children and Families, the Department of Corrections, and the Department of Health.

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[14] PharmaBoardroom.com, Mexico: Healthcare & Life Sciences Review, Nov. 2015, p.39.
[15] Wallace D, India Curbs Exports Amid Coronavirus, Restricted Products, Include Paracetamol API and Formulations, Generics Bulletin, Mar 4, 2020.
[16] Tripathi S, The World Needs to Change How It Trades Drugs, Foreign Policy, April 21, 2020..
[17]

Prior to approval of the Florida plan, the FDA did not permit importation of prescription drugs from Canada although there were a few very specific exceptions. Upon hearing of the FDA approval of the Florida reimportation plan, the Canadian government took action to ban export of prescription drugs from Canada, if the export would leave Canadians without needed medications.

This FDA-Florida-Canada interaction over importation of prescription drugs from Canada at a low cost will need active intervention by the U.S. administration including the FDA, the U.S. Trade Representative, and the Department of Commerce, if it's going to work. Keep in mind that Florida has a population of 21.8 million while Canada's population is 38.5 million. A robust importation program by Florida could deplete a major portion of the drugs in the Canadian market--and Canada is not likely to let that happen.

Strategies to Minimize Geopolitical Risks & Other Vulnerabilities

Just as the U.S. would not rely on its enemy for bullets, neither should we rely on a major geopolitical rival for critical drugs to treat the U.S. population or military forces—the source of our drug supply is a matter of national security. The U.S. needs to have a strategic plan for drug supply with policies and incentives to ensure a secure and resilient supply of all essential and necessary drugs. Continuous work is needed to identify risks and secure the supply of key starting materials and API for critical pharmaceuticals. The U.S. needs improved quality inspection and enforcement to prevent unintentional drug quality problems from lack of voluntary compliance and inadequate regulatory oversight (e.g., India, China, or even at facilities in the U.S.). The U.S. needs intensified security and quality monitoring to prevent deliberate attacks and threats posed by drug production in politically adverse settings.

The U.S. needs to encourage more re-shoring, near-shoring and friend-shoring of API and finished drug production especially for critical drugs, increased transparency of drug production sourcing, and de-risking of the supply chain. The U.S. lacks a centralized system to effectively map, track, predict, and respond to drug shortages. The FDA itself reports difficulties monitoring the production, quality, and distribution of active pharmaceutical ingredients (APIs) in foreign countries, especially in locations such as China and India.

The upstream drug supply chain in the U.S. needs to be mapped in order to identify vulnerabilities, to prevent disruptions, and to prepare coordinated responses. There is a need for an international global system for addressing drug shortages and their causes so that preemptive action can be taken to prevent future drug shortages. Comprehensive information on drug supply and drug shortages is needed to provide awareness of vulnerabilities that is timely and transparent enough to predict and respond to drug shortages before the public faces real and significant consequences.

Chairman SMITH. Thank you.
Dr. Gralow, you are recognized.

STATEMENT OF JULIE GRALOW, MD, CHIEF MEDICAL OFFICER AND EXECUTIVE VICE PRESIDENT, ASCO

Dr. GRALOW. Thank you, Chairman Smith, Ranking Member Neal, and members of the committee. It is my pleasure to appear before you to discuss the drug shortage crisis. I am Dr. Julie Gralow, chief medical officer and executive vice president of the Association for Clinical Oncology, or ASCO. I am a professor emeritus of medical oncology and global health at the University of Washington School of Medicine.

ASCO is a leading professional organization representing nearly 50,000 oncology professionals dedicated to improving cancer care. We appreciate the committee's dedication to addressing drug shortages. Every day, we hear from oncologists about the challenges they and their patients are facing. The drug shortage crisis is forcing providers to make impossible choices, including deciding which patients receive lifesaving and life-prolonging cancer drugs on schedule and in established doses, or whether they are left to use suboptimal alternatives, reduce doses, delay treatments, and, in the worst situations, are unable to provide necessary therapies.

An oncologist in Texas shared that a patient's breast cancer was responding to a commonly used oncology drug, carboplatin, in combination with immunotherapy. After four cycles, the cancer was under control. She stopped receiving the carboplatin due to the shortage, but continued the immunotherapy, and unfortunately, her cancer quickly progressed.

An oncologist in California sent a patient with bladder cancer to an academic center to participate in a clinical trial, primarily because that was the only way to guarantee access to cisplatin, another drug in shortage. The oncologist saw clinical trial enrollment as the only way to achieve the standard of care that his office could not provide.

An oncologist in Puerto Rico could not treat a head and neck cancer patient with the preferred regimen because the practice was projected to run out of the drug during the treatment. The physician and the patient were forced to select an alternative.

You can imagine the tremendous emotional toll this places on patients and their families. These deeply troubling choices my colleagues frequently face amid the drug shortage crisis are emotionally taxing the entire health care team. The staff time and expense of managing shortages includes looking for supply, allocating limited drugs, changing treatment plans, and counseling patients.

The U.S. must establish a more resilient pharmaceutical supply chain. Most oncology drugs in shortage are generic, sterile injectables that sell for $1 to $8 per dose, leaving these drugs with slim profit margins, sometimes with production costs exceeding the selling price, and often driving manufacturers out of the market or looking to manufacture outside of the U.S. to keep costs down. There are few manufacturers of sterile injectables, and they face significant costs to stay in business.

The leading cause of drug shortages is manufacturing quality issues, largely driven by economic factors. Disruption from quality

issues can leave the manufacturer unable to ramp up production for months and at significant expense. When one manufacturer experiences quality issues, the entire market is impacted. If another manufacturer is willing to enter the market to shore up, supply can take months to get FDA approval and get production up and running due to the complexity of sterile production requirements.

Current drug payment policies compound quality issues. Purchasers have limited information, typically only price data, and don't have access to manufacturing quality or supply information. This creates adverse market incentives for manufacturers to prioritize cost cutting over quality improvements or capital investments. It is particularly challenging for generic oncology drug manufacturers who operate on a slim or even negative profit margin.

Approximately half of all newly diagnosed cancer patients are over 65 years old, making Medicare the largest payer of cancer care in the country. As such, Congress can take immediate action in three areas: payment, manufacturing, and quality. Congress could explore alternative payment methodologies to provide relief from artificially low generic reimbursement rates, encouraging a more reliable supply of drug. Payment reform should factor in quality and reliability of supply.

In manufacturing, Congress could encourage the adoption of advanced technology, such as continuous manufacturing for critical drugs and Active Pharmaceutical Ingredients. Incentives such as tax credits or government contracts could help increase manufacturing in the U.S.

Finally, in the area of quality, Congress could consider stronger requirements for risk management plans and incentives for purchasers to contract with manufacturers who demonstrate quality and the ability to provide reliable supply.

The shortage of critical cancer drugs is a crisis. Cancer patients and their families deserve to know that they will get the care they need without delay. Providers should not have to make heartbreaking choices about patient care. We must act. ASCO stands ready to collaborate with you to advance comprehensive solutions.

[The statement of Dr. Gralow follows:]

Testimony of

Julie R. Gralow, MD, FACP, FASCO

Chief Medical Officer and Executive Vice President

Association for Clinical Oncology

Before the

United States House Committee on Ways and Means

Examining Chronic Drug Shortages in the United States

February 6, 2024

Chairman Smith, Ranking Member Neal, 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. Julie Gralow, Chief Medical Officer, and Executive Vice President for the Association for Clinical Oncology (ASCO). I am Professor (emeritus), Medical Oncology and Global Health, at the University of Washington School of Medicine. Previously, I was the Jill Bennett Endowed Professor of Breast Cancer at the University of Washington School of Medicine, Professor in the Clinical Research Division of the Fred Hutchinson Cancer Research Center, as well as Director of Breast Medical Oncology at the Seattle Cancer Care Alliance.

ASCO is a leading professional organization representing nearly 50,000 oncology professionals, including physicians, researchers, and other healthcare providers dedicated to improving cancer care. ASCO appreciates the Committee's dedication to addressing drug shortages.

Every day we hear from oncologists around the country about the challenges cancer patients and their providers are facing, amid some of the worst oncology drug shortages to date. This crisis is forcing providers to make impossible choices, including having to decide which patients receive lifesaving and life-prolonging oncology drugs on schedule and in the established doses or whether we're left to use sub-optimal alternatives, reduce doses, delay treatments, and in the worst situations, are unable to provide any of the necessary therapies.

An oncologist in Texas shared that a patient's metastatic breast cancer was responding to a commonly used oncology drug, carboplatin, in combination with immunotherapy. After four cycles, her cancer was under control. She stopped receiving carboplatin because of the shortage, but continued immunotherapy and unfortunately, her cancer has progressed.

Another oncologist in California sent a patient with bladder cancer to an academic center to participate in a clinical trial because that was the only way to guarantee they would have access to cisplatin, another drug in shortage. Clinical trials assess whether an experimental treatment *is better*

than the traditional standard of care. In this case, though, the oncologist saw clinical trial enrollment as the only way to achieve *at least* the standard-of-care that his office could not provide.

An oncologist in Puerto Rico could not treat a head and neck cancer patient with the preferred regimen because the practice was projected to run out of the required drug during the treatment cycle. The physician and patient were forced to select an alternative. As you can imagine, this places a tremendous emotional toll on patients and their families.

These are the deeply troubling choices that my colleagues frequently face amid the drug shortage crisis, emotionally taxing the entire health care team. The oncology care team is compelled to deviate from recommended practice guidelines, either by working with unconventional and unproven treatments or by determining the allocation of scarce resources. When physicians are forced to opt for the non-standard of care, the already burdensome process of acquiring prior authorization from payers becomes even more intrusive, creating additional obstacles for patients in accessing necessary care. Further, the staff time and expense of managing shortages – looking for supply, allocating limited drugs, changing treatment plans, counseling patients and their families – is a tremendous cost to the system. As we consider these solutions, we also recognize concerns around increased costs to the health care system. We will pay a greater long-term cost in the form of delayed or denied care if we do not address the underlying economic forces driving these shortages of generic drugs. While 90 percent of prescriptions were filled in 2022 with generic or biosimilar medicines, they accounted for less than 18 percent of total prescription drug spending[1]; furthermore, at least one analysis showed that over half of the drugs actively in shortage were some of the very cheapest on the market. In addition to the cost to patients' health, hospitals have seen an increase in costs – an estimated $230 million a year – in additional costs to purchase alternatives and to manage the shortages and $360 million a year in labor to

[1] https://accessiblemeds.org/resources/blog/2022-savings-report#:~:text=91%25%3A%20Portion%20of%20U.S.,country%27s%20spending%20on%20prescription%20drugs.

handle the shortages[2]. These staggering numbers only include hospitals, not other settings of care such as private practice or other community settings. To avert future shortages, the United States (U.S.) must establish a more resilient pharmaceutical supply chain, especially for generic drugs. Most oncology drugs in shortage are generic sterile 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[3] often driving U.S. manufacturers out of the market or looking to manufacture outside the U.S. to keep costs down. 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. When one manufacturer 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. Even if another manufacturer is willing to enter the market to help shore up supply, that too can take weeks or months to get Food and Drug Administration (FDA) approval and get production up and running, due to the complexity of sterile production requirements.

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

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[2] https://www.aha.org/news/headline/2019-06-27-survey-drug-shortages-cost-hospitals-360m-annually#:~:text=Hospitals%20spend%20close%20to%20%24360,this%20week%20by%20Vizient%20Inc. https://www.acpjournals.org/doi/abs/10.7326/M18-1137?journalCode=aim

[3] https://accessiblemeds.org/resources/blog/2022-savings-report#:~:text=91%25%3A%20Portion%20of%20U.S.,country%27s%20spending%20on%20prescription%20drugs

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.

Approximately half of newly diagnosed cancer patients are over 65 years old, which makes Medicare the largest single payer of cancer care in the country.[4] As such, there are three areas where Congress can take immediate action: payment, manufacturing, and quality. In the area of payment, Congress could explore alternative payment methodologies that would provide relief from artificially low generic reimbursement rates, thereby encouraging a more reliable supply of drugs. Payment reforms should factor in quality and reliability of supply. With respect to manufacturing, Congress could encourage the adoption of advanced technology, for example, continuous manufacturing for critical drugs and active pharmaceutical ingredients (APIs). There could also be incentives such as tax credits or government contracts to increase manufacturing in the U.S. Finally, in the important area of quality, Congress could consider stronger requirements for risk management plans and incentives for purchasers to contract with manufacturers who demonstrate quality and the ability to provide reliable supply. These are only a few recommendations that have been proposed. Most are not new, and they are on a long list of suggestions made by stakeholders over the past decade. The shortage of critical cancer drugs is an urgent crisis. We must act. Cancer patients, and their families, deserve to know that they will get the care they need without delay, and for as long as they need it. Providers should not have to make these heartbreaking choices about patient care. ASCO stands ready to collaborate with you to advance comprehensive solutions that ensure individuals with cancer receive the lifesaving and life-prolonging treatments they require.

[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7318119/

Chairman SMITH. Thank you.
Dr. Ballreich.

STATEMENT OF JEROMIE BALLREICH, PHD, ASSOCIATE RESEARCH PROFESSOR, JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

Mr. BALLREICH. Thank you, Chairman Smith, Ranking Member Neal, and honorable members of this committee. Thank you for the opportunity to testify about chronic drug shortages. I am an associate research professor specializing in the economics of the U.S. pharmaceutical market.

I recommend Congress consider four policy solution sets to address chronic drug shortages: first, consider policies that improve the transparency of drug supply chains, notably around the source of drug raw materials; second, consider policies that incentivizes long-term market commitments and investment in the supply chain; third, consider policies to incentivize the onshoring of drug and ingredient manufacturing; lastly, consider the implementation of a supply safety net either in the form of a stockpile or buffer stocks of essential drugs.

Legislation should require drug manufacturers to disclose information on key supply chain attributes, including site and capacity of drug manufacturing facilities and the source of drug ingredients. A recent study identified 87 percent of drug ingredients and 60 percent of finished products were manufactured overseas, principally in India and China. This study used proprietary data. This type of information should be disclosed to the FDA and shared with key stakeholders in the drug supply chain, which will allow the identification of supply chain threats and possible remediation of supply chain threats.

Congress should consider changes in generic drug reimbursement to incorporate incentives for manufacturers to invest in more resilient supply chains. These policies could include higher payment levels for manufacturers who demonstrate commitment for resilient supply chains and higher payment levels for generic drugs with complex manufacturing and small markets. Currently, the generic market rewards manufacturers who offer the lowest price. This does not consider long-term market commitments by manufacturers, nor incentivizes investment in the supply chain.

One mechanism for incorporating incentives could be payment which incorporates a grading system based on supply chain resiliency, where Medicare and Medicaid pay higher prices for generics with resilient supply chains. This is similar to the quality measures that Medicare considers for paying hospitals and Medicare Advantage plans.

Related to payments, I am concerned that provisions of the Inflation Reduction Act, specifically penalty—inflation rebate penalties, may incentivize shortages. If a drug company signals to the FDA that their drug is in shortage, then their drug could be exempt from inflation rebates. This policy could be improved by limiting the exemption to shortages that are caused by external factors to the supply chain and not just simply a higher demand.

Congress should consider policies to incentivize domestic drug ingredient manufacturing. These policies could come in the form of

subsidized loans, tax incentives, or even higher payment rates for drugs produced in the U.S. Onshoring of the drug supply chain will increase its resilience.

Lastly, policies should be enacted to create a supply safety net in the form of either stockpile or buffer stock of essential drugs and/or ingredients. A national stockpile will provide a centralized location of essential drugs and can be accessed in times of shortages. In addition, having a single purchaser of a national stockpile will improve the economy of scale and lower operating costs.

Alternatively, Congress could also opt for a more decentralized approach by providing financial incentives in the forms of grants or tax incentives to wholesalers or hospitals to increase their inventory of essential drugs beyond short-term demand needs. CMS has recently proposed a rule to encourage buffer stocks at hospitals, but this could be broadened to other intermediary suppliers such as wholesalers.

I applaud the efforts of this committee to consider policies to improve the supply chain of drugs and improve supply chain resiliency. Immediate priorities should be the creation of a national stockpile of essential medicines, greater transparency of the supply chain, and reform generic drug reimbursement to incentivize supply chain investments. Thank you.

[The statement of Mr. Ballreich follows:]

Testimony for the Record

Submitted to the U.S. Congress

House Committee on Ways and Means

For Hearings on Examining Chronic Drug Shortages in the United States

February 6, 2024

Jeromie Ballreich, Ph.D., M.H.S.

Associate Research Professor

Johns Hopkins University

Chairman Smith, Ranking Member Neal, and Honorable Members of the U.S. House Ways and Means Committee, thank you for the opportunity to testify about chronic drug shortages. I am Jeromie Ballreich, and I am an Associate Research Professor in the Department of Health Policy and Management at the Johns Hopkins Bloomberg School of Public Health. I direct the master's program in health economics. I am a core faculty member of the Johns Hopkins Drug Access and Affordability Initiative, which is a research center evaluating US drug shortages and incentives for drug innovation. My research focuses on the US pharmaceutical market, pharmacoeconomics, and economic evaluation. The views expressed within my testimony do not necessarily represent the views of Johns Hopkins University.

As a researcher in this field, I recognize the health problem of chronic drug shortages and have studied the complex array of factors that contribute to drug shortages. My objective for this testimony is to provide an overview and rationale for actions the Congress can take to reduce the number of chronic drug shortages.

I recommend Congress consider four policy solution sets addressing chronic drug shortages:

- **Improve transparency of drug supply chains**
- **Address generic market resilience through demand-oriented policies.**
- **Increase supply chain resilience through supply-oriented policies.**
- **Ensure continued patient access via the establishment of a supply safety net.**

Improving the transparency of the drug supply chain will allow for the identification of supply chain vulnerabilities for key stakeholders of the US drug market. Demand-oriented solutions will encourage long-term market commitment of generic manufacturers and incentivize investment for supply chain resilience through the use of financial incentives directed towards the generic market. Supply-oriented policies include financial incentives for US drug and active ingredient manufacturing. Providing a safety net for US patients could be done by establishing supply buffers or stockpiles to mitigate the impact of any sudden changes to the drug supply chain.

Causes of drug shortages

Drug shortages are a serious public health problem affecting providers, payors, and most importantly, patients. It is essential that patients have immediate access to quality medicines to treat their diseases and conditions. Disruptions to access can interrupt plans of care, cause additional financial costs, and put patients' lives at jeopardy. According to a 2023 report commissioned by the Office of the Assistant Secretary for Planning and Evaluation, the average drug shortage affects nearly half a million patients, many of which are over the age of 65.[i] Not only does a single drug shortage affect a significant patient population, but the number of drug shortages occurring annually are in the hundreds. The University of Utah Drug Information Service, which tracks real-time drug shortages, identified, and tracked over 300 shortages in 2023-the highest annual level in the past decade.[ii]

The problem of drug shortages is not a new public health problem. In 2012, Congress passed the Preserving Access to Life-Saving Medications Act, which improved shortage notification and provided the US Food and Drug Administration (FDA) additional authority to address shortages. This law improves the transparency of the drug supply chain and addressed some of the causes of shortages; however, drug shortages continue to be a major public health problem. The stubbornness of this problem is a testament to the complexity of the US drug market and the root causes of drug shortages.

The reasons behind drug shortages can broadly be categorized into supply chain factors and quality issues. On the supply chain side, shortages occur when there is a disruption in manufacturing due to changes in financial circumstance, geopolitical events, or natural disasters. For example, in 2017, Hurricane Maria devastated Puerto Rico and the pharmaceutical industry located there. This significantly disrupted the supply chain for hundreds of drugs since many drugs are manufactured in only one location. This natural disaster and supply chain disruption resulted in shortages of crucial medicines, such as the injectable antibiotic, azithromycin.[iii] **However, according to FDA data, these external factors are responsible for only a small portion of the drug shortages. Most of the shortages are caused by the actions of the manufacturers**.[iv]

Most commonly drug shortages occur due to problems with manufacturing and quality concerns. The manufacturing of drugs is a complex process involving chemical or biological processes which need to occur in sterile environments. If these processes are not kept to the highest standard of quality, the drugs can become contaminated, and patients' safety is compromised.

Quality issues cause shortages across a variety of different drugs, including both branded and generic drugs. Quality issues were the primary cause of shortages for many important life-saving cancer medications. In 2023, the drug manufacturer Intas was a major supplier of cisplatin, an important chemotherapy drug. The company relied on one manufacturing plant in India to produce these drugs. A series of FDA inspections raised several red flags for the safety and quality of the manufacturing, ultimately leading to a shutdown of the plant in India which caused nearly immediate shortages of cisplatin. The quality issues were so numerous and severe that the FDA called it a "cascade of failure" for the quality and safety of manufacturing and required significant time and investment to remediate.[v]

The generic drug industry is responsible for nearly 90% of prescriptions dispensed.[vi] Unlike branded drugs, which have patent protection and can charge high prices for the drugs, the generic industry relies on competition to keep prices low. However, this reliance on competition can result in drug shortages. There is nothing to differentiate one generic drug from another since they all must replicate the active ingredients of the branded drug to get FDA approval. As a result, generic companies compete solely on price and competitive forces maintain constant downward pricing pressure. Hospitals, clinicians, wholesalers, and pharmacies are incentivized to procure generic drugs at the cheapest possible prices. The low prices and thin profit margins can result in generic companies exiting the market potentially causing a drug shortage and generally reducing overall supply capacity. A recent study showed that over half of generic manufacturers exit the market within four years of entering the market.[vii] The current market rewards companies who offer the lowest price but offers no rewards for long-term market commitment, improving supply chain resilience, or maintaining high quality manufacturing standards.

Changes in the demand for certain drugs and a reliance on just in time manufacturing, slim inventories, and other supply chain efficiencies exacerbate drug shortages especially if there is a limited supply capacity to respond to changes in the demand of a drug. There were shortages for drugs treating conditions such as attention deficit hyperactivity disorder caused in part due to increased demand because of proliferation of mental health telehealth providers and increased prescribing of stimulants.[viii] We have also seen shortages for the diabetic and weight loss medications due to sharp changes of demand for weight loss.

Proposed Policy Solutions

Improved Transparency

Legislation should be enacted to require that drug manufacturers disclose information on key attributes of the drug supply chain including site and capacity of drug manufacturing facilities and the source of the raw materials used to manufacture the drugs. **According to a 2023 study by my Johns Hopkins colleagues, two countries India and China – provide the greatest percentage of raw materials used in the manufacture of drugs sold in the US**.[ix] When there is a pandemic or geopolitical strife there can easily be a disruption to the supply chain. The US needs to develop its own supply of the components necessary to manufacture the drugs sold in the US. We should not be relying solely on other countries for the raw materials used to manufacture the drugs treating US patients.

The supply chain behind each patient's drug can be complex and opaque. The lack of transparency precludes key stakeholders from identifying vulnerabilities and possible solutions. The supply chain threat due to lack of transparency can be illustrated by an example that often occurs. Suppose there are 10 generic manufacturers for a single drug. At first glance, stakeholders could assume the supply chain has good resilience, since multiple manufactures can cover any supply disruptions. But that assumption breaks down if all 10 manufacturers source their raw materials from a single producer. Even if these manufacturers source from two or three

different producers, the assumption of good supply chain resilience could still breakdown if the producers of APIs are in the same country.

Demand-oriented policies

Changes in how generic drugs are paid could incorporate incentives for manufacturers to invest in more resilient supply chains. These policies could include higher payment levels for manufacturers who demonstrate a commitment for resilient supply chains and higher payment levels for generic drugs with complex manufacturing in small markets.

The generic market rewards manufacturers who offer the lowest price. The current payment system does not take into account long-term market commitments by manufacturers, nor does it incentivize manufactures to invest in more resilient supply chains. One mechanism for incorporating incentives for manufacturers to invest in the supply chain could be payment which incorporates a grading system based on supply chain resiliency where payers, notably Medicare and Medicaid, pay for generics at a higher price if they score high on the grading system. The Medicare program does this for hospitals and Medicare Advantage plans that score well on certain measures.[x]

In recent years, a major drug shortage occurred for generic sterile injectables (GSIs). Researchers attributed this shortage to the small market size for these injectables, price competition, and complex manufacturing, which limited market entrants. The causes for GSI shortages are similar for the generic market in general, except GSI's tend to require higher manufacturing investment due to the complex manufacturing process. Reimbursement is also typically through hospital or outpatient payments, which often bundle drug payments with other services. CMS should consider ways to incorporate quality payments to improve supply chain resilience for GSI's and incentivize manufacturer to invest in resilience. Several researchers have identified specific mechanisms to address GSI's.[xi]

I am concerned with the incentives created by the Inflation Reduction Act's (IRA) penalties for price increases. My concern is not that there are provisions to limit price increases to the rate of inflation, but the fact that drugs in shortage can be exempt from the penalties if they increase

prices faster than inflation. Drug companies signal to the FDA that they believe their drug is in shortage and typically the FDA places that drug on a shortage list. This is appropriate since hospital and clinicians want to know they could be a shortage of a specific drug. However, the Inflation Reduction Act exempts drugs with a shortage designation from price increase penalties. This exemption may incentivize drug manufacturers to self-identify shortages. This policy could be improved by limiting the exemption to shortages which are not caused by changes in demand. CMS needs to take a careful look at the drugs in shortage to determine the reason for the shortage.

Supply-oriented policies

Policies should be enacted to incentivize domestic drug and ingredient manufacturing and encourage supply chain resilience.

In 2019, 87% of facilities producing the raw materials used to manufacture the drugs and 60% of facilities producing finished generic drugs were outside of the US.[xii] The large concentration of API production in China and India leaves our drug supply chain vulnerable to geopolitical risks. The best way to mitigate these risks is to diversify manufacturing to other countries and given the impact on patients due to drug shortages, policies should prioritize a move to strengthen domestic drug and ingredient manufacturing. These policies could come in the form of subsidized loans, tax incentives, or even higher payment rates for drugs produced in the US or have a US based supply chain.

Supply safety net

Policies should be enacted to create a supply safety net in the form of either a stockpile of essential drugs or the raw materials used to manufacture the drugs; or incentivize the purchase of buffer stocks by hospital or wholesalers.

As noted earlier, there exists several causes of drug shortages in the US. Policies have been proposed to increase supply chain resilience, with the intent of mitigating future drug shortages. Given that patients depend on these drugs, Congress should also consider creating a national stockpile of essential drugs or raw materials in case of any significant sudden disruption to the

supply chain. Congress could also opt for a more decentralized approach by providing financial incentives to wholesalers or hospitals to increase their inventory of essential drugs beyond short-term demand needs. CMS as recently proposed a rule to encourage buffer stocks at hospitals, but this rule could be broadened to other intermediary suppliers, such as wholesalers. These financial incentives could be in the form of grants or tax incentives to increase inventory levels.

There are benefits to a national stockpile including coordination of supply and economy of scale. A national stockpile will provide a centralized accounting of available drugs and can be accessed in times of shortages. In addition, having a single purchaser in charge of a national stockpile will improve the economy of scale and lower operating costs.

Conclusion

Congress needs to consider policies to improve the supply of drugs and improve supply chain resilience. **Immediate priorities should be decoration of a national stockpile of essential medicines, greater transparency of the supply, chain, and reform generic drug reimbursement to incentivize supply chain investment.**

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[i] Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health & Human Services. Impact of Drug Shortages on Consumer Costs. May 2023. https://aspe.hhs.gov/

[ii] https://www.ashp.org/-/media/assets/drug-shortages/docs/ASHP-2023-Drug-Shortages-Survey-Report.pdf

[iii] https://www.nytimes.com/2017/10/23/health/puerto-rico-hurricane-maria-drug-shortage.html

[iv] https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions

[v] https://www.nytimes.com/2023/12/19/health/cancer-drug-shortage.html?bgrp=c&smid=url-share

[vi] Food and Drug Administration. Office of Generic Drugs 2021 annual report [Internet]. Silver Spring (MD): FDA; 2022 Feb 14. Available from: https://www.fda.gov/drugs/generic-drugs/office-generic-drugs-2021-annual-report

[vii] Frank RG, McGuire TG, Nason I. The evolution of supply and demand in markets forgeneric drugs. *Milbank Q*. 2021;99(3):828-852.

[viii] https://www.nbcnews.com/health/mental-health/adderall-shortage-adhd-medication-2023-rcna99019

[ix] Socal, M. P., Ahn, K., Greene, J. A., & Anderson, G. F. (2023). Competition And Vulnerabilities In The Global Supply Chain For US Generic Active Pharmaceutical Ingredients: Study examines the competition and vulnerabilities in the global supply chain for US generic active pharmaceutical ingredients. *Health Affairs*, *42*(3), 407-415.

[x] https://www.cms.gov/newsroom/fact-sheets/cy-2024-medicare-hospital-outpatient-prospective-payment-system-and-ambulatory-surgical-center-0

[xi] https://www.brookings.edu/articles/federal-policies-to-address-persistent-generic-drug-shortages/

[xii] Kaygisiz NB, Shivdasani Y, Conti RM, Berndt ER. The geography of prescription pharmaceuticals supplied to the U.S.: levels, trends, and implications [Internet]. Cambridge (MA): National Bureau of Economic Research; 2019 Dec. (NBER Working Paper No. 26524). https://www.nber.org/system/files/working_papers/w26524/w26524.pdf

Chairman SMITH. Thank you all for your testimony. We will now proceed to the question-and-answer session.

As I noted in my opening statement, most of the Active Pharmaceutical Ingredients that make up our essential medicines are sourced from outside our country, and China is a leading source of pharmaceutical product imports. Dr. Schondelmeyer, can you speak to what dangers we face by being reliant on foreign sources for our medical supply chain, and how can we better onshore more production, or at least be less reliant on hostile countries like China?

Mr. SCHONDELMEYER. Thank you, Mr. Chairman. That is a great question. There is no simple answer, but we are reliant—we have to realize you can't just set up a factory and make tablets or capsules without the chemicals and the raw ingredients that are needed to make that. And, with the majority of those made outside of the U.S., then we have to obtain those from other countries.

Now, remember in my presentation I talked about India put a ban on export of certain drugs out of India because they wanted to make sure they had enough for themselves. And, if that ban had stayed in place, we would have seen shortages over the next three or four months develop in the U.S., and we would have been without certain products. And so, if India and/or China and/or a country that makes a lot of the generics that we need puts bans or trade embargoes on exporting drugs, we are going to be without the drug.

And yes, Civica or other drug companies in the U.S. could begin making them, but they can't do it tomorrow. It is going to—we can ask Mr. Coukell how long it would take, but it is months to years to repair that. So we could have patients—cancer patients or pediatric patients or other patients—without the drugs they need because a country simply blocks us from having access to those drugs.

And that is—you know, we don't rely on other countries to make the bullets when we fight wars, especially our sworn enemies, and so we want to make sure that the drugs we need to keep our public and our military healthy are coming from sources that we have control of.

Chairman SMITH. Thank you. It is easy to get caught up in the logistical challenges or market forces when discussing drug shortages, but we have to remember at the end of the supply chain sits a patient waiting for a treatment to a cure. Dr. Schleicher, please describe the impact on patients and providers when they are forced to navigate drug shortages on top of managing their needed treatments.

And how is this challenge worse in smaller and rural areas?

Dr. SCHLEICHER. Yes, thank you, Chairman. So it is extremely challenging, especially when you don't know when the end of the shortage is coming.

A lot of people talk about delaying treatment. For us, in the peak of this, we thought it might be months until we would get carboplatin back, so you couldn't delay. So you are just treating without. And sometimes there are substitutions, but often there are not. So you are really having to treat patients without the evidence-based treatment regimen that we are used to giving, which is incredibly hard, as the oncologist and the team, of course, having to deliver that news once you have gained trust with that patient, but obviously way worse for the patient him or herself.

In addition, all of us are used to evidence, clinical guidelines, and we were at the first time not having those. Organizations like ASCO and others did kind of put out consensus guidelines, but often shortages happened before we had that. Our group were emailing back and forth, "How would you treat this? How would you treat this?" We had advanced analytics to help us at least the best way possible figure out where the drugs were.

Now, if you are a one-doc or two-doc practice in rural America, one, you don't have access to colleagues to ask for help on. I can't imagine treating without a certain drug or knowing what substitution to give if I don't have people to ask.

Two, inventory management is complicated enough. Tennessee Oncology had to carry and give 200 different drug formulations last year to our patients. Being able to add that with also stockpiling drugs that might be in shortage is almost an impossible task, even for a group as large as us.

But a one or two-doc practice in rural America would have—I don't even know how it would be possible to navigate, one, what to do clinically; and then two, how to actually manage the inventory.

Chairman SMITH. Thank you.

Mr. Coukell, we heard from your statement that Civica represents an alternative way of sourcing essential drugs for health care providers. How are your contracting practices with manufacturers different from traditional large group purchasing organizations, and how can these models be implemented in smaller rural communities?

Mr. COUKELL. Thank you, Mr. Chairman. Let me actually start with the rural community component.

We have some large for-profit and non-profit health systems who are part of Civica, but we also have some small rural hospitals. They have the same access to our drugs at the same price, which may even be an advantage for the small hospital, since they don't normally have the buying power. And we hold stock for them based on whatever volume they have committed.

In terms of our contracting processes, we do a number of things that are different. One is that we have long-term purchase and supply contracts. So, when we contract with a contract manufacturer, they have typically a five-year volume commitment from us. So they know they are in the game for five years, and they can invest in their production and they know that they have stable demand and price. So it creates that stability in the marketplace.

But we go further. We actually go out and do a physical audit of a manufacturing facility that we are going to contract with. Our team goes in, they look at the facility, they look at the cleanliness, they look at the protocols, they review documentation, and then we sign a contract—a quality agreement with them. So on an ongoing basis they are submitting data to us on product deviations, inspectional reports, all kinds of things that give us insight into the quality in that facility.

And then finally, sir, each batch of drug, we make a batch-by-batch decision to release that onto the market based on a review of the quality documentation associated with that batch.

Chairman SMITH. Thank you. I now recognize the ranking member, Mr. Neal, for any questions he might have.

Mr. NEAL. Thank you, Mr. Chairman.

Dr. Ballreich, I know you are going to hear a lot today about the potential for onshoring the manufacture of medicines to address drug shortages and the need to provide tax incentives for manufacturers to do so. And one of the most critical steps is to address the shortage of generic, sterile injectable drugs in the manufacturing quality arena. What do you think Congress ought to be doing to consider improving the reliability and quality of the finished product to mitigate shortages?

Mr. BALLREICH. Yes, excellent question. Thank you, Ranking Member Neal.

I think Congress should consider looking at the reimbursement mechanism for GSIs, or Generic Sterile Injectables. These are very—these tend to be small-market-type injectables. Having better transparency of the supply chain, having a potential scorecard to incentivize quality, rather than simply let's identify the lowest cost are all possible solutions to improve the resiliency of the Generic Sterile Injectable market.

So I think there are a number of potential policy options for GSIs, and I—out of those, I think increased transparency, quality scorecard are the two best approaches to improve the market.

Mr. NEAL. And, as you know, Joe Biden has taken advantage of the opportunity with the Defense Production Act to enable more domestic manufacturing of these essential medicines.

Dr. Gralow, you said something that captured my attention during the testimony. By the way, the testimony was really good. You said that Medicare is now the biggest provider of cancer care, or something to that extent, in your comments. Can you elaborate on that? That is pretty important for members of the committee to hear.

Would you turn on your——

Dr. GRALOW. Sorry. For the most part, cancer is a disease of aging. Of course, it can occur in younger people, but the longer we live the more likely we are to get cancer.

So, with our aging population, more than half of cancers right now in the United States are being diagnosed at age 65 or greater. So Medicare can play a big role in how we actually help strengthen these sterile injectables that are dirt cheap, and it can build up the whole system.

Mr. NEAL. Thank you. That was really important.

I yield back.

Chairman SMITH. Thank you.

Mr. Buchanan.

Mr. BUCHANAN. Thank you, and I want to thank the chairman and thank the witnesses today.

As someone that has been in business for a lot of years before I got here, we had tens of millions of dollars' worth of inventory that had to be managed. I think we have got a disaster on our hands in terms of moving forward. That is just my opinion. We have got to find a way for American companies to get back in the game.

My point in bringing up the idea of the inventory, I don't care if you are a two-store, or you are just a small—2 docs or you have got 500 docs, there is the technology, I have got to believe, out there. You should have a six-month supply. We always had a fill rate.

And so we have got to find a way. Frankly—we have got to be candid about this—you have got India and China producing 70, 80 percent, it depends on what number you want to have, in terms of the raw materials. That has got to change, and we have got to get more of our control locally. I represent Sarasota or the Manatee County Tampa Bay area, and I can tell you I have 200,000-plus seniors there. And this has been going on for quite a while with the docs in that area, especially as it relates to cancer. So we have to find a way we can come together, work together, set the incentives up so we can get more of our American companies in there.

The other thing I will just say, when you have seen what happened with COVID, what happened to the inflation? It went out of sight, and it is because there was no inventory. And that is what is going to happen here. They said it is 50 percent or something up—the Chinese have been up the last couple of years in some of their products or whatever, but that is going to happen here. When the cupboard is bare and there is no inventory, people are going to pay the difference.

So we have to have adequate supplies. We have got to stop kidding ourselves and figure out how, looking as we go forward, how we are going to be in this game in a bigger way, especially American companies. It means American jobs.

So, Mr. Schondelmeyer, why don't—could you explain to me, you know, a little bit more your thoughts on just inventory management—because it was brought up a little bit earlier today—and why that is such a big problem for this industry?

[Pause.]

Mr. BUCHANAN. Hit your——

Mr. SCHONDELMEYER. Yes, I do think this industry does a great job of managing inventory, in general. But we have moved to what you call just-in-time inventory, where you minimize the amount you keep on hand because one of the fastest ways for a business to lose money is to have too much sitting in inventory. But, when you start to run short and have shortages of raw materials or production, then that small inventory catches you and leaves you without product. And so we need to better be able to predict when demand changes will stress that inventory.

And what really caught us in the pandemic, there were demand changes that affected the inventory and availability, but there were also supply disruptions we didn't anticipate. When a whole city in China was closed on lockdown because of COVID, and they quit producing products where they made pharmaceuticals, then we didn't have them. That wasn't a demand issue, that was a supply issue.

So I think we do need to control the inventory and know how much—what I look at is the agricultural industry. If we, you know, are worried about food supplies, we can tell you how much soybeans we expect to be produced next year, and how much corn, and which field in Missouri or Arkansas is going to produce those, or

in Iowa, wherever it is coming from. We know that. But for pharmaceuticals, as a government, we don't have a single agency that knows where all of our drug products come from——

Mr. BUCHANAN. Let me——

Mr. SCHONDELMEYER [continuing]. How much is being produced.

Mr. BUCHANAN. I have just got five minutes.

Mr. SCHONDELMEYER. Yes.

Mr. BUCHANAN. So Mr. Coukell——

Mr. SCHONDELMEYER. Sorry.

Mr. BUCHANAN [continuing]. Could you add on to that? You have talked about inventory management of that, and just your thought, and your background. And how do we create the incentives to have more American companies and more American jobs here in the States?

And I know there is a cost to wages and all these other factors that come into play, but I am concerned about us not being at the table because, you know, when I first got in the business it was all about oil and gas, and they had it, and we had pay—you got to pay whatever you have got to pay to get it, and I just don't like that, being backed into a corner, and that is where I feel, as Americans, we are at right now.

Mr. COUKELL. Thank you. As Dr. Schondelmeyer says, it costs money to have inventory sitting around in a warehouse, which is why people mostly try not to do it. But, if somebody drops out of the market, it takes drug production a long time to increase. So we need that buffer stock as an insurance policy.

I think we probably shouldn't try to have that sitting in an individual doctor's office or hospital. They are not set up, they don't have the space, they don't have the systems, they don't want the risk of expired inventory. But, if that inventory buffer is sitting in the supply chain, we are constantly putting new stock in and selling the older stock, and we are really managing it, there is an incremental cost to doing that but it is an incremental cost that would really compensate for the added resiliency we would have.

Mr. BUCHANAN. Yes. The only thing I would say is that there is a turn rate and everything else, and maybe it is not six months, maybe it is three, but to keep things that tight, I think, is the wrong way going forward.

Thank you, and I yield back.

Chairman SMITH. Thank you. I now recognize my friend and 49ers fan, Mr. Thompson.

Mr. THOMPSON. I am going to enjoy that steak you are going to buy me after the Super Bowl, Mr. Chairman. [Laughter.]

Mr. THOMPSON. Mr. Chairman, thank you very, very much for this hearing today. It is timely and important.

Prescription drugs is one of the things that I hear the most about from my constituents. And, as we all know, when you need a drug, you need it, and you need it fast. The price of the drug is only part of the battle. It has to be affordable, but it also has to be accessible. And the witnesses have all made that an important point—part of their testimony. And they all seem to agree that fixing current and preventing future drug shortages requires both transparency and stronger supply chains.

Dr. Gralow, I think many of us on both sides of the aisle are frustrated at the lack of transparency in our healthcare system. Can you talk a little bit more about how increased transparency would help in this specific area in preventing drug shortages and ameliorating the ones that we already face?

Dr. GRALOW. Thanks for that question.

There is a severe problem with transparency in where the raw materials come from, what the manufacturers are doing. We know which manufacturers the FDA has approved. We can get, but it can be complicated to understand, what percent of the market each of the manufacturers are supplying and where each of them are getting the Active Pharmaceutical Ingredients. That is not really known.

So, for example, what happened with the cisplatin case is the Active Pharmaceutical Ingredients made in one plant in India, that plant was shut down by a surprise FDA visit that found some major quality problems. We did not know, there was no transparency that that company supplied the majority of Active Pharmaceutical Ingredients for all of the manufacturers across the board. Knowing that up front, we could have reacted much, much sooner. And it wasn't until we saw the implications of that with now drug dropping from most of the manufacturers, that we realized just how much that one plant impacted everyone.

Mr. THOMPSON. Well, I think that is a good spot for me to ask you and any of the other witnesses that would like to comment, what specific things can Congress do to make pharmaceutical supply chains more resilient?

Dr. GRALOW. I think a better early detection system, which relies on exactly your initial question on transparency, on what comes from where. Early notification when there is a problem so that we can react, we can maybe gear up with some of our manufacturing. We could even look at sites—to the FDA to approve manufacturers who aren't currently approved to bring in lots, for example. So a better early detection system.

What Congress can do is—we are going to have to pay more money for these drugs, these sterile injectables that are generic, that cost—you know, this bottle of water costs more than some of them. We are going to have to. But that is going to be an exchange for resiliency across the system, you know, good quality manufacturing, where the plant is——

Mr. THOMPSON. So, in your testimony, you had mentioned the generic drugs, and the appeal to those for many is in fact the price. But at the same time, that discourages manufacturers because they can make more money in other than generic. How do we fix that?

Dr. GRALOW. So that was to me?

Mr. THOMPSON. Well——

Dr. GRALOW. Everyone?

Mr. THOMPSON. I will ask that to anyone who wants to jump in.

Mr. CAVACINI. I could offer a comment, sir. Thank you.

Mr. THOMPSON. Please.

Mr. CAVACINI. I think it is important to remember that the vast majority of generic medications are in strong supply, and we

don't have an issue, and the market works very effectively to balance cost, quality, and access.

There is a subset of complex and inexpensive and therapeutically important molecules, largely Generic Sterile Injectables, that make up the vast majority. I think two-thirds of generic shortages are in the category of Generic Sterile Injectables, and I think that is an opportunity to inject some of the ideas that we have heard from the panel today that are really consistent around transparency and economic stability and incenting additional capacity and supply and thinking about buffer or safety stocks for those subset of molecules.

Mr. THOMPSON. Yes, sir.

Mr. COUKELL. You know the saying. If something seems too good to be true, it probably is. So, if somebody is offering to sell you a vial of medicine for $0.40, you probably have to wonder, am I getting a really good quality drug? But, right now, the system drives providers, purchasers to chase that to $0.40. And, if they can get it down to 38, they go there.

We have to take a step back and say we are going to pay you, so at least some share of your purchasing. It is not price insensitive, but it also takes into account some knowledge of the quality and the facility where that drug is coming from.

Mr. THOMPSON. Thank you.

I yield back. Go 49ers.

Chairman SMITH. We will see about that.

Mr. Smith is recognized.

Mr. SMITH of Nebraska. Thank you, Mr. Chairman. Thank you to our entire panel here for sharing your insight and expertise.

Obviously, these issues aren't easy. And certainly, Dr. Schleicher, thank you for your opening and sharing very real impacts on patients. And it is hard to believe that, as much technology as we have, and ingenuity, that we are still facing these shortages, and it should be concerning for all of us.

I happen to deal with a very rural and often times remote constituency. In fact, my district covers enough area that I have—I represent over 50 critical access hospitals, over 100 rural health clinics. So to say it is rural is a bit of an understatement because, like I said, some of those facilities are in remote locations, and obviously not large enough to develop an inventory to prevent a shortage. And so, hopefully, we can find some agility, if you will, and—in that ability to meet the needs of—the very diverse needs of our patients. And I know that this is often times exacerbated with, you know, workforce issues, inflation, and I would say some government-centered over-regulation, as well.

So I hope that—and I am told that—compounding pharmacies actually can be a part of the solution, at least. I would appreciate hearing your perspective on that. But I hope that we can work together to address these issues.

But, Dr. Schleicher, can you describe perhaps the capital investment that is needed to keep the steady supply of drugs available for patients in your practice, such as an oncology practice, and perhaps how smaller, more rural providers might have more difficulty with this?

Dr. SCHLEICHER. Great question, thank you very much, Congressman.

So, as we all talk about the complexities of cancer drugs—and some are extremely expensive, some are the ones we are talking about today—the very expensive ones, the capital requirements to stock, say immunotherapies, are very high because you purchase the drug first. A large group of 200 providers like us, we can do that because we know if a patient shows up to the door and doesn't—isn't able to get that medicine due to toxicity, there is going to be another patient that comes to our door or to one of our 35 clinics elsewhere and be able to give it.

With the 200 different drugs that cancer patients need right now, it is hard to have different inventory strategies for different types of drugs because we are already trying to balance patient demand, payers, which drugs they want us to use, et cetera, but we are able to have some buffer.

If you are—I was visiting a practice, a single physician in rural Kentucky, a few months ago, and he has actually stopped even doing traditional buy and build to have the drugs because he was so scared about buying a drug, a patient coming up, not being able to get it, and then he is on the hook for the price of that drug.

So the smaller practice it gets, which often is in rural America, as you are describing, it becomes very difficult to afford to have the inventory for all the different categories of patients you are going to see, especially the high price of lots of inventory, which is different than these drugs. But navigating those differences is very challenging to a practice.

Mr. SMITH of Nebraska. Thank you.

Mr. Coukell, could you perhaps reflect on, from your perspective on distribution and purchasing, how might—your ideas for addressing rural shortages?

Mr. COUKELL. Thank you. I think if Congress incentivizes hospitals to purchase in a different way that takes quality into account, then the market will respond by creating those pathways to market. And I have given the example of Civica, which is equally accessible on the same price basis to a rural hospital as to an urban or a hospital chain.

Mr. SMITH of Nebraska. Okay, thank you.

Mr. Chairman, I yield back.

Chairman SMITH. Mr. Doggett.

Mr. DOGGETT. Thank you, Mr. Chairman, and thanks to each of our witnesses for testifying.

However, I must say I think the most pressing shortage that we have in America is the shortage of access of patients here to brand-name drugs, for which we pay the highest prices in the world, with one in four patients in our country skipping or rationing their prescriptions because their unaffordable access to these drugs is a really pressing challenge.

Claiming outrageous prices are necessary to fund innovation, many pharma manufacturers spend more enriching themselves with stock buybacks and dividends than on research and development. They have invested in this Congress, outspending every other industry with hundreds of millions lobbying each year and generous campaign funding. Now, they are wasting resources on

nine separate lawsuits to block an extremely modest Medicare drug price negotiation program.

At the same time, like our witnesses today, I have heard from constituents, particularly those unable to access Adderall for children struggling in school. Many first pointed fingers at the Drug Enforcement Agency for this shortage, claiming that their quotas were too low to meet demand, yet DEA has confirmed that manufacturers did not meet production quotas in 2022, resulting in a shortfall of about a billion doses. And similar trends followed last year.

Meanwhile, Teva, the leading manufacturer of generic and branded forms of Adderall, reported $15.8 billion in revenue in 2023, an increase of 7 percent from the prior year. So they are certainly not short of profits. Adderall has been in shortage since October of 2022. So, while children suffer, Teva's billions did not go to that worthy cause. Teva spent less than $1 billion in 2023 on research and development, yet its overall selling and marketing expenses were more than twice that.

We need greater responsibility and less hypocrisy from the pharmaceutical industry. Studies have found that the overwhelming majority of shortages, about three-fourths of them, were due to increased demand. This is not a problem caused by low prices; it is a failure to invest in capacity and track and report increased demand. An FDA drug shortages task force found shortages "persist after supply disruptions, despite some price increases. Remarkably, only 42 percent of drugs in shortage were found to have seen significant production increases to restore supplies, and only about a third reached pre-shortage supply levels, even a year after being in shortage.

With this committee enabling most pharma manufacturers to pay some of the lowest tax rates in America, much less than what a mother trying to support two children would pay if she earned the average wage, with giant tax subsidies that we provide for research and development, it is difficult to imagine what other tax incentives this committee could provide. But I am sure we will get some lobbying help to find them.

Pharma is once again in search of a boogeyman to hide its wrongdoing, condemning the modest progress that was made in dealing with unjustified price hikes that, unfortunately, include only a handful of drugs, none of which are generics. Nor do the inflation rebates apply to generics in part B, which is the program most oncology shortages fall under. For part D inflation rebates, which do encompass generics, there is an exception for drugs experiencing or at risk of shortage.

Dr. Ballreich, Big Pharma has launched misleading attacks on the inflation rebates designed to prevent these price spikes. Can you please elaborate on your shared concern and your recommendation to further strengthen the rebates to prevent pharma gaming?

Mr. BALLREICH. Thank you, excellent question.

So, in the Inflation Reduction Act, as you noted, there are inflation rebates. If a drug is identified in shortage, they are exempt from the inflation rebates. There are certain situations—a natural disaster, or other external supply chain effects—that make a lot of

sense. However, one of the biggest drugs in terms of sales that was in shortage last year was the new, popular ozempic, the GLP 1 inhibitor, initially, for type 2 diabetes and now for weight loss.

So I think in situations where there is a sudden change in demand that drives the shortage, these inflation rebates don't make any economic—the inflation rebate exemption does not make any economic sense. That exemption should be restricted for drugs which are facing shortages due to external factors and not because a branded pharma company did not invest enough in their own supply manufacturing capacity because they are, in fact, incentivized to get that drug already to market. Inflation rebate exemptions are not going to change that.

Mr. DOGGETT. Thank you.

Thank you, Mr. Chairman.

Chairman SMITH. Mr. Kelly.

Mr. KELLY. Thank you, Mr. Chairman, and thank you all for being here.

At the risk of sounding insensitive, I am in the automobile business. They currently have 35 cars sitting in our lot that belong to customers who are waiting for parts to come in to fix them. When I look at your business and what you are talking about, we all have the same problems. The global supply chain that we all rely on has found—that is fine, as long as the chain doesn't get broken. Once it is broken, it is almost impossible to take care of.

Now, I am assuming that a lot of the medicines that are on the shelf have a clock-out time, or a time where they are no longer effective and they probably have to be discarded at—somebody does something with them. I am imagining that. But I know we have these conversations. Each of you have pretty much said the same thing. And it is about the economy, stupid. We are talking about the price of drugs, the price of drugs, and why aren't there more available, and why aren't these people producing them for less money, and why, and why, and why, and all they are doing is getting fat and happy over people who are sick and need these drugs.

I happen to sit on a board for Hyundai Motor Company. It is called the Hope on Wheels, and it is an effort to make sure that pediatric cancer gets cured. We have about an 80 percent cure rate right now, but that also means that 20 percent do not get cured. We have come out with a lot of different pharmaceuticals. We come up with some amazing new drugs.

I would just suggest that the boogeyman isn't the people who produce the drugs, it is the fact that these are products that age out and need to be replaced, and you rely on a parts change that is not always consistent. When I hear that India decided to hang on to their own supply, well, charity always does begin at home. I would hate to be living in India and saying, you know what? We found there was a better price in America, so we sold those drugs to them, our people will just have to do without them.

I know we have these hearings, and we like to try to get to the bottom of things, but the real price issue that we are talking about right now is demand and supply chains. And I got to tell you, I don't care if it is in the automobile business, or in the pharmaceutical business, or if you are in the appliance business, or whatever business you are in. It is all reliant right now on a global sup-

ply chain that we didn't have in the past, but we have now. And why do we rely on it? Because we can get those parts cheaper someplace else in the world.

I really appreciate you all coming here today, but, listen, I am a diabetic. You know, I would hate to hear that I can't get a hold of insulin, or I would hate to hear that we don't want to go with a generic form. I would like to go back to 1933, when those scientists at the University of Toronto decided to sell the patent for $1 because they thought the value was so important to the American—to humanity that they would never try to make a profit on it. Unfortunately, this is an economic problem. This is a business problem.

And again, I said earlier, at the risk of sounding insensitive, I am not. But I also am not going to be impractical, thinking that people are going to produce things and supply them and not make a profit on it and that they would think that they could stay open for long periods of times by losing money. That just isn't the way it works.

So, if any of you can help me, is it the supply chain? Is it the fact that we found other places in the world that can produce things for less money than we can produce them here at home, and we rely on them to supply that, as—what we need? If anybody—if there is something opposite of that—I have listened to all of you, and your testimonies are all the same.

I will just tell you again, going back to Hope on Wheels, if you really want to see, go into a children's hospital, where a small child has no chance of surviving because we don't have the ability to cure him or her of what it is that they have. It does come down to dollars and cents, unfortunately.

Do you have any way we can fix this global supply chain, other than the fact that, if we are willing to pay more for an American-made product that is actually made in America and sourced in America, that that may be part of the answer?

Anybody?

Dr. GRALOW. I think that is absolutely part of the answer. I think bringing the manufacturing and the raw materials back to the U.S. could be part of the solution.

But I think also rewarding those that are offshore for good, quality manufacturing, not good-quality drugs—hopefully, all the drugs themselves are good quality, but for good quality manufacturing, updating your machinery, and resiliency in the system.

So this buffer of three, six months, whatever, you know, it is very hard to have a national stockpile when these drugs expire. And they do. They do not last long. You would have to keep changing it out. That is not realistic, but rewarding companies who have a guaranteed, multiple-month backup supply, they update their machinery, it is transparent——

Mr. KELLY. So if I could just ask you, who is—would reward these companies?

Dr. GRALOW. Who would be?

Mr. KELLY. Who would reward these companies?

Dr. GRALOW. We would.

Mr. KELLY. Who is we?

Dr. GRALOW. Well, Medicare pays for half of these drugs——

Mr. KELLY. And that would be the American taxpayer.

Dr. GRALOW. That—the American taxpayer——

Mr. KELLY. Yes.

Dr. GRALOW. The private payers, as well.

Mr. KELLY. No, I mean, it comes down to—every single penny that we talk about that the government is going to spend comes out of some hardworking American taxpayer's pocket, okay?

Let's get to the realistics of all this thing. I agree with you. I am not disagreeing with you. The question is what price are we willing to pay and when is it that we are going to say it doesn't matter what the cost is, we are going to produce it, even if we are losing, and we are still going to do it just because we have great hearts?

I really start to wonder sometimes when we have these discussions. It really does come down to the economy, and I don't say it is about being stupid, it is about being realistic about it.

There is nothing harder than to watch a loved one pass away because he or she does not have access to a lifesaving pharmaceutical. That is why I thought the Trump Administration with the right to try had a great idea.

Chairman SMITH. Thank you.

Mr. Larson.

Mr. LARSON. Thank you, Mr. Chairman, and I thank you for this important hearing. I think it underscores what Martin Luther King would say is the fierce urgency of now and acting upon this.

I would like to point out, listening to our colleagues talk and the questions here as well, that this underscores another specific reason why we shouldn't be shutting down government because this is so vitally important, as we have just heard, just on the Medicare side alone.

Also, we have learned—and Mr. Chairman, I would like to submit for the record an article entitled, "University of Connecticut Researchers Lead the National Effort to Improve Drug Manufacturing for the record.

Chairman SMITH. Without objection.

[The information follows:]

FEBRUARY 5, 2024

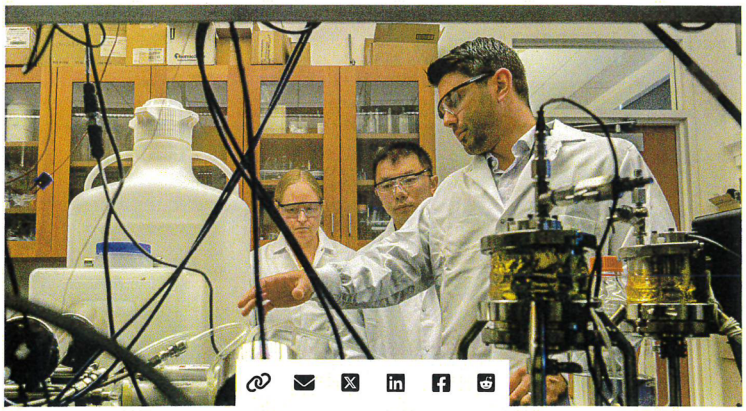
ENTREPRENEURSHIP RESEARCH & DISCOVERY

Continuous Manufacturing as opposed to batch processing

May 17, 2018 | *Colin Poitras - UConn Communications*

UConn Researchers Lead National Effort to Improve Drug Manufacturing

Researchers in the School of Pharmacy are adapting the techniques of continuous manufacturing used in the electronics, chemical, and automobile industries to the production of complex drugs.



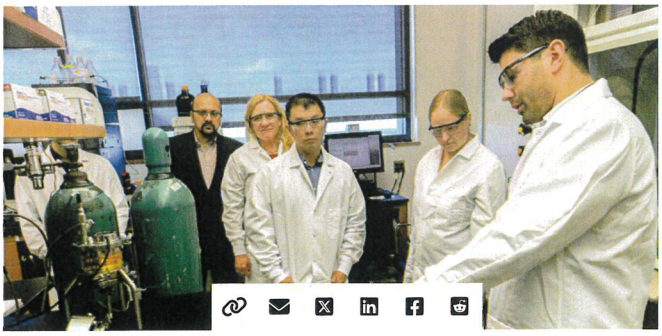


Antonio Costa, assistant research professor of pharmaceutical science, right, explains the apparatus for continuous processing of liposome drug products to officials from the FDA's Office of Pharmaceutical Quality as part of a quarterly presentation to the funding agency. (Peter Morenus/UConn Photo)

esearchers from UConn's School of Pharmacy are leading a national effort to improve pharmaceutical manufacturing.

Research teams led by pharmaceutics professors Diane Burgess and Bodhisattwa "Bodhi" Chaudhuri are adapting the techniques of continuous manufacturing, which has long been used in electronics, chemical, and automobile manufacturing, to the production of complex drugs. With these techniques, drugs are made in a single uninterrupted process, unlike the batch-processing technology that is commonly used, in which medications are produced in a series of separate steps.

The new technologies being created at UConn could dramatically change the way today's complex drug dosages are made, offering manufacturers a more responsive and reliable production platform to keep pace with the rapid advances taking place in medicine.





Antonio Costa, assistant research professor of pharmaceutical science, right, explains the apparatus for continuous processing of liposome drug products at the Pharmacy/Biology Building. From left are Bodhi Chaudhuri, associate professor of pharmacy, Diane Burgess, Board of Trustees Distinguished Professor of Pharmaceutics, and Su-Lin Lee and Katherine Tyner, both of the FDA's Office of Pharmaceutical Quality. (Peter Morenus/UConn Photo)

For years, drug makers have relied on decades-old batch-processing technology, in which medications are produced in steps, with many stops and starts along the way. But this method has had its share of problems, from errors caused by lapses in human supervision to production delays. Contamination risks are a constant concern, due to the open transfer of materials between stages. In some instances, whole batches of inferior or contaminated drugs have been thrown out, contributing to critical drug shortages and increasing costs for manufacturers and consumers alike.

The U.S. Food and Drug Administration has made improving pharmaceutical manufacturing a national priority. The FDA is counting on major academic research laboratories, like those in UConn's School of Pharmacy, to create state-of-the-art manufacturing systems that can produce today's complex new drug products quickly, reliably, and efficiently.

As part of that effort, researchers in UConn's School of Pharmacy recently secured a highly competitive $3.3 million FDA grant to develop a continuous manufacturing platform for complex drug dosages that will eliminate many of the problems associated with batch processing of these products. The three-year grant recognizes UConn's leadership in pharmaceutical manufacturing research, and was the first to be awarded under the 21st Century Cures Act, which was passed by Congress in 2016 to spur innovation in drug manufacturing and development.

"Complex drug products have unique characteristics that have greatly enhanced human health," says Burgess, Boar sor of Pharmaceutics.

"However, due to their complex formulation and processing requirements, their manufacturing cost is very high. Creating a more robust and modern production platform is absolutely essential if we are going to meet the growing demand for these important new products."

The drug tablets and capsules that most of us are familiar with are considered simple dosage forms and are relatively easy to manufacture. Complex drug dosages, on the other hand, are often sophisticated precision medications that must be carefully produced as well as carefully administered.

They include a class of drugs known as parenteral preparations that cannot be taken orally. In some cases, these medications are rendered into nanosized particles such as liposomes that must be injected into the patient. Liposomes are made out of the same type of materials as the membranes of cells. They are widely used in HIV and cancer treatments because of their ability to travel to specific, targeted sites in the body – such as tumor locations – to release their medication, thereby reducing the occurrence of potentially harmful side effects.

But it is the very nature of these complex drugs – their sophistication and precision – that makes them a challenge to make at a commercial scale.

In continuous manufacturing, drugs are made in a single uninterrupted process from raw material to finished product. The system is highly automated, self-contained, and closed, significantly reducing the risk of human error and possible contamination. Multiple, built-in quality control features allow manufacturers to monitor quality during production, increasing efficiency.

In batch processing, quality control tests often are not performed until all of the steps in the process are complete, leading to significant production delays when entire batches are found to be inferior or contaminated and the process must be restarted.

The batch process is also ill-suited to new drug development, as manufacturers sometimes need to make significant adjustments in their production lines to accommodate new drug de platforms are engineered

to be more flexible, and would accelerate new drug development.

Continuous manufacturing is not new to Burgess's lab. Her research team spent the past four years successfully developing a prototype continuous manufacturing platform for liposome-based drug products. This effort started with the thesis work of former Ph.D. student Antonio Costa, who is now an assistant research professor in the Burgess lab. With the support of UConn's National Science Foundation I-Corps site, Accelerate UConn, the team is commercializing this platform. A patent for the technology is pending.

With the new FDA grant, Burgess and her team intend to leverage that technical foundation to create a more versatile modular continuous manufacturing platform that can be used to make a broader range of complex drugs.

In addition, a team led by co-principal investigator Chaudhuri, associate professor of pharmaceutics with expertise in chemical engineering and multi-scale computer modeling, is building multi-scale computer models that will predict the liposome size and encapsulation needed for a wide variety of drugs under different processing conditions (fluid flow rates, mixture concentrations, and temperature changes). Those predictions, along with experimental findings, will be systematically loaded into an extensive database. Information in the database will then be used to "train" an artificially intelligent (AI) computer system that will allow industry representatives and the FDA to clearly see how continuous manufacturing can be adopted for a multitude of complex pharmaceuticals.

Because the process is so new, federal regulations and policies regarding continuous manufacturing of complex drug products are currently limited. This has contributed to some manufacturers' reluctance in adopting the technology, as it is largely untested and unregulated.

Chaudhuri says that in building the database and artificially intelligent neural network, the team will better understand the underlying molecular and fluid dynamics involved in the process, which are critical to making sure complex drug formulations are made properly.



"By using multi-scale computer models, we can see exactly how and where these nanoparticles and liposomes are being formed, which is almost impossible to observe or ascertain experimentally," Chaudhuri says. "We can then run different simulations, varying such things as temperature, input pressure, velocity, or other factors until we get the precise outcomes – such as particle size distribution, concentration, and drug encapsulation."

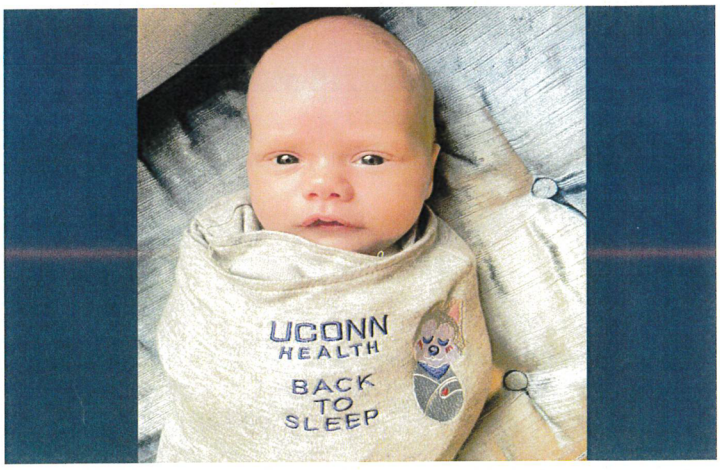
The AI network and database will allow users to input different drug elements, design parameters, and processing conditions to see how complex drugs can be made using continuous processing. It will serve as a road map for manufacturers seeking to adopt the new technology. It also will provide federal officials at the FDA with a clear scientific framework upon which to base new policies and regulations related to using continuous manufacturing for complex drug dosages.

"Developing a more robust and modern manufacturing technology that provides no interruption in production is essential to meeting today's diverse therapeutic needs," Burgess says. "The knowledge we will gain through this research will not only encourage future drug innovation, it should help guide federal authorities on future policy."

Jie Shen, a former researcher in Burgess's lab who is now an assistant professor of pharmacy at the University of Rhode Island, is also working on the continuous manufacturing project. Shen specializes in the development of advanced drug delivery systems such as those used in making complex dosages, and will test the prototype manufacturing system in her lab.

This project is funded by the federal Food and Drug Administration, grant #1U01FD005773-01.

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Mr. LARSON. And the reason I do that is because, in last year's spending bill, we authorized the FDA to designate five higher education institutions as national centers for excellence in advanced and continuous pharmaceutical manufacturing. This designation would mean investing in domestic manufacturing and innovation.

Unfortunately, when we continue to struggle to fully fund the government, the program remains unfunded. So we are here talking about a problem that needs specific attention. And yes, Mr. Kelly is right, it does require government funding. But to not fund these programs creates enormous problem.

Dr. Gralow, in your comments, you talked about continuing manufacturing and why that is so vitally important. It should be of interest to everyone. But could you also explain the current process of batching and why that leads to extra costs and inefficiency?

Dr. GRALOW. So continuous manufacturing would mean you have always got ongoing processing of either the active pharmaceuticals or of the drug. The batching that you referred to, which is a more standard practice, older model, there is—every time you shift in and out, these—these are sterile injectable drugs that go into patients. So, when you have to switch your assembly line, there is a cost involved with switching to another drug, switching, you know, to another ingredient, whatever. And that shuts it down. So the fits and starts have inherent cost in the system.

So the continuous process of in the background it is always being made is just more efficient and more resilient because if something happens, and it disrupts the whole supply chain, you don't have big batches of something and then not enough of another.

Mr. LARSON. Mr. Cavacini, has that been your experience at McKesson, that the process of batching must be an enormous cost, as opposed to continuous manufacturing?

Mr. CAVACINI. Thank you for the question.

I would like to emphasize that McKesson is a distributor of pharmaceuticals and not a manufacturer. We sit between the manufacturer and providers like hospitals and pharmacies and community providers. We run distribution centers and invest in inventory to make sure that needed medications are available to providers and patients where and when they need them.

But, you know, as we look at the generic market—and I think many generic manufacturers do share their production lines——

Mr. LARSON. Right.

Mr. CAVACINI [continuing]. And that process, as described by the doctor, can contribute to cost and waste and delays in when we need to surge into new products.

Mr. LARSON. Well, thank you. And I remain concerned that we have to get on top of this process, and all of you have talked about the raw materials, et cetera. Is it a question that the United States does not have the raw materials that China and India have, or do we have the raw materials, we are just not producing them?

Anyone who would care to——

Mr. CAVACINI. Thanks for that question. I would say that the U.S. has raw materials, carbon and oxygen and, you know, chemicals, but we don't have a lot of the formulated ingredients to make the drugs that we have.

As I said in my comments, there are at least 100 Active Pharmaceutical Ingredients that the only place you can acquire those in the world and they are ready to incorporate in a drug product form is in China. And there is another set of maybe 250 that are only available from India. There are over 600 that are not available in the U.S. anywhere. So sometimes it is that the ingredients do not exist in the U.S. We could set up companies to make those, but it takes considerable amount of time and will require a lot of investment in those operations.

Mr. LARSON. Thank you, sir.

I yield back.

Chairman SMITH. Mr. Schweikert.

Mr. SCHWEIKERT. Thank you, Mr. Chairman. I would like—with your permission, I have a number of articles I would like to submit for the record.

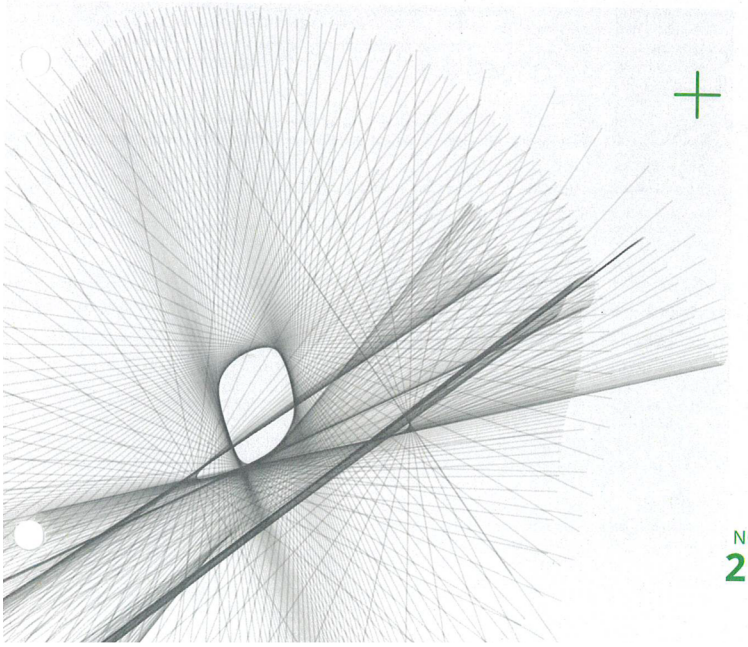
Chairman SMITH. Without objection.

[The information follows:]

IQVIA INSTITUTE FOR HUMAN DATA SCIENCE

Drug Shortages in the U.S. 2023

A CLOSER LOOK AT VOLUME AND PRICE DYNAMICS



NOVEMBER
2023

Introduction

Drug shortages have recently received widespread news coverage for their impact on patient care and public health. The number of drug shortages in the U.S. is increasing as more shortages continue to be reported than resolved. Stakeholders have recommended various approaches to mitigate shortages, such as prioritizing essential medicines, stockpiling, and making changes to reimbursement or statutory rebates. Shortages appear to be driven by a variety of causes that need to be better understood, as they may impact which solutions will best address them.

In this report, shortages reported by the Food and Drug Administration are assessed in conjunction with sales and volume data of these medicines in the U.S. market. Characteristics of shortages, including product type, form, and the number of manufacturers are evaluated. Market concentration is assessed for molecules with shortages based on current sales data. The causes and impacts of shortages across a range of therapy areas are analyzed and presented here.

We intend for this report to provide a foundation for meaningful discussion about the mechanisms that can be put in place to mitigate shortages in the future and steps stakeholders can take to ensure patient access to medicines.

This study was produced independently by the IQVIA Institute for Human Data Science, drawing on IQVIA proprietary data. Funding for this research and report has been provided by the Association for Accessible Medicines. The contributions to this report of Vibhu Tewary, Tizita Zeleke, and others at IQVIA are gratefully acknowledged.

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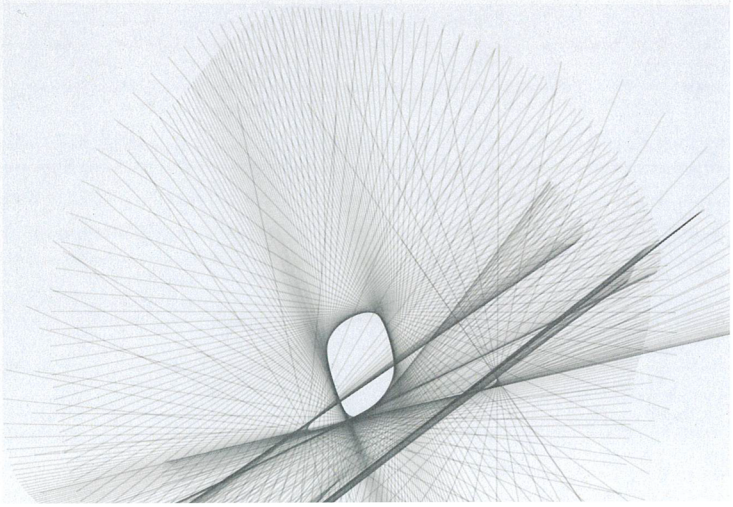
MURRAY AITKEN
Executive Director
IQVIA Institute for Human Data Science

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Overview

Drug shortages occur when the demand of a drug exceeds the supply and are an ongoing issue in the U.S. healthcare system, although the number and severity of shortages has changed over time. While the overall number of shortages may be lower than it was more than a decade ago, the causes and impacts have shifted, requiring different strategies to resolve and prevent shortages. All stakeholders involved in the supply and distribution of medicines, from active ingredient manufacturers to pharmacists, play a role in preventing shortages and ensuring patient access to medicines.

OVERVIEW OF SHORTAGES IN THE U.S.

As of June 2023, there are 132 molecules in the U.S. market with active shortages, impacting a range of therapy areas including pain/anesthesia, oncology, central nervous system, and infectious disease. Over the past five-and-a-half years, three times as many new molecule shortages have occurred as have been resolved, with shortages typically lasting more than a year.

Shortages tend to be in generic (84%) and injectable drugs (67%) and are more frequently multi-source, while shortages were more often single-source generics in 2011, reflecting efforts by regulators and industry to increase generic approvals. Despite shortage molecules predominantly being multi-source, markets remain highly concentrated in a few suppliers, impacting the ability to readily resolve shortages when a leading supplier is affected, and new or existing manufacturers must build or expand manufacturing capacity to account for the gap in supply.

Shortages more frequently occur in multi-source generics where markets are highly concentrated in a few suppliers, impacting resilience and prolonging shortages.

Shortages are more common at lower prices, with 56% of molecules in shortage priced less than $1.00 per unit. An extended unit measured in these analyses is a volume metric, which varies by the type of form a drug takes (oral, injectable, etc.). As injectables are typically measured in milliliters and doses often comprise multiple units, the cost for a dose may be more for an injection than for an oral drug where extended units measure a pill or capsule, which is effectively reflecting a dosage unit. These costs, while not directly comparable, reflect that competition may be driving some of these drugs below their cost of production and distribution. The resulting underinvestment by manufacturers in maintenance and quality or forced exits from the market further constrain competition and challenge market resilience, as well as disincentivizing new entrants.

The planned discontinuations of drug packs rarely lead to shortages and may be a result of strategic business decisions or medicines being withdrawn from the market; however, market exits can disrupt other participants, although regulatory requirements to notify the FDA of planned discontinuations play a key role in enabling other companies to react appropriately.

ONCOLOGY SHORTAGES

Although oncology shortages have only impacted a small share of overall volume, inspection-driven disruptions and market exits have led to significant shortages in older genericized chemotherapeutics and particularly platinum-based chemotherapeutics. Treatment for cancer patients is strongly impacted and may be delayed by chemotherapy shortages, given their use as backbone therapies across multiple indications and limited options for therapeutic interchangeability.

Oncology drugs with significant shortages have highly concentrated markets despite multiple suppliers. Additionally, prices are low, making it more difficult for new or existing suppliers to achieve a return on investment for building or increasing manufacturing capacity to address shortages when major players have

had disruptions. Despite reported shortages, overall oncology volume has continued to increase signaling shortages as a potential issue of disparate drug availability among regional health centers and individual providers, causing patients to delay receiving timely treatments.

SHORTAGES ACROSS OTHER THERAPY AREAS

Drug shortages have occurred across several therapy areas with causes ranging from increased demand to manufacturing disruptions, meaning a single solution may not prevent or resolve future shortages.

Public health measures during the COVID-19 pandemic disrupted the seasonal pattern of bacterial infections, particularly in children, and a return to historic infection levels in late 2022 led to a shortage in pediatric oral liquid antibacterials as the pandemic resulted in unpredictable demand. Conversely, injectable antibacterial shortages began in late 2021 when market share leaders experienced manufacturing delays while overall injectable antibacterial volume has been declining. Continued antibacterial shortages could inadvertently contribute to antimicrobial resistance, as changes in prescription behavior may lead to an increased use of broad-spectrum antibacterials, potentially exacerbating this global concern.

Anesthetic shortages have been persistent since 2017, particularly in local anesthetics, driven by a lidocaine shortage. General anesthetics and muscle relaxants have seen pandemic related shortages as these medicines have been utilized in hospitalized COVID-19 patients, resulting in supply-chain shocks that drove volumes up substantially. Though shortages remain in general anesthetics and muscle relaxants, the impact has lessened as these pandemic waves have subsided.

Psychiatric medicines have seen significant volume increases in recent years following greater awareness among the general public and increased modes of accessibility to providers (e.g., telehealth). Overall ADHD volume has increased 12% since 2017, leading to shortages due to increased demand, particularly in amphetamine salts, despite regulators noting available manufacturing capacity. Shortages in mental health have been confined to a limited number of molecules and generally resolved quickly, despite significant growth in mental health prescriptions in recent years.

GLP-1 agonists are a novel mechanism and illustrate that shortages can also affect new drugs prior to patent expiry, despite innovators strong incentives to always have excess stock available. These drugs have shown such significant promise for people living with diabetes and obesity that use has more than doubled since the end of 2020, driven by new patients across diabetes and obesity. This unprecedented surge in new patients and demand has caused shortages across many of these innovative medicines, limiting access for existing patients and new patients wishing to start therapy.

Shortages can have different causes depending on the market dynamics at play and require a variety of solutions and participation from all stakeholders to resolve and prevent future shortages from occurring.

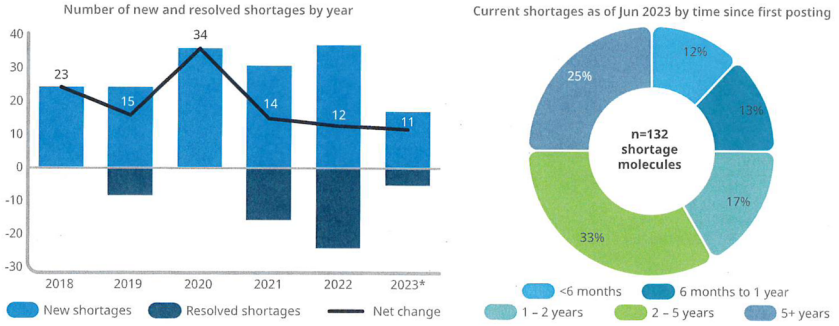
Overview of shortages in the U.S.

- Drug shortages are an ongoing issue in the U.S. healthcare system, although the number and severity of shortages have changed over time, with 132 active shortages as of June 2023.
- Over the past five-and-a-half years, 160 new molecule shortages have occurred through June 2023 while only 51 have resolved, and more than half of current shortages have been ongoing for more than two years.
- Shortages tend to be in generic and injectable drugs, with 84% and 67% of shortages, respectively, while shortages in oral drugs are less common. Of the 132 drugs in shortage, 12 are branded and the remaining 120 are generic, and generic shortages most often affect injectable medicines.
- Multi-source generic molecules are more likely to be in shortage than single-source molecules, while shortages were more often single-source generics in 2011, reflecting efforts by regulators and industry to increase generic approvals over the last decade.
- Despite shortage molecules predominantly being multi-source, markets remain highly concentrated in a few suppliers, impacting the ability to readily resolve shortages when a leading supplier is affected, and new or existing manufacturers must build or expand manufacturing capacity to account for the gap in supply.
- Shortages are more common at lower prices, with 56% of molecules in shortage priced less than $1.00 per unit, where competition may be driving some of these drugs below their cost of production and distribution, causing manufacturers to exit the market and disincentivizing new entrants.
- Planned pack discontinuations rarely lead to shortages, but market exits can disrupt other participants, although regulatory requirements to notify the FDA of planned discontinuations play a key role in enabling other companies to react appropriately.

Drug shortages have been an ongoing issue in the U.S. healthcare system for more than a decade, with 132 active shortages as of June 2023.

More shortages continue to be reported than resolved with 58% of current shortages ongoing for more than two years

Exhibit 1: Net shortage increase by year and time since first posting of current shortages



*2023 is through June

Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

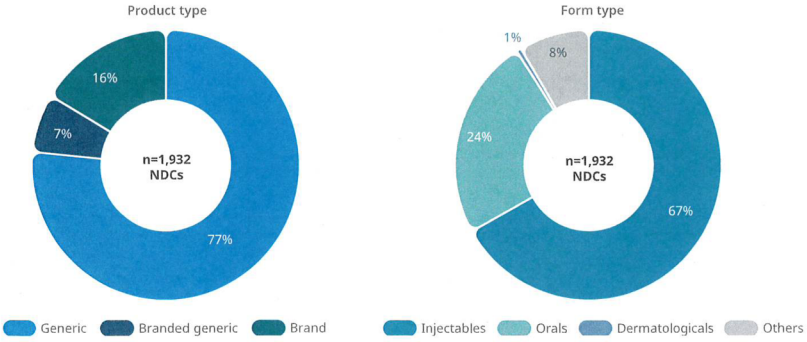
- Over the past five-and-a-half years, an average of more than 25 new molecule shortages have occurred annually, with 160 in total added through June of 2023 and only 51 resolved.
- Resolved shortages have been more clustered in time without a steady pattern, with the largest number being resolved in the second and third year of the COVID-19 pandemic.
- For the currently active shortages affecting 132 molecules, 75% have been active for more than a year and 58% have been ongoing for more than two years.
- Many shortages are affecting medicines with complex manufacturing processes, and the limited ability of new or existing manufacturers to increase or add new capacity is an underlying reason for extended durations of shortages.
- While some shortages are short-term and may be related to unexpected seasonal demand, others are more systemic and suggest more complex drivers of the shortages.

Notes: Molecules are included as new in the year the shortage was initially posted to the FDA Drug Shortages Database. Molecules are included as resolved when the shortage has resolved and included in the year of the date of update for the shortage. Molecules where a shortage occurred and was resolved and a subsequent shortage occurred in the following years would be represented more than once.

OVERVIEW OF SHORTAGES IN THE U.S.

84% of the drugs in shortage in the last six years are generics, 67% injectables, and 24% orals

Exhibit 2: FDA shortages by product type and form, 2017–Jun 2023



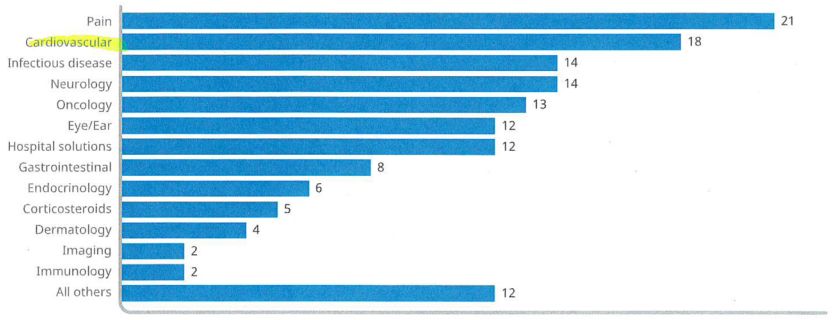
Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

- The vast majority of shortages — 84% of national drug codes (NDCs), which are unique identifiers for individual pharmaceutical packs for each company — are generic or branded generic drugs. Injectables represent 67% of shortage NDCs.
- Generic injectables represent 65% of generic NDCs in shortage, similar to injectables, and 67% of shortages overall.
- Generally generic medicines are much lower cost than brands and some observers have begun to suggest that some generic prices may be too low to support sustainable markets.
- The FDA commissioner in August 2023 said "...the fundamental problem is that we have two drug industries in the U.S. — the innovator industry...[and] the generic side, and a lot of the prices are too low... the price has been driven down below the cost of manufacturing and distributing the drug."[1]
- Prices driven below the cost of manufacturing and distributing can result in some competitors discontinuing production of molecules, reducing necessary maintenance activities and generally contributing to less resilience in manufacturing supply of those medicines.

Notes: See Definitions for more information about national drug codes (NDCs).

Shortages are concentrated in pain, including anesthesia, cardiovascular, infectious diseases, neurology and oncology

Exhibit 3: Molecules with current shortages as of June 2023 by therapy area



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

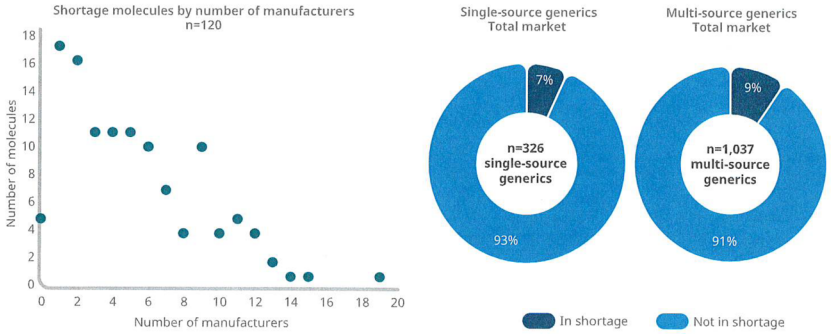
- Many shortages are focused in just a few therapy areas, including pain/anesthesia, cardiovascular, infectious diseases, central nervous system, and oncology, and these areas have been leading causes of shortages over the past decade.[2]
- A dozen years ago, a peak of shortages drove significant levels of attention and several policy responses, including increased generic approvals and the creation of the current FDA shortage reporting system.
- Current oncology shortages, including those in supportive care, are concentrated in platinum-based chemotherapies, and while there are 13 active shortages now compared to 28 in 2011, there are important similarities in the two periods a dozen years apart.
- Shortages have continued to be concentrated in sterile injectables and in generic drugs, and the same classes leading shortages today were also impacted the most in that earlier period.
- Antibacterial shortages, whether pharmacy or hospital-dispensed, are a significant concern affecting multiple aspects of healthcare delivery and have occurred throughout the past decade. These shortages impact treatment choices, requiring shifts to more potent treatments earlier for a patient, reducing future escalation opportunities and worsening issues related to antimicrobial resistance.

Notes: Molecules used to treat diseases across different therapy areas may be represented in multiple therapy areas. Oncology includes supportive care.

OVERVIEW OF SHORTAGES IN THE U.S.

Multi-source generic molecules are more likely to be in shortage than single-source molecules

Exhibit 4: Generic molecules by shortage status and number of manufacturers, Jan–Jun 2023



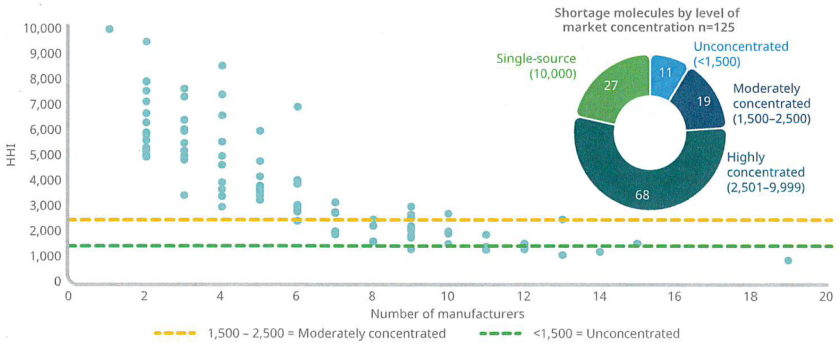
Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

- Current shortages are more often affecting molecules with multi-source manufacturing, reflecting that market resilience is driven by diversified supply, not only the number of companies involved. Of the medicines with generics available and affected by shortages, only 17 of them were single-source, while the vast majority were multi-source, one with 19 companies involved.
- Single-source generic medicines are much less common today than they were in 2011,[2] largely as a result of sustained efforts by the FDA and industry to increase generic approvals for previously single-source drugs.
- Those efforts further contributed to the lower frequency of single-source generics in shortage, which represents 7% of those medicines in the market compared to 9% of multi-source generics being in shortage.
- Single-source generic makers' market predictability may be allowing them to manage buffer stocks and mitigate the impacts of market volatility with less financial risk than is possible in multi-source markets.
- The multi-source generics in shortage are a further illustration that the presence of a company as a manufacturer does not always translate into the ability to react to a competitors' shortage and fill a gap in supply.

Notes: Generic molecules are those where generics or branded generics are available, and brands may still be available. Brand molecules are those where only brands are available. Manufacturers included if they represent at least 1% of volume in the first six months of 2023.

Most molecules with shortages are multi-source but remain highly concentrated, impacting resilience to shortages

Exhibit 5: Shortage molecule Herfindahl-Hirschman Index (HHI) and number of companies, Jan–Jun 2023



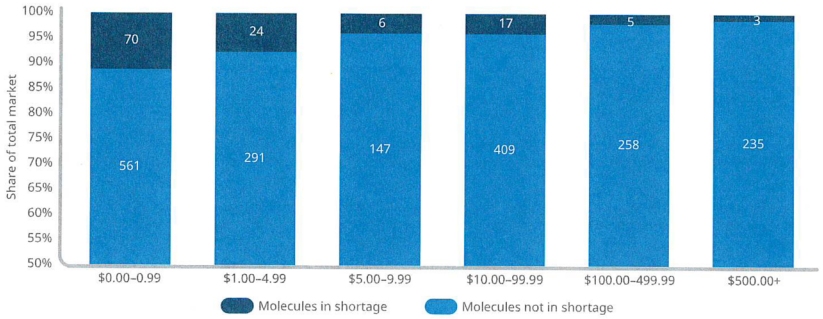
Source: FDA Drug Shortages Database, Jun 2023; IQVIA National Sales Perspective, Jul 2023; IQVIA Institute, Jul 2023.

- The concentration of market share among competitors is a key indicator of the potential resilience of the market to an unexpected driver of shortages and can be measured with the Herfindahl-Hirschman Index (HHI).
- Natural disasters, active or inactive ingredient supply issues, as well as disruptions to packaging materials such as vials can all contribute to manufacturing supply issues, and when those issues affect a significant share of a molecule, shortages may result.
- Another driver of disruptions has been regulatory oversight, where FDA inspections have triggered shutdowns of some sites and where those companies are leading suppliers of a medicine, the shortages are difficult for their peers to resolve.
- Over three-quarters of current shortages are in highly concentrated markets (including single-source), indicating that issues in supply from leading suppliers or the only supplier may result in prolonged shortages as significant lead-time is needed for a new or existing company to build or expand capacity in a complex generic, not accounting for further delays that may be driven by commercial uncertainties delaying investment decisions.

Notes: Seven molecules with current shortages have no sales in the first six months of 2023 and are not included here. Manufacturers included if they represent at least 1% of volume in the first six months of 2023. See Definitions for more information about Herfindahl-Hirschman Index (HHI).

Shortages are more common at lower prices with 56% of molecules in shortage priced less than $1.00 per unit

Exhibit 6: Average invoice price per extended unit of molecules, Jan–Jun 2023, n=2,026



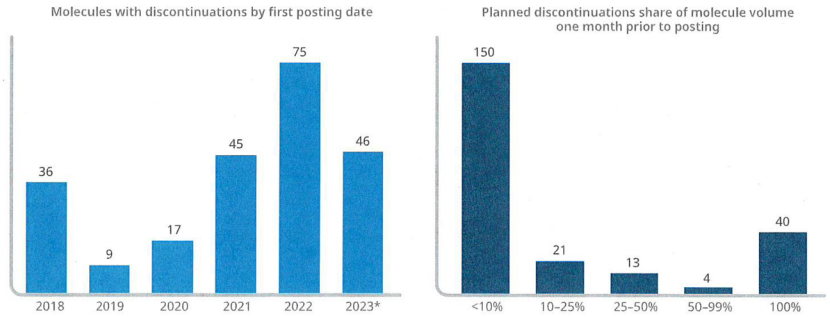
Source: FDA Drug Shortages Database, Jun 2023; IQVIA National Sales Perspective, Jul 2023; IQVIA Institute, Jul 2023.

- Shortages are more common in drugs with very low list prices, with 11% (70 of 631) of drugs priced less than $1.00 per extended unit in shortage, compared to 1.3% (3 of 238) of those priced more than $500 per unit.
- Low priced drugs (<$1) accounted for 56% of the 125 drugs in shortage with reported volume in this analysis.
- An extended unit is defined as a milliliter for some injections, and as a pill for oral solids (see Definitions for more details). These variations notwithstanding, more than half of shortages are affecting drugs with very low list prices.
- These list prices do not take into account discounts and rebates, which apply in the supply chain and further erode a manufacturer's realized prices.
- With the list prices of these medicines eroded to very low levels, returns on investments in new facilities or increased capacity are among the more challenging decisions being made in the generic sector.
- Competition in generic molecules may be driving some of these drugs below their cost of production and distribution, although these details are opaque and unclear, causing manufacturers to exit the market and disincentivizing new entrants.

Notes: Seven molecules with current shortages have no sales in the first six months of 2023 and are not included here.

Planned pack discontinuations rarely lead to shortages, but market exits can disrupt other participants and affect resilience

Exhibit 7: Planned discontinuations by first posting date and volume share prior to posting



*2023 is through June

Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

- As prices have declined, one suggestion has been that companies will discontinue manufacturing where they are not making a profit and this does appear to be a fairly common occurrence, with companies discontinuing at least one form/strength of 228 molecules since the end of 2017.
- These discontinuations have not resulted in shortages, although other drugs reported as current shortages have a history of company discontinuations in the months or years leading up to the start of their shortages.
- Nearly two-thirds of discontinuations were of NDCs with <10% share of their molecule, reflecting rational business decisions of companies failing to achieve sustainable market shares.
- The remaining one-third of discontinuations have had more significant market shares and there could be multiple reasons why these have not resulted in a shortage, although they are not precluded from it happening in the future.
- The FDA requirements to notify the agency of planned discontinuations plays a key role in enabling other companies to react appropriately.
- Reformulations and transitions to newer or better treatments options, where the planned discontinuation is part of a strategic shift, make a discontinuation less likely to result in a market disruption.
- Finally, there are cases where a medicine is being withdrawn for clinical reasons, and the planned discontinuation does not result in a shortage.

Notes: Molecules with discontinuations and current or resolved shortages have been defined as shortages and are not plotted here. Molecules may have more than one planned discontinuation but are only plotted once based on earliest discontinuation posting on FDA Drug Shortages Database. Nineteen molecules with planned discontinuations had no volume one month prior to posting of the discontinuation and are assumed to have represented 100% of molecule volume prior to discontinuation.

Oncology shortages

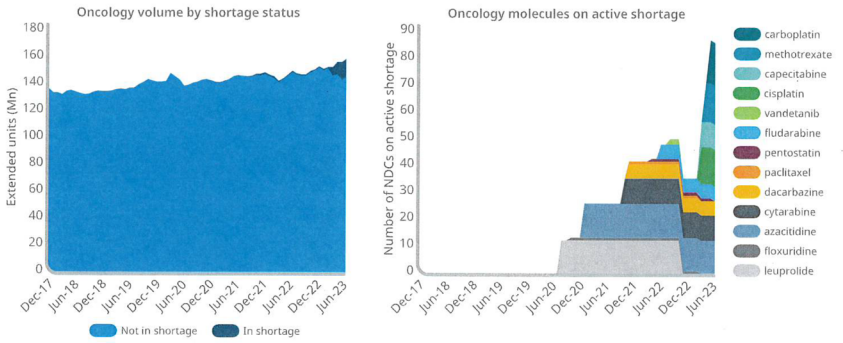
- Oncology shortages were exacerbated during the COVID-19 pandemic and although only a small share of overall oncology volume has been impacted, shortages have been concentrated in older genericized chemotherapeutics and particularly platinum-based chemotherapeutics, raising concerns for patients needing these medicines as part of their cancer care.
- Twelve oncology molecules have had shortages over the last 18 months and impacting 1% to 100% of the volume over that period, with 11 injectable and one oral shortage.
- Inspection-driven disruptions and market exits have led to shortages of oncology molecules, leaving other manufacturers to increase production to fill the supply gaps.
- Oncology drugs with significant shortages are highly concentrated markets despite multiple suppliers with low prices, making it more difficult for new or existing suppliers to achieve a return on investment for building or increasing manufacturing capacity to address shortages.
- The manufacturing complexity associated with some oncology medicines and highly commoditized prices have reduced the number of active manufacturers in many molecules over a period of years.
- Competitive pressures have most often created markets with high concentration, where one or just a few companies have a majority of the market, limiting the resilience of the market to any unexpected disruptions.

Platinum-based chemotherapy shortages have had an outsized impact on patient care because of their central position in a wide range of regimens across tumors and multiple lines of therapy, often where there are few therapeutic alternatives.

ONCOLOGY SHORTAGES

Oncology shortages exacerbated during the COVID-19 pandemic but represent a small share of overall oncology volume

Exhibit 8: Oncology volume and molecules by shortage status, Dec 2017–Jun 2023



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

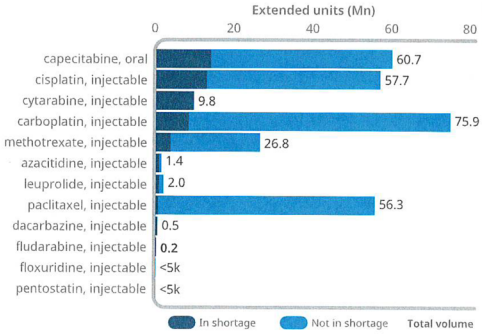
- As of June 2023, there are eight cancer medicines with active shortages while five other medicines have seen shortages over the last five years that have resolved.
- Oncology has seen a growing number of shortages since 2020, with four new molecule shortages between March and June 2023: cisplatin, methotrexate, capecitabine, and carboplatin.
- Although there are shortages having significant impacts across these molecules, the volume in shortage accounts for only 9% of the total oncology volume in June 2023, and overall oncology volume continues to grow, up 6% from June 2022.
- Oncology shortages have been concentrated in older genericized chemotherapeutics, and platinum-based chemotherapeutics — carboplatin and cisplatin — have been particularly impacted by shortages beginning in February 2023, causing concerns for patients who rely on these life-saving medications.

Notes: Analysis includes medicines with a focus on cancer therapeutics and does not include supportive care. Shortages are determined at the pack level and included only during the period for which the pack was in shortage.

ONCOLOGY SHORTAGES

Oncology shortages are primarily impacting injectables with 100% of cytarabine volume in shortage over the last 18 months

Exhibit 9: Oncology molecule volume in shortage, Jan 2022–Jun 2023, extended units (Mn)



% volume in shortage Jan 2022–Jun 2023	Month shortage first reported
23%	Feb 2023
23%	Feb 2023
100%	Sep 2021
11%	Apr 2023
14%	Mar 2023
63%	Dec 2023
44%	Jul 2020 (resolved Oct 2022)
1%	Oct 2021 (resolved Feb 2023)
89%	Oct 2021
65%	May 2022
100%	Sep 2020 (resolved Feb 2023)
83%	Mar 2022 (resolved May 2023)

Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

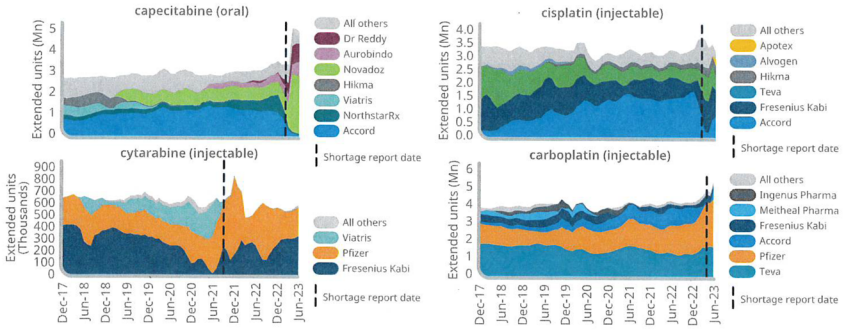
- Twelve molecules have had shortages over the last 18 months, impacting 1% to 100% of the volume over that period, with 11 injectable and one oral shortage.
- Four molecules account for 87% of the shortage volume since January 2022: capecitabine, cisplatin, cytarabine, and carboplatin.
- While capecitabine and cisplatin shortages have impacted 23% of the total volume and carboplatin shortages 11%, cytarabine shortages have impacted 100% of the volume, raising concerns for access to this medicine for patients with hematological cancers.
- While other medicines with shortages in the last 18 months account for less volume, many of these are used to treat rare cancers with smaller patient populations where shortages can have significant impacts for these patients.
- Dacarbazine, used in the treatment of malignant melanoma and Hodgkin lymphoma, has been in shortage since late 2021, with 89% of the volume in the last 18 months impacted by shortages. Dacarbazine is included in the treatment regimen used most commonly for Hodgkin lymphoma,[3] raising concerns for consistent treatment of patients with this rare cancer.

Notes: Analysis includes medicines with a focus on cancer therapeutics and does not include supportive care. Vandetanib had no sales during the period it was in shortage and is not included here. Shortages are determined at the pack level and included only during the period for which the pack was in shortage.

ONCOLOGY SHORTAGES

Oncology shortages likely due to inspection driven disruptions and market exits of major players

Exhibit 10: Volume by corporation for select oncology shortages, Dec 2017–Jun 2023, 3-month rolling avg extended units (Mn)



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

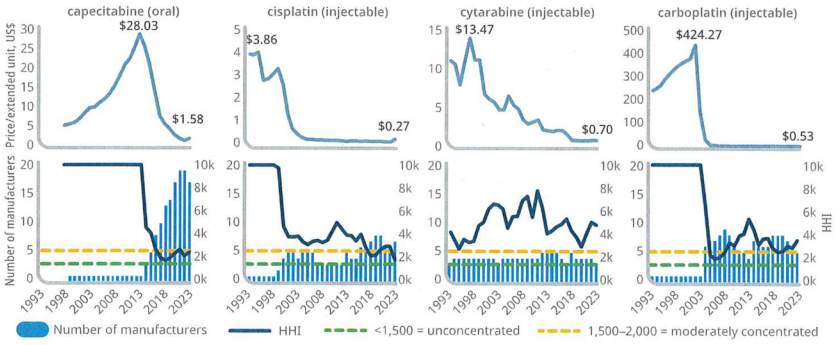
- The most significant shortages by volume in oncology have been the result of manufacturing disruptions and exits from manufacturers accounting for significant market shares.
- For capecitabine, cisplatin, and carboplatin, these shortages began between February and April 2023, shortly after FDA facility inspections in late 2022 noted deficiencies at Intas Pharmaceuticals — which sells medicines in the U.S. market under Accord Healthcare — leading to import restrictions on these drugs and many others.[4]
- Prior to this, Accord entered these markets during the period 2015–2017, following abbreviated new drug application (ANDA) approvals. Leading up to the shortage events, Accord accounted for 22% of the carboplatin market, 33% of the capecitabine market, and 53% of the cisplatin market.
- As a result of inspections, Intas (Accord) took the manufacturing line out of production, leading to significant disruptions to these medicines and requiring other manufacturers to increase production to account for the lost volume, which they largely were able to do.
- The cytarabine shortage began in 2021 following the exit of Viatris which accounted for 44% of the market prior to discontinuation, leaving the other two manufacturers to increase production.
- Notably, supply typically rises exponentially following the announcement of a shortage, rather than falling. This is likely a result of stockpiling by healthcare organizations due to fear of limited future access. Generally larger, better resourced purchasers have been better able to adapt to disruptions, whereas smaller community oncology providers have reported shortages and, in some cases, have had to suspend or delay treatments or refer patients to be treated elsewhere.

Notes: Manufacturers with less than 3% of total volume and repackagers are included in all others. Shortage report date represents the earliest initial posting date of the shortage in the FDA Drug Shortages Database.

ONCOLOGY SHORTAGES

Oncology markets are highly concentrated, inhibiting responses to address shortages and extending the effects

Exhibit 11: Invoice price of select oncology shortages and Herfindahl-Hirschman Index (HHI), 1993–Jun 2023



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

- Following brand loss of exclusivity, oncology medicines with shortages have seen overall declines in price despite variable market participants and market concentration.
- Prices for injectable oncology shortages dropped significantly after generic entry, stabilizing at prices of less than $1.00 per extended unit in recent years.
- These pricing dynamics make it difficult for manufacturers to get a return on the investment needed to increase production when a shortage is ongoing, often leading to prolonged shortages.
- Despite four to ten manufacturers for these injectable generic medicines, the markets have remained moderately to highly concentrated with one or two of these manufacturers maintaining a majority of the market share.
- Oral capecitabine has seen a similar rapid decline in price with generic entry and an increasing number of competitors — up to 19 in 2021 and 2022 — but the market has remained moderately concentrated with a few manufacturers.
- The low prices and high degree of market concentration exposes the market to significant disruptions when a major player experiences a manufacturing disruption or exits. These factors reduce resiliency, as other manufacturers in the market and new entrants would need to invest in increasing manufacturing capacity in a low margin product.

Notes: 2023 data shown here is based on sales data from the first six months of 2023. See Definitions for more information about Herfindahl-Hirschman Index (HHI).

Shortages across other therapy areas

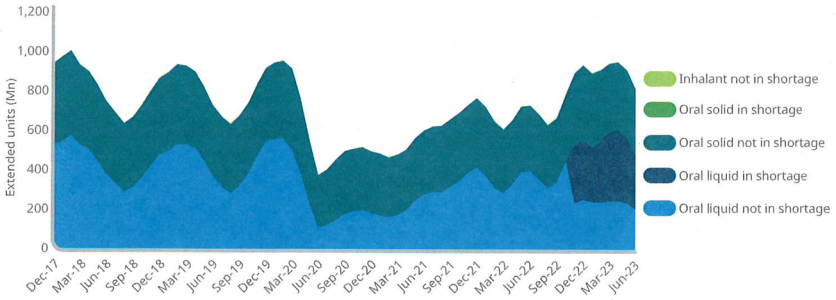
- Shortages have occurred across a number of other therapy areas with causes ranging from increased demand to manufacturing disruptions, meaning a single solution may not prevent or resolve future shortages.
- Public health measures during the COVID-19 pandemic disrupted the seasonal pattern of bacterial infections, particularly in children, and a return to historic infection levels in late 2022 led to a shortage in oral pediatric antibacterials.
- Increasing injectable antibacterial shortages began in late 2021 when market share leaders experienced manufacturing delays and have yet to be resolved.
- Anesthetic shortages have been persistent since 2017, with local anesthetics particularly affected and general anesthetics impacted with successive waves of COVID-19 hospitalizations.
- Overall ADHD medicine volume has increased 12% since 2017, leading to shortages due to increased demand, despite available manufacturing capacity.
- Despite growth in overall mental health prescriptions, shortages have been confined to a limited number of molecules and generally resolved quickly.
- GLP-1 agonist use has more than doubled since the end of 2020, driven by new patients in both diabetes and obesity and contributing to ongoing shortages in these novel medicines.

Shortages have been the result of various causes, including increased demand and manufacturing disruptions.

SHORTAGES ACROSS OTHER THERAPY AREAS

Oral antibacterial shortages driven by increased pediatric use in late 2022 following lower demand during the pandemic

Exhibit 12: Non-injectable antibacterial volume by form and shortage status, Dec 2017–Jun 2023, 3-month rolling avg extended units (Mn)



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

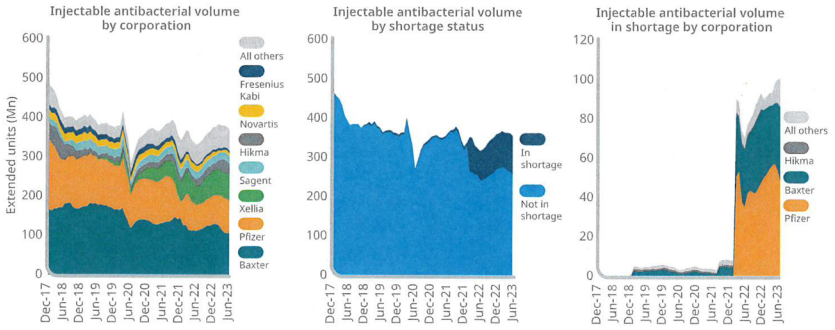
- Antibacterial usage was down over 20% during 2020 and 2021 as social distancing and other public health measures used to combat COVID-19 were effective at decreasing bacterial infections. As these measures were phased out, antibacterial use began to rise again in 2022 and was up 2% in the first half of 2023 compared to pre-pandemic levels.
- Children under the age of 19 saw the most dramatic changes in usage throughout the pandemic, with a 50% decline in prescriptions early on followed by a significant increase as children returned to school and other activities, ending 2022 with prescriptions 8% above pre-pandemic levels.[5]
- The significant disruption during the pandemic in pediatric use of antibacterials led to a shortage in oral liquid formulations starting in October 2022 as the health system was not able to predict demand for the fall/winter respiratory illness season, which was more severe than prior years.
- One consequence of antibacterial shortages, reported by researchers at Boston Children's Hospital, is a shift in prescribing to more broad spectrum antibacterials, which can increase the likelihood of antimicrobial resistance.[6]

Notes: Shortages are determined at the pack level and included only during the period for which the pack was in shortage.

SHORTAGES ACROSS OTHER THERAPY AREAS

Increasing injectable antibacterial shortages began in late 2021 when market share leaders experienced manufacturing delays

Exhibit 13: Injectable antibacterial volume by corporation and shortage status, Dec 2017–Jun 2023, 3-month rolling avg extended units (Mn)



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

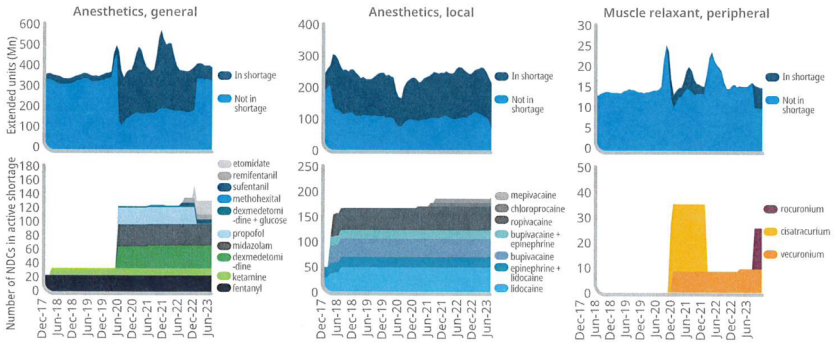
- Injectable antibacterials have seen declining volume over the last five years as efforts have been made to more appropriately use antibacterials to reduce the development of antimicrobial resistance.
- Baxter Healthcare and Pfizer account for more than half of the injectable antibacterial volume in the U.S., with Xellia Pharmaceuticals the next largest manufacturer at 17% of the market.
- Shortages of injectable antibacterials have been ongoing since 2017 but have impacted less than 3% of volume until early 2022 when a shortage of injectable metronidazole began, and shortages now impact 28% of overall volume.
- Injectable metronidazole shortages accounted for 91% of injectable antibacterial volume in shortage as of June 2023, with Pfizer and Baxter Healthcare shortages contributing the most.
- Additionally, Pfizer, which accounts for 38% of the injectable penicillin market, warned of a shortage in June 2023 due to manufacturing delays and rising syphilis infections, with the shortage expected to last through 2024,[7] adding further stresses on healthcare providers trying to navigate the injectable antibacterial market.

Notes: Manufacturers with less than 3% of total volume and repackagers are included in all others. Shortages are determined at the pack level and included only during the period for which the pack was in shortage.

SHORTAGES ACROSS OTHER THERAPY AREAS

Anesthetic shortages have been persistent since 2017 with local anesthetics particularly affected

Exhibit 14: Anesthetic volume by shortage status and molecules in shortage, Dec 2017–Jun 2023



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

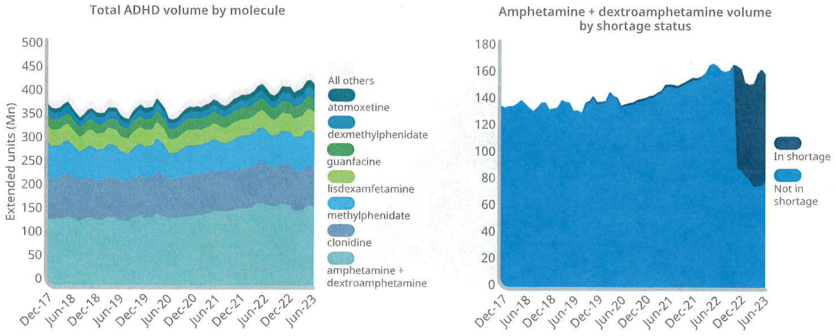
- Anesthesia medicines, including general, local, and muscle relaxants, are foundational to inpatient and outpatient surgical procedures, and shortages in these medicines can result in delays for patients receiving procedures and hospitals making prioritization decisions based on available supply.
- General anesthesia has had shortages for many years for fentanyl, which as a controlled substance has additional supply chain complications.
- At the start of the COVID-19 pandemic, reported shortages for medicines needed for ICU patients resulted in supply-chain shocks that drove volumes up substantially and then had seasonal spikes for several years.
- Local anesthesia has been dominated by a many-years-long lidocaine shortage, which in turn has its roots in companies' challenges in manufacturing sufficient supplies of long-acting versions such as bupivacaine, resulting in shortages of both molecules.
- Muscle relaxants are a common medicine for intubating patients, among other uses, and the pandemic surge in demand generated shortages which were resolved, despite annual spikes in volume.
- Shortages across these medicines complicate scheduling of a wide range of procedures and surgeries, which may be part of a broad-based reduction observed in elective procedures in post-pandemic periods.

Notes: Includes prescription medicines only; OTC medicines are not included. Shortages are determined at the pack level and included only during the period for which the pack was in shortage.

SHORTAGES ACROSS OTHER THERAPY AREAS

Overall ADHD volume has increased 12% since 2017 leading to shortages due to increased demand

Exhibit 15: ADHD volume by molecule and shortage status, Dec 2017–Jun 2023, 3-month rolling avg extended units (Mn)



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

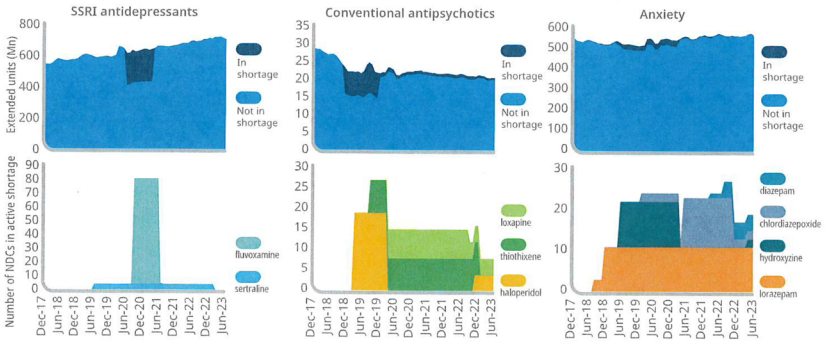
- Overall use of medicines for attention-deficit/hyperactivity disorder (ADHD) has grown 12% since 2017 and amphetamine + dextroamphetamine (amphetamine salts) account for 37% of ADHD medicine use.
- Use of ADHD medicines rose significantly throughout the pandemic, particularly in women aged 20–64, with an increase in remote work and clinician awareness contributing and continued use from previously diagnosed patients.[5]
- Shortages in ADHD have primarily impacted amphetamine salts, where half of volume was in shortage as of June 2023. Other ADHD medicines, including novel treatments Qelbree and Azstarys launched in 2021, remain available.
- Because amphetamine salts are Schedule II drugs, their manufacturing is highly controlled, however the FDA and Drug Enforcement Administration (DEA) have indicated that manufacturers produced only 70% of their amphetamine salt quota in 2022, leaving nearly 1 billion additional doses that could have been supplied.[8]
- An additional complicating factor is the spring 2022 opioid crisis settlement, which required drug wholesalers to exercise more scrutiny over the volumes of controlled substances they ship to pharmacies. Most affected organizations implemented algorithmic volume caps, with some pharmacies and/or prescribers with volatile prescription demand resulting in canceled orders and patients unable to acquire prescribed medications.[9]

Notes: Includes prescription medicines only; OTC medicines are not included. Shortages are determined at the pack level and included only during the period for which the pack was in shortage.

SHORTAGES ACROSS OTHER THERAPY AREAS

Mental health molecules have been on shortage since 2018 with some classes showing sharp increase in shortage due to demand

Exhibit 16: Mental health volume by shortage status and molecules in shortage, Dec 2017–Jun 2023



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

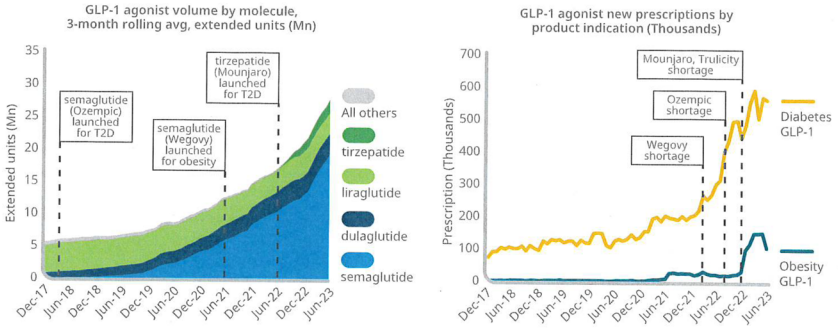
- Despite significant growth in overall mental health prescriptions since 2019,[5] shortages have been confined to a limited number of molecules and generally resolved quickly.
- For the most part, antidepressants are dispensed as oral solids, and oral medicines can be characterized as lower complexity for manufacturing and thus more easily addressed by a company increasing supply compared to injectable drugs.
- The lack of substantial impact on the market level trend suggests there may be other therapeutic alternatives, which could include newer branded therapies that may benefit from shortages of older generic drugs.
- Anxiety drugs have seen a notable increase in volume over the past five years, particularly during the pandemic, and while there have been shortages, the impacts have been relatively isolated and resolved within a couple of years.
- Notably, an ongoing shortage in injectable lorazepam could have impacts on patients undergoing surgeries, experiencing seizures, or admitted in the ICU, however other benzodiazepines for injection are available as therapeutic alternatives.[10]

Notes: Shortages are determined at the pack level and included only during the period for which the pack was in shortage.

SHORTAGES ACROSS OTHER THERAPY AREAS

GLP-1 use has more than doubled since the end of 2020 driven by new patients in both diabetes and obesity

Exhibit 17: GLP-1 agonist volume by molecule and new prescriptions by indication, Dec 2017–Jun 2023



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, IQVIA National Prescription Audit, Jun 2023; IQVIA Institute, Oct 2023.

- The first GLP-1 agonist for treatment of type II diabetes launched in 2005, however GLP-1 agonist use has increased rapidly since the launch of Ozempic in 2018 and the subsequent launch of Wegovy for treatment of obesity in 2021, with current GLP-1 agonist volume nearly four times that in 2017 and GLP-1 agonists the fastest growing mechanism in diabetes.[5]
- Since the launch of Wegovy, new prescriptions are up 181% for diabetes GLP-1s and 257% for obesity GLP-1s as increasing awareness of these medicines has increased patient demand.
- Wegovy, Ozempic, Trulicity, and Mounjaro are all experiencing shortages as new patient demand across both diabetes and obesity outpaces supply, potentially causing difficulties in filling prescriptions for patients already on therapy.
- Novo Nordisk, the manufacturer of Wegovy, indicated in May 2023 that it was limiting supply of lower doses of Wegovy used as starting doses to ensure adequate supply of higher doses for existing patients.[11]
- New data highlighting the effectiveness of GLP-1s in preventing cardiovascular events[12] and the early termination of a trial for chronic kidney disease due to efficacy[13] indicate a likely expansion of use of GLP-1s, further increasing demand.

Notes: GLP-1 agonist products are grouped based on indication listed on latest FDA label and do not reflect off-label use.

Notes on sources

THIS REPORT IS BASED ON THE IQVIA SERVICES DETAILED BELOW

NATIONAL PRESCRIPTION AUDIT (NPA):
NPA is the industry standard source of national prescription activity for all pharmaceutical products. It measures demand for prescription drugs, including dispensed pharmaceuticals to consumers across three unique channels: retail, mail service, and long-term care pharmacies. From sample pharmacies, IQVIA collects new and refilled prescription data daily. NPA represents and captures over 92% of all outpatient prescription activity in the United States and covers all products, classes, and manufacturers.

NATIONAL SALES PERSPECTIVES (NSP) measures revenue within the U.S. pharmaceutical market by pharmacies, clinics, hospitals and other healthcare providers. NSP reports 100% coverage of the retail and non-retail channels for national pharmaceutical sales at actual transaction prices. The prices do not reflect off-invoice price concessions that reduce the net amount received by manufacturers.

THIRD-PARTY INFORMATION:
FOOD AND DRUG ADMINISTRATION DRUG SHORTAGES DATABASE is a searchable database to provide stakeholders with easy access to information about drugs in shortage and includes information about current drugs in shortage, resolved shortages, discontinuations of specific drug products, and other relevant product information. Information in the database is predominantly provided to FDA by manufacturers and the database is updated daily. For this report, the information analyzed from the database was that provided as of June 8, 2023. The database can be accessed from: https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.

Defintions

HERFINDAHL-HIRSCHMAN INDEX (HHI) is a measure of market concentration and is often used to measure the impact of mergers on competitiveness in a market. The HHI is the sum of the squares of each market participants market share. The U.S. Department of Justice and Federal Trade Commission define markets as unconcentrated when the HHI is below 1,500, moderately concentrated when the HHI is between 1,500 and 2,500, and highly concentrated when the HHI is above 2,500.[14]

SALES AT INVOICE PRICES are used throughout this report and reflect sales at prices paid by outlets (i.e., pharmacies, hospital, clinics), whether purchased directly from a manufacturer or indirectly via a wholesaler. Invoice line-item discounts are included. Other discounts and rebates are not reflected.

EXTENDED UNITS are the number of tablets, capsules, milliliters, ounces, etc. of a product shipped in each unit and can be used to measure volume. For oral solid formulations, extended units are equal to the number of tablets or capsules. For wet vials, extended units are equal to the number of milliliters. For dry vials, extended units are equal to the number of vials.

NATIONAL DRUG CODES (NDCS) are assigned by the FDA and serve as universal product identifiers for prescription drugs. Each NDC code is a 10-digit number that identifies the labeler, product, and package. The labeler code identifies the firm that manufactures, repackages or distributes a drug product. The product code identifies the specific strength and form for a product. The package code identifies the trade package size.

Methodologies

DEFINING SHORTAGES

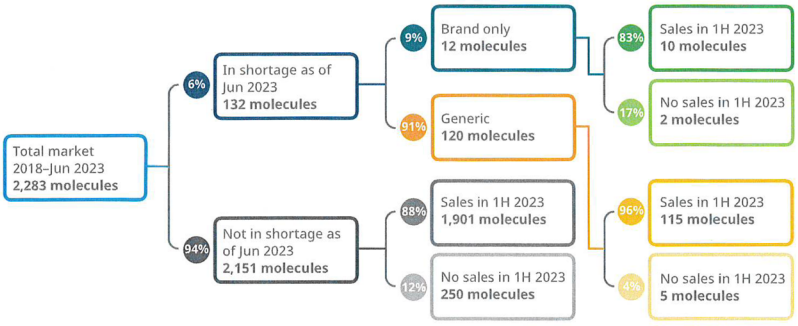
Shortages are defined throughout this report based on information provided in the FDA Drug Shortages Database as of June 8, 2023. NDCs are provided in the Drug Shortages Database and were matched to NDCs available in IQVIA National Sales Perspective. Volume and product characteristics were assessed for shortages at the NDC level.

Shortages were determined and further characterized at the molecule, or active ingredient, level. Molecules with "current" or "resolved" statuses in the Drug Shortages Database were determined to be shortage molecules, regardless of the presence of discontinuations within that molecule. Molecules that had only "discontinued" statuses were not included as shortages and are reported as discontinuations.

For "current" shortages, shortages were considered active from the initial posting date included in the Drug Shortages Database. For "resolved" shortages, shortages were considered active from the initial posting date to the date of update included in the Drug Shortages Database.

Shortages were only included in volume and sales analyses where sales occurred in the observed period. For current shortages, volume and sales analyses are based on 1H 2023 data (Jan–Jun 2023). Total market analyses are based on prescription drugs only where volume/sales were observed in the period. The segmentation of molecules in the market is provided in Exhibit 18.

Exhibit 18: Molecules in U.S. market segmented by shortage status and sales in 1H 2023



Source: FDA Drug Shortages Database, IQVIA National Sales Perspective, Jun 2023; IQVIA Institute, Oct 2023.

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Murray Aitken is Executive Director, IQVIA Institute for Human Data Science, which provides policy setters and decisionmakers in the global health sector with objective insights into healthcare dynamics. He led the IMS Institute for Healthcare Informatics, now the IQVIA Institute, since its inception in January 2011. Murray previously was Senior Vice President, Healthcare Insight, leading IMS Health's thought leadership initiatives worldwide. Before that, he served as Senior Vice President, Corporate Strategy, from 2004 to 2007. Murray joined IMS Health in 2001 with responsibility for developing the company's consulting and services businesses. Prior to IMS Health, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray writes and speaks regularly on the challenges facing the healthcare industry. He is editor of Health IQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.



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Michael Kleinrock serves as Research Director for the IQVIA Institute for Human Data Science, setting the research agenda for the Institute, leading the development of reports and projects focused on the current and future role of human data science in healthcare in the United States and globally. Kleinrock leads the research development included in Institute reports published throughout the year. The research is focused on advancing the understanding of healthcare and the complex systems and markets around the world that deliver it. Throughout his tenure at IMS Health, which began in 1999, he has held roles in customer service, marketing, product management, and in 2006 joined the Market Insights team, which is now the IQVIA Institute for Human Data Science. He holds a B.A. degree in History and Political Science from the University of Essex, Colchester, UK, and an M.A. in Journalism and Radio Production from Goldsmiths College, University of London, UK.



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Jamie Pritchett is Thought Leadership Manager for the IQVIA Institute, managing aspects of IQVIA Institute projects and conducting research and analysis within global healthcare. Prior to joining IQVIA in 2021, he held positions with the North Carolina Department of Health and Human Services and the Duke Human Vaccine Institute, where he developed skills in understanding and addressing the array of physical, environmental, and social contributors to individual health. Jamie uses his experience in public health, health communication, and drug development and research to understand current trends in healthcare and the life sciences industry. He holds a Bachelor of Science in Animal Science and Zoology and a Master of Toxicology from North Carolina State University.

About the Institute

The IQVIA Institute for Human Data Science contributes to the advancement of human health globally through timely research, insightful analysis and scientific expertise applied to granular non-identified patient-level data.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved human outcomes. With access to IQVIA's institutional knowledge, advanced analytics, technology and unparalleled data the Institute works in tandem with a broad set of healthcare stakeholders to drive a research agenda focused on Human Data Science including government agencies, academic institutions, the life sciences industry, and payers.

Research agenda

The research agenda for the Institute centers on five areas considered vital to contributing to the advancement of human health globally:

- Improving decision-making across health systems through the effective use of advanced analytics and methodologies applied to timely, relevant data.
- Addressing opportunities to improve clinical development productivity focused on innovative treatments that advance healthcare globally.
- Optimizing the performance of health systems by focusing on patient centricity, precision medicine and better understanding disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.
- Understanding the future role for biopharmaceuticals in human health, market dynamics, and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of technology in health system products, processes and delivery systems and the business and policy systems that drive innovation.

Guiding principles

The Institute operates from a set of guiding principles:

- Healthcare solutions of the future require fact based scientific evidence, expert analysis of information, technology, ingenuity and a focus on individuals.
- Rigorous analysis must be applied to vast amounts of timely, high quality and relevant data to provide value and move healthcare forward.
- Collaboration across all stakeholders in the public and private sectors is critical to advancing healthcare solutions.
- Insights gained from information and analysis should be made widely available to healthcare stakeholders.
- Protecting individual privacy is essential, so research will be based on the use of non-identified patient information and provider information will be aggregated.
- Information will be used responsibly to advance research, inform discourse, achieve better healthcare and improve the health of all people.

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A message from PhRMA

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4 hours ago - Health

Pharmacies are struggling to refill their own ranks



Tina Reed, author of Axios Vitals

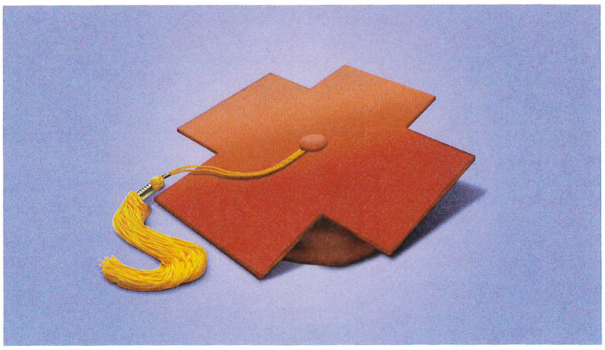


Illustration: Sarah Grillo/Axios

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the industry.

Why it matters: The pharmacies' ambitions to become go-to providers for vaccinations, patient monitoring and even prescribing are being threatened by workforce shortages and burnout, as well as a flagging talent pipeline from the nation's pharmacy schools.

Driving the news: Walgreens on Monday announced a partnership with pharmacy school deans at 17 universities to better align training with the changing pharmacy business model.

- But the goal is also, in part, to address the industry's image problem.

What they're saying: "We have got to evolve this to get people excited to get back in the industry," Rick Gates, chief pharmacy officer at Walgreens, told Axios.

The big picture: There's been a steady drop in applications to pharmacy schools, falling 64% from nearly 100,000 in 2012 to about 36,000 in 2022, according to the American Association of Colleges of Pharmacy.

- In 2022, there were 13,323 graduates from four-year pharmacy programs, down from 14,223 the previous year and the largest drop since 1983, per AACP data.
- Widely publicized staff walkouts in recent months have called attention to increased workload demands that pharmacists warned are making them more prone to errors.
- There's been a big shift from the time when pharmacists were revered members of their community, said Frank Harvey, CEO of Surescripts and a pharmacist. Expanding the services that

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- "We've gone through this 20- or 30- or 40-year span where the pharmacists' job got diluted," he said. "If we could just get it back to what the perception was 50 years ago."

- "We were seen as the doc, you know? I had a ton of my patients who used to call me, 'Doc, can you help me out with this?'"

Zoom in: The University of North Carolina's Eshelman School of Pharmacy, which is part of the new Walgreens initiative, two years ago added more comprehensive education around the business of health care.

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- "They didn't really understand the business of health care in this country. How does a drug get from a manufacturer to a patient?" Angela Kashuba, the school's dean, told Axios.

- It's an example of the kind of updates that need to take place in pharmacy schools, she said.

Between the lines: In response to concerns about overwork, national retailers including Walgreens and CVS Health are trying to streamline and eliminate some tasks by investing heavily in automation and micro-fulfillment centers where robots do most of the work.

- They've also begun making headway in getting insurers to recognize pharmacies' ability to furnish care amid shortages of other providers and to pay for this work, said Walgreens' Gates.

- The industry's attempts to transform itself, he said, should ultimately help pharmacists prioritize what's usually the most

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Go deeper



Emily Peck, author of Axios Markets
2 hours ago - Economy

The Taylor Swift Economy is now a high school curriculum

AXIOS



Photo illustration: Aïda Amer/Axios. Photo: James Devaney/GC Images and David Eulitt/Getty Images

Taylor Swift's relationship with Kansas City Chiefs tight end Travis Kelce is more than just a love affair, it's an economics case study, says University of Kansas professor Misty Heggeness.

What's happening: She's created a Taylor Swift curriculum — Swiftynomics 101 — to help high school and college teachers convey economics lessons by analyzing the 34-year-old pop star's effect on the NFL's business.

Go deeper (2 min. read) ⟶



Andrew Freedman, author of Axios Generate
Updated 3 hours ago - Energy & Environment

Deadly storm pummels California with "catastrophic" flooding

AXIOS



An aerial view of a home destroyed by a mudslide as a powerful long-duration atmospheric river storm, the second in less than a week, continues to impact Southern California on Feb. 5, 2024 in Los Angeles, California. Photo: Mario Tama/Getty Images

A "dangerous" atmospheric river event is slowly releasing its grip on parts of Southern California, where it is brought a rare "high risk" of potentially deadly flooding to Los Angeles County into Tuesday.

The big picture: The storm that rapidly intensified Sunday off California's coast has resulted in at least three deaths and disrupted travel across the state. A Los Angeles fire official said crews had responded to over 130 incidents related to flooding and 49 related to mud and debris flows.

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Andrew Solender
3 hours ago - Politics & Policy

AXIOS



House Foreign Affairs Committee Chair Michael McCaul. Photo: Anna Moneymaker/Getty Images.

Even the House Republicans who would be the most prone to support the Senate's Israel, Ukraine, Taiwan and border security funding package — the staunch Ukraine supporters — are distancing from it.

Why it matters: It cements the almost certain demise of the package as most Republicans in both chambers, as well as some Democrats, position against it.

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The Washington Post
Democracy Dies in Darkness

BUSINESS

Just How Dangerous Are India's Generic Drugs? Very

Analysis by Ruth Pollard | Bloomberg
April 4, 2023 at 3:21 p.m. EDT

For a nation that seeks to claim the mantle of "pharmacy to the world," India is scandalously short on regulatory oversight. In the last six months alone, its generic cough syrups have killed dozens of children, its eye drops have caused blindness and its chemotherapy drugs have been contaminated.

India

The children who died — mostly under the age of five years — were given Indian-made over-the-counter products contaminated with industrial solvents and antifreeze agents that are fatal in even small amounts. The eye drops that contained extensively drug-resistant bacteria? So far 68 patients across 16 US states have been affected. Three people died, several had to have their eyeballs removed, some went blind, the Centers for Disease Control and Prevention reported on March 21. The Indian company, Global Pharma Healthcare, issued a voluntary nationwide recall for the drops.

India is the largest provider of generic medicines, producing 20% of the world's supply, according to the government's Economic Survey. Its $50 billion drug-manufacturing industry exports medicines to over 200 nations and makes 60% of all vaccines. It boasts "the highest number" of US Food and Drug Administration compliant plants outside America, and indeed, some of its generic pharmaceutical companies produce high-quality medicines.

That may well provide consumers with a level of comfort, but history suggests it is unwise to trust that feeling.

The latest drug recalls just add to a long line of scandals that have tainted the sector. In 2013, a US subsidiary of major Indian drug manufacturer Ranbaxy Laboratories Ltd. pleaded guilty to US federal criminal charges and agreed to pay $500 million for selling adulterated generic drugs, fabricating data, and committing fraud. Serious flaws in the FDA compliance regime allowed these breaches to go undiscovered, until a years-long investigation laid bare the endemic corruption. A generic drug made in India and modeled on Lipitor sold in the US to treat high cholesterol, for example, was contaminated with shards of blue glass, as journalist Katherine Eban documented in her book, Bottle of Lies: The Inside Story of the Generic Drug Boom. Her book draws in part on the experience of whistleblower Dinesh Thakur, who worked at Ranbaxy.

You would think such a damning indictment would prompt India to develop a safer, better pharmaceutical oversight regime. Think again. The systemic fraud exposed by the investigation — where data was routinely falsified to fool inspectors, increase production and maximize profit — did not result in a regulatory overhaul.

Still, a two-day "brainstorming session" held in February appeared to acknowledge the system's inherent weaknesses, with Health Minister Mansukh Mandaviya telling participants India needed to "move from generic to quality-generic drugs." Discussions involved "how to make the country's drugs regulatory systems transparent, predictable and verifiable," according to a health ministry media release. Consumers shouldn't hold their breath, hough. A national law on drug recalls has been under discussion since 1976 without resolution, and the government — at least publicly — remains in denial:

Since the Ranbaxy scandal, Thakur has campaigned for the reform of India's main regulator, the Central Drugs Standard Control Organisation, and, with lawyer T. Prashant Reddy, has written his own book, The Truth Pill: The Myth of Drug Regulation in India, which was published in October.

They note that adulterated Indian drugs aren't just killing children in developing-world export markets like Gambia and Uzbekistan. They're also killing children at home: In 2019, at least 11 infants died in the state of Jammu because of cough syrup containing diethylene glycol. Indeed, as Thakur notes, the mass poisoning of children with medication containing DEG has happened in India on five previous occasions — in one 1998 case, 36 children died due to acute renal failure after consuming contaminated cough syrup.

And here we are.

The World Health Organization sent alerts in October and January, asking for the cough medicine to be removed from the shelves. (It also issued a warning last year for cough syrups made by four Indonesian manufacturers sold in that country, where 203 children died in similar circumstances.)

Maiden Pharmaceuticals, whose medicines were sold in Gambia and linked by the WHO to the deaths of at least 70 children, has denied wrongdoing. And India's regulator rejected the WHO's findings, saying no toxic substances had been found in samples taken from Maiden's plant. CDSCO Director General V.G. Somani said the warning caused "irreparable damage" to the reputation of the Indian pharmaceutical industry, Bloomberg News reported in January.

Then came the reports of at least 18 deaths in Uzbekistan linked to another batch of children's cough syrup manufactured by another Indian company, Marion Biotech Ltd. This time there was some action, and on March 22, the company's manufacturing license was revoked.

It shouldn't have taken more deaths for Prime Minister Narendra Modi's administration to act. The red flags have been there for years. What's lacking is political will, and transparency. The FDA publishes different reviews of new drug applications on its website, along with detailed notes. The European Medical Agency gives similarly expansive information. There is no such openness in India.

As Thakur explained to me, the pharmaceutical industry is India's manufacturing success story, providing a major source of foreign exchange and soft power. Any criticism is seen through the lens of nationalism, he said, and framed as defaming the industry. So why does contamination with such deadly substances occur so regularly? "The simple nswer is that Indian pharmaceutical companies quite often fail to test either the raw materials or the final formulation before shipping it to market," Thakur said.

India relies on the weak oversight of developing countries that make up the bulk of its exports — that's how it can continue to push substandard and often deadly medicines there. As a paper on the Gambia poisonings published in March by the CDC noted, "inadequate regulatory structures make the sale of medications from international markets an especially high-risk activity in low-resource settings." But what about countries with supposedly strong regulatory systems, like the US? This latest scare should prompt further reform of the FDA's overseas inspections regime.

In the absence of a global framework for pharmaceutical safety, what can be done to make the generic drugs that consumers around the world have come to rely on safer and effective? For a start, the WHO's prequalification program, which facilitates the purchase of billions of dollars' worth of medicines through international agencies such as Unicef, must be overhauled. Then there's the question of holding these companies to account for the harm they cause inside and outside India via legal avenues and victim's compensation.

In a year that India holds the Group of 20 presidency, it should drag its pharmaceutical industry out of the dark ages and into the real world — one that is driven by transparent, evidence-based medicine and real safety data shared across borders. Its export partners should demand nothing less.

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Ruth Pollard is a Bloomberg Opinion editor. Previously she was South and Southeast Asia government team leader at Bloomberg News and Middle East correspondent for the Sydney Morning Herald.

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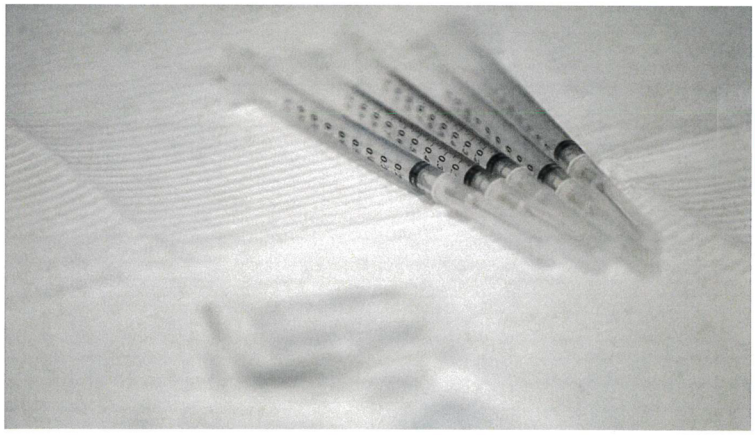
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PHARMACEUTICALS

U.S. dependence on China for lifesaving drugs grows

Treatments for cancer, cardiovascular diseases drive rising imports

china dependence



The U.S. has been importing more chemotherapy treatments, immunosuppressants and other lifesaving drugs from China. © Reuters

RINTARO TOBITA, Nikkei staff writer
August 2, 2023 02:21 JST

WASHINGTON -- U.S. imports of Chinese-made pharmaceuticals are soaring to meet

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"We will continue the importation until approved manufacturers can meet all patient needs," an FDA spokesperson said.

The U.S. imported $6.95 billion worth of pharmaceuticals from China in 2022, up more than eightfold from $820 million the year before, official data shows. Demand has remained strong, with imports over the first five months of this year alone totaling more than double the annual tally from 2021.

The surge is being driven largely by chemotherapy drugs, immunosuppressants and cardiovascular drugs. Growing demand for chemotherapy drugs has led to shortages in the U.S. Quality control problems in India, a major pharmaceutical exporter, have exacerbated the supply troubles.

China has helped to fill the gap. Until 2021, its share of U.S. pharmaceutical imports by value stood at around 1%; by 2022, that figure had grown to 9.6%.

"The largest contributing factor to China's market share growth has been domestic policies China has implemented with the goal of building a world-class advanced pharmaceutical manufacturing industry," said Niels Graham, a China economy expert at the Washington-based Atlantic Council.

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To some, America's growing dependence on China for lifesaving drugs poses a potential national security risk.

U.S. President Joe Biden last September signed an executive order aimed at expanding domestic production capacity, but the order did not include enforceable requirements for companies and has had a limited effect.

In Congress, Democratic lawmakers on June 22 introduced a bill that would lower tariffs on pharmaceutical imports from U.S. allies, which could help Japanese and European products compete with cheaper Chinese alternatives.

The U.S.'s increased imports of pharmaceuticals from China resemble to a lesser extent its dependence on the country for electric-vehicle components, amid soaring demand for EVs.

U.S. imports of lithium-ion batteries from China more than doubled in 2022 to $9.04 billion. This amounted to 12.5% of all U.S. imports of lithium-ion batteries, five times as much as in 2018, official data shows. China's share of imports has continued to grow, reaching nearly 20% in the January-May period of this year.

The U.S. also relied on China for around 80% of nickel, graphite and other key minerals used in EVs last year.

Washington is offering big subsidies to encourage automakers and battery makers to expand domestic production. But constructing new plants takes time.

"[Domestic] supplies are not expected to increase significantly until after 2025," said Kensuke Abe, a Washington-based analyst for Japanese trading house Marubeni.

White House national security adviser Jake Sullivan said in April: "Clean-energy supply chains are at risk of being weaponized in the same way as oil in the 1970s, or natural gas in Europe in 2022."

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MANUFACTURING

AstraZeneca to drop $26.5M in China for new production line for diabetes drugs: report

By **Joseph Keenan**
Jan 18, 2024 9:09am

AstraZeneca | China | diabetes drugs | plant expansion



AstraZeneca is reported to be spending $26.5 million to build a new production line in Taizhou, China, to bolster supply of its diabetes drugs. (China News Service/Getty Images)

Pharma giant AstraZeneca will spend $26.5 million to build a new production line for its diabetes treatments dapagliflozin and metformin hydrochloride at the Taizhou National Medical High-tech Development Zone in Jiangsu, China Daily reports (https://www.chinadaily.com.cn/a/202401/15/WS65a4fd12a3105f21a507c5b6.html).

The facility is forecast to have an annual output value of $1.4 billion and is expected to become a global manufacturing outpost for the company's diabetes therapies, according to the publication.

Marketed in the U.S. as Farxiga, dapagliflozin helps prevent absorption of glucose in the kidneys to help lower blood sugar. Metformin, meanwhile, reduces the absorption of sugar from the stomach. As a combination therapy, the medicines are marketed as Xigduo.

Fierce Pharma Manufacturing has reached out to AstraZeneca for additional details on the project.

AstraZeneca's operations in China were the focus of market speculation last summer when the Financial Times reported (https://www.ft.com/content/d195f3d0-0101-414e-b190-9691e6c5661d) that the company had explored separating its business in the country amid increasing geopolitical tensions in the region. However, the company's international and China president, Leon Wang, quickly rebutted the report.

Elsewhere, AstraZeneca in November said (https://www.fiercepharma.com/pharma/astrazeneca-subsidiary-exit-beating-heart-indian-operations-bangalore) it would exit a production plant in Bangalore, India, "in due course." AstraZeneca said it would auction off the site to a buyer who can serve as a contract manufacturer for the products made there.

AstraZeneca | China | diabetes drugs | plant expansion | Facilities

ATTEND EVENTS

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18-20 MAR — **Trial Master File Summit** — Savannah, GA

06-08 MAY — **Medical Affairs Strategic Summit East** — Jersey City, NJ

Empower bolsters compounded drug manufacturing capacity with purchase of Eugia site in New Jersey

By **Kevin Dunleavy**
Feb 5, 2024 04:26pm

Aurobindo Pharma | plant sale | compounding | contract manufacturing



Houston-based Empower Pharma, a manufacturer of compounded drugs, has bolstered its production capacity with the acquisition of a plant in New Jersey from Eugia, a subsidiary of Indian generics manufacturer Aurobindo. (WorSangJun/GettyImages)

Only a few weeks after an Eugia manufacturing site in New Jersey received an FDA reprimand, it's set to change hands under a newly revealed transaction.

Empower Pharmacy on Monday revealed a plan (https://www.prnewswire.com/news-releases/empower-pharma-to-purchase-eugia-manufacturing-facility-in-new-jersey-for-large-scale-expansion-of-personalized-compounded-medicine-302053371.html) to buy Eugia's new site in East Windsor. The purchase comes six weeks after the FDA cited Eugia's site with 10 observations in a Form 483 write-up.

Empower, which produces compounded drugs, will receive Eugia's 170,000-square-foot plant and will take over its workforce. Along with the plant sale, the companies will form a "contract manufacturing relationship," Empower said.

The site opened last year and boasts bulk manufacturing and automated fill-finish production capabilities, according to Empower.

"We anticipate welcoming the talented team in East Windsor to Empower shortly and we intend to use these capabilities to support our strategic growth initiatives," Shaun Noorian, the CEO of Empower, said in a release.

Noorian, who founded the company in 2009, added that the acquisition of Eugia's site will allow it to meet the growing demand for compounded drugs.

Eugia is a subsidiary of generics manufacturer Aurobindo.

The manufacture of compounded drugs has come under increased attention with the surge in the popularity of diabetes and obesity drugs. The FDA allows these knockoff treatments to be produced when there is a shortage of a drug, such as the case with Novo Nordisk's Ozempic and Wegovy and Eli Lilly's Mounjaro.

In its December inspection of Eugia's plant, the FDA found issues with a construction project that posed a contamination risk. Inspectors also found ceiling leaks and damage to an HVAC system located near an aseptic processing line. Further, the company lacked quality control documentation to prevent contamination, according (https://www.fda.gov/media/175809/download?attachment) to the FDA's report.

Empower did not immediately respond to a request for comment on the issues the FDA cited during its December inspection of Eugia's site.

In 2021, Empower opened (https://www.prnewswire.com/news-releases/empower-pharmacy-opens-north-americas-most-advanced-compounding-pharmacy-in-houston-301364032.html) a new $55 million plant in Houston. The company called the 85,000-square-foot site one of the largest compounding facilities in the U.S.

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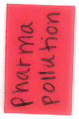
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NEWS HEALTH CARE

Undrugging the environment: Europe's plan to cut pharma pollution

For the first time, new drugs could be denied approval on the basis of environmental harm.



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The EU is looking to crack down on pollution from medicines by ratcheting up environmental requirements | Diptendu Dutta/AFP via Getty Images

APRIL 17, 2023 6:00 AM CET
BY CARLO MARTUSCELLI AND LEONIE CATER

The world's rivers are full of drugs — and it's making the world sick.

A leaked draft of the European Commission's revision of the bloc's pharmaceutical rules shows the EU is looking to crack down on pollution from medicines by ratcheting up environmental requirements. But its plans are facing internal resistance, pushback from industry and questions over methodology — and it remains to be seen which measures make the cut when the proposal is finally published on April 26.

It's not a trivial problem. One study published last year monitored over 1,000 sampling sites along 258 rivers in 104 countries across all continents for active

pharmaceutical ingredients. Only an indigenous village in Venezuela — where modern medicines aren't used — and Iceland were unscathed.

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While not immediately lethal, drug-laced rivers harm wildlife, such as fish, frogs and birds, as the chemicals can alter their growth, reproduction and behavior.

And when antibiotics go into waterways, it can increase bacterial resistance to these lifesaving medicines, harming people's ability to fight common infections. The U.N. estimates that up to 10 million deaths could be caused by superbugs by 2050, matching the annual death toll of cancer.

In its draft plans, the Commission wants to allow the EU's drug regulator to turn down medicines approval on environmental grounds, and require drug companies to measure the environmental impact of their production process.

It would be a step-change in attempts to curb pharmaceutical-linked pollution.

Tug-of-war

For environmental activists, stricter standards can't come soon enough.

Scientists in recent years have warned that pharmaceuticals constitute a "weakly regulated global environmental risk." And a February U.N. Environmental Program report on antimicrobial resistance (AMR) found that "the pharmaceutical industry is considered largely an unregulated sector in terms of environmental pollution."

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"I don't think that [pharmaceutical pollution] has been taken yet seriously enough [by policymakers] — it should be taken more seriously," said Mirella Miettinen, a senior researcher in environmental law at the University of Eastern Finland's law school. "And quite fast hopefully."

But the new rules are not a sure thing. A document seen by POLITICO showed that the proposed changes have already been caught in an internal tug-of-war, with the Commission's environment department pushing for a greater focus on environmental risks and the industry department skeptical of more stringent rules.

Meanwhile, the pharmaceutical industry has already pushed back against the leaked draft.

Hubertus Cranz, director general of the German Medicines Manufacturers' Association, called the proposals "very problematic," saying that while his group is committed to objectives around environmental sustainability, the industry is really "struggling a lot with the administrative burden."



The pharmaceutical industry has already pushed back against the leaked draft | Thibaud Moritz/AFP via Getty Images

Linking environmental risk assessments to drug approvals risks detracting from drug efficacy and safety — the main metrics by which to judge new drugs until now, he added.

'Meaningless' risk assessments

Under current rules for drug approvals, pharmaceutical companies have to submit an environmental risk assessment (ERA) detailing how toxic the

chemicals in a new medicine are, how long they linger in the environment, and what their impact is on plants, animals and microbes.

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They're also required to estimate how much of these ingredients will leak into the environment through normal use and disposal, and can be asked to put in place mitigation measures if they exceed certain levels.

But Laure Herold, a communications official for the European Medicines Agency (EMA), said that while companies are required to submit an environmental risk assessment, and would be marked down for a missing one, marketing authorization can't currently be denied on the basis of an "incomplete ERA."

An analysis by the Pharmaceutical Journal found that one in five new medicines approved by the EMA in 2021 were submitted without all environmental data. And drugs approved before October 30, 2005 were never required to carry out an assessment.

"So far, it's pretty meaningless, and we're really hoping that with this new legislation that is going to change," said Dorothea Baltruks, a research associate at the Centre for Planetary Health Policy, a German think tank.

Under the proposed rules, drug companies will need to estimate — for the first time — the environmental impact of their manufacturing process, beyond use and disposal of the medicines. They will be asked to propose risk

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A bigger problem?

Perhaps a bigger problem is that there's disagreement about how risks are actually assessed and what the permissible levels of chemicals are — something it will be up to regulators to decide.

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Herold said the risk assessments are based on worst-case scenarios of environmental exposure, and that "only a very small minority of human medicinal products have been shown to constitute a potential threat to the environment."

But Alistair Boxall, one of the co-authors of the study on pharmaceutical pollution in rivers, takes issue with the "underlying science" of the current risk assessments, saying they're not sensitive enough to calculate a drug's pollution footprint correctly.

The anti-inflammatory drug Diclofenac, for example, is a widely used over-the-counter medicine that is known to pose a threat to certain animals and plants — it gets flushed into wastewater systems after digestion. But based on the standard studies necessary to conduct an environmental risk assessment under EU law, the data suggests the drug holds little danger for rivers.

"I think some of the models we use are probably not giving necessarily the right answers," Boxall said.



A placard reading "There begins the sea, protect it", on the bank of the Seine river, in Rouen, northwestern France | Lou Benoist/AFP via Getty Images

What's more, while the proposed risk assessments will — for the first time — consider the impact of antibiotics production on AMR, more research is needed before policymakers can introduce binding targets, according to one of the authors of the U.N. report on AMR in the environment.

Too stringent standards could drive up prices and negatively impact antibiotic access, but it's also not yet clear what the effects of persistent lower levels of antibiotic pollution are.

"We know that, in the long run, releasing chemicals into the environment isn't a good thing," said David Graham, professor of ecosystems engineering at Newcastle University. But "it's very much a matter of almost professional opinion, as to the level and extent of effects you might see."

MARKETING

Making us thinner will see fatter profits for pharma as Bloomberg's crystal ball predicts obesity drug sales hitting $44B by 2030

By **Ben Adams**
May 31, 2023 9:10am

Saxenda | Wegovy | Mounjaro | Eli Lilly



Nearly 70% of total sales of anti-obesity drugs will stem from the U.S., according to Bloomberg Intelligence. (imyskin/GettyImage)

Novo Nordisk has lit the tinder of a new megablockbuster market with Saxenda and Wegovy as new, branded anti-obesity drugs are set to haul in $44 billion by this decade's end.

That's according to the latest projections in a new report by Bloomberg Intelligence, which found sales of branded anti-obesity drugs could hit $44 billion, when risk adjusted, in 2030. That would be a major ballooning of a market that was worth just $2.5 billion last year.

According to Bloomberg Intelligence, nearly 70% of that figure will stem from the U.S. The analysts said they expect a slower ramp-up in Europe and a 20% price discount to the U.S., given the use of health technology assessors on the continent.

The market is set to be dominated by Novo's Saxenda and, more notably, its newer semaglutide-based drug Wegovy, both GLP-1s, as well as Eli Lilly's tirzepatide. Lilly's drug, which works as a dual GLP-1/GIP (glucose-dependent insulinotropic polypeptide), is currently marketed as Mounjaro in diabetes but will likely soon see a filing for obesity, with a potential launch by late this year or early 2024.

"We expect Novo Nordisk's franchise and Eli Lilly's tirzepatide to dominate with shares of 54% and 46% respectively, while contributions from less-effective anti-obesity drugs are negligible," said Michael Shah, senior industry analyst at Bloomberg Intelligence, in the report.

But more drugs are on the horizon that could bump these estimates up. "Pipeline developments such as oral GLP-1s by Lilly and Pfizer, and Amgen and Lilly's dual- and triple-combination drugs represent upside to our view," Shah said in the report.

The newest class of drugs from Novo and Lilly are all injectable but both are also now working on oral versions. Pfizer, yet to market an anti-obesity drug, is also working on an oral-only drug called danuglipron, a small-molecule GLP-1R agonist, and encouraging early-stage data could see it enter the market later this decade.

Analysts said in the report that "securing broad reimbursement and supply are key" when it comes to marketing these drugs, with "possible upside from further innovations including combination products." They added that the anti-obesity market could "mirror those seen in diabetes," where Novo and Lilly are already the biggest players.

Shah continued: "Unprecedented demand in obesity coupled with the strong relaunch of Wegovy, which serves as a benchmark for future launches, underpins our upgraded sales view for the market. Our previous scenario, published in early February, called for $28 billion in obesity sales in 2030 (or $33 billion if we don't adjust for clinical failure risk)."

Saxenda | Wegovy | Mounjaro | Eli Lilly | Novo Nordisk | obesity drugs | Pfizer | Bloomberg | GLP-1 | weight loss | Pharma

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An Ongoing Crisis: Semaglutide Shortage Raises Dual Concerns for Obesity and Diabetes Treatment

December 21, 2023
Hayden E. Klein

Feature *Article*

An in-depth look into what the drug is being used for and what has contributed to the shortage.

Between celebrity endorsements, before-and-after TikToks, and the increasing evidence of its weight-loss benefits, it is no surprise that the rapidly growing popularity of semaglutide as a weight loss tool has led to a nationwide shortage of the glucagon-like peptide 1 (GLP-1) receptor agonist.

But what does this mean for patients who are finding it more and more difficult to access this drug?



Ozempic injection | Image credit: mbruxelle – stock.adobe.com

Semaglutide is sold under the brand names Ozempic, Rybelsus, and Wegovy—all manufactured and sold by Novo Nordisk. Ozempic injection and Rybelsus tablets are FDA approved as a supplement to diet and exercise to improve glycemic control in adults with type 2 diabetes (T2D).[1] Meanwhile, the 2.4 mg Wegovy injection is indicated for weight loss for individuals with overweight or obesity with a body mass index (BMI) of at least 27 kg/m^2 and at least 1 weight-related complication, or a BMI of at least 30 kg/m^2.[2,2] While Wegovy can benefit patients with T2D through weight management, it is not meant to directly treat T2D in the same way as Ozempic and Rybelsus.

Despite the different indications, people have been using Ozempic and Rybelsus for weight loss, which has contributed to decreased access for patients with T2D who need it to manage their condition.[3] An analysis of electronic health records shared with CNN by Epic Records estimates that around 1.7% of all Americans have been prescribed a semaglutide medication in 2023 alone, reflecting a nearly 40-times increase over the past 5 years.[3] Additionally, the increased popularity of Wegovy is making it harder for patients with overweight or obesity who have been using it for weight loss to access the treatment that has been working for them.

According to data collected between 2017 and 2020, 41.9% of US adults have obesity, and nearly 20% of American children and adolescents have obesity.[4] Zoomed out, the World Health Organization (WHO) estimates that more than a billion people have obesity worldwide, including 650 million adults, 340 million adolescents, and 39 million children.[5]

Trends in Weight Loss Drug Use

According to data published in the 2023 Trends Shaping the Health Economy Report in September, national spending on semaglutide reached a total of $10.7 billion in 2021, making it the fourth highest across drug classes in terms of spending.[6]

Ozempic is also the most prescribed GLP-1 receptor agonist.[6] In Q4 of 2022, health care providers in the United States wrote more than 9 million prescriptions for semaglutide, tirzepatide (Mounjaro), and liraglutide (Saxenda) in just 3 months, with semaglutide accounting for around 7 million of these prescriptions. With the May 2022 approval of tirzepatide for T2D and its increasing use among patients without diabetes looking to manage their weight, there is potential for it to eventually take the spot Ozempic currently holds. On the other hand, liraglutide was found to be less effective for weight loss compared with the other 2 drugs, leading to a slow decline in use.

Across major markets, there has been a rise in the count of individuals using Ozempic who have a background of overweight, obesity, or experiencing other forms of hyperalimentation, according to the report. This surge varies, showing an increase of 48% in Minneapolis, Minnesota, to as much as 481% in Cleveland, Ohio.[6] The prevalence of both on-label and off-label usage also differs across various markets.

"From 2020 to 2022, the quarter-over-quarter percent change for GLP-1 prescriptions has increased but the rate of future utilization will depend on manufacturer supply, cost and prioritization of on- and off-label use," the report said. "Notably, just over half of patients taking these medications have a history of type 2 diabetes or have an associated medical visit with their prescription."

How Do Celebrity Endorsements Contribute to the Uptake Boom?

According to *People*, household names like Oprah Winfrey and Tracy Morgan have used and encourage the use of semaglutide for people who are overweight or obese who feel like nothing else has helped them take off and keep off the weight.[7] On the other hand, Sharon Osbourne and Amy Schumer are among those who have used the drug for that purpose and have regrets around it, including losing more weight than expected and generally feeling unwell. Meanwhile, actor Anthony Anderson noted how the drug's increasing use for weight loss negatively impacts people like him who are living with T2D, telling *People*, "It's creating a shortage for those of us who need the medicine that we need and not for weight loss issues, but for our health."

Anderson's statement aligns with what others with T2D are experiencing when trying to access Ozempic, as opposed to the rich and famous who can access these treatments much more easily.

Many patients with T2D are experiencing challenges in getting reimbursed for drugs like Ozempic due to US insurers implementing restrictions to discourage prescribing the medication for weight loss.[8] Novo Nordisk acknowledged tighter health plan management of GLP-1 drugs, contributing to a recent decline in US prescriptions.[9] Patients have reported delays and obstacles, including prior authorization requirements and the need to try alternative medications, which raises concerns about potential impacts on diabetes management and overall health outcomes.

In fact, these issues did not just start this year, as Ozempic became a celebrity weight loss sensation back in 2022.[10]

Marketed as a potential solution to the obesity epidemic, Ozempic gained public attention after being featured on The Dr. Oz Show in an episode from February 2021.[11] Initially

approved by the FDA for diabetes treatment in December 2017, the higher-dose form, semaglutide 2.4mg, branded as Wegovy, was later approved for weight loss in June 2021. Elon Musk's Twitter endorsement of "fasting and Wegovy" on October 1, 2022, further intensified interest.[12] However, a shortage of Wegovy—which was put on the FDA's drug shortage list in March 2022—led health care providers to prescribe Ozempic for weight loss as an alternative.

Using Semaglutide for Weight Loss

To learn more about what patients and physicians are experiencing amid this shortage, *The American Journal of Managed Care®* (*AJMC®*) spoke with Ian Neeland, MD, director of cardiovascular prevention and co-director of the Center for Integrated and Novel Approaches in Vascular-Metabolic Disease, University Hospitals Harrington Heart & Vascular Institute, and associate professor of medicine at Case Western Reserve University School of Medicine.

Neeland mentioned a noticeable increase in interest in semaglutide for weight loss in his practice over the past year, noting that, as a cardiologist, he doesn't specifically work in chronic weight management but gets a lot of patient referrals for it as cardiovascular health and weight are often linked. In general, he will often start the patient on a GLP-1 receptor agonist if it is indicated for the treatment of obesity. However, it can be a difficult conversation to have with the patient when insurance does not cover chronic management for these medications, causing them to have to pay out of pocket.

"Some of my patients are well-to-do and can afford that cost, [but] many others cannot," Neeland said. "It's unfortunate because we have something to offer individuals but many times they can't get it, and not because of the shortage per se, just because of the cost of the medication. Certainly, over time with more options in the market, those costs will likely come down and as things go generic, but for the meantime, it can be a difficult conversation to have with patients that we have effective medications, but I'm not sure you can utilize it because you can't necessarily afford it or that insurance will cover it."

When patients with overweight or obesity seek assistance for weight loss, Neeland described a comprehensive evaluation involving a thorough examination of medical history and potential indications or contraindications for GLP-1 receptor

agonists, emphasizing the importance of counseling and education about potential side effects, and addressing concerns and offering strategies to mitigate these effects. University Hospitals has a pharmacist-led dose escalation protocol, as Neeland explained, emphasizing the pharmacist's role in assessing side effects and ensuring a smooth transition to higher doses. This approach aims to facilitate patients' progress toward the maximum tolerated and most effective dose, tailored to individual needs.

It's also important to know that not everyone will respond to semaglutide for weight loss, and guidelines for the treatment of obesity include other approaches for those who may need them.[2]

If patients using semaglutide are not experiencing weight loss within a specific timeframe, the decision to discontinue the medication depends on the underlying reasons for the lack of efficacy. According to Neeland, if the achieved dose is deemed insufficient, dose escalation might be considered as an option, or if individuals show a limited response to this particular medication, switching to a different GLP-1 receptor agonist could be a suitable alternative. Additionally, modifying dietary habits and lifestyle behaviors may be essential for optimizing weight loss outcomes. The course of action depends on the context, and the conversation about discontinuation involves exploring various factors influencing the patient's success on the medication, with the option to switch to an alternative agent if deemed beneficial.

How Does the Shortage Affect Individuals With Diabetes?

When it comes to helping his patients with T2D navigate their diabetes management during the shortage, Neeland said there is no one-size-fits-all approach, but there are steps he takes to help patients avoid going completely off semaglutide. This includes reducing the dose to the next available dose, trying to access the drug through other pharmacies, or getting the drug out of country. It's important to note that semaglutide works by uptitrating the dose, so when patients with diabetes have their regimen interrupted or disrupted completely for a long period of time—even as little as 2 to 3 weeks—due to these shortages, that's when there are concerns for the patient's ability to maintain glycemic control. When this happens, patients typically have to start over from the lowest original dose and escalate doses all over again, since stopping the regimen and going back to a higher dose commonly leads to

adverse events, and patients may have reduced glycemic control during this time.

Neeland also mentioned that there is an oral semaglutide option that is not currently experiencing shortages and is indicated for diabetes management. The pills have not been tested for a weight loss indication, which he said is likely why patients looking to lose weight are not asking for them instead of the injection, but they are a good alternative for when patients with diabetes are having trouble accessing the injection.

Oral semaglutide has a few limitations not present in injectable semaglutide. First, it requires daily administration compared with the once-weekly injectable form. Additionally, it must be taken with minimal water and without any other medications or food, making the timing of ingestion potentially challenging. This could pose adherence difficulties, especially for individuals who prefer a more structured morning routine or struggle with coordinating multiple medication schedules. Further, there are essentially 3 fixed doses for oral semaglutide, whereas the injectable form offers a bit more flexibility in dosing.

Despite these considerations, oral semaglutide remains a viable and effective option, particularly for managing T2D and, depending on whether future clinical trials test for this and yield positive results, potentially for off-label use in weight loss.

The Role of the Employer

In an interview with *AJMC*, Dawn Weddle, vice president of the Midwest Business Group on Health (MBGH), was frank on her views of the semaglutide shortage.

"From an employer perspective, we feel that the priority should always be given to patients that have diabetes and not necessarily being used just for weight loss, especially when there are shortages," she said.

Weddle explained that employer plans typically do not cover off-label drug use, making it challenging for individuals to obtain Ozempic for weight loss. The national shortage seems more pronounced in higher-dose pens used for severe cases diabetes, creating concerns for patients who rely on these medications. While manufacturers are working to address the shortage, challenges with the supply of plastic pens persist,

and the FDA approval process for manufacturing new pens adds complexity to resolving the issue.

In a recent learning network event by MBGH titled "Obesity, the Employer Conundrum," a session focused on how employers make informed decisions regarding the coverage of GLP-1 weight loss medications, with a particular emphasis on semaglutide as the most prescribed GLP-1. The discussion highlighted the evolving scientific understanding of obesity, emphasizing the shift from solely lifestyle interventions to recognizing obesity as a chronic condition. The featured expert, a registered dietitian, emphasized the effectiveness of GLP-1 medications in helping employees manage their weight, stressing that treating obesity as a chronic condition requires a long-term approach.

The session acknowledged the conundrum employers face in navigating the challenges of covering GLP-1 medications. Employers recognize the efficacy of these medications in weight management and understand the broader impact on various health conditions associated with obesity. However, the high prevalence of obesity in the workforce, affecting nearly 70% of the population, poses a considerable challenge. The lack of a standard of care for obesity adds complexity for employers, who must determine appropriate guardrails for medication use. Various strategies, such as BMI thresholds, comorbidities, pre-authorizations, and directing employees to specialized medical centers, were discussed as potential approaches to ensure the right medication reaches the right patient at the right time.

"I think one of the reasons that [using diabetes drugs for weight loss] has become so popular is, number one, they're effective," Weddle said. "There have been other medications out there for a long time, other anti-obesity medications that are pretty cheap, they're less than $100 a month, but they don't even come close to the results of Wegovy in terms of weight loss. Patients on Wegovy are seeing a 15% reduction in their weight and, and these other anti-obesity medications aren't even coming close to that."

How Will the Shortage Carry Into 2024?

The semaglutide shortage issue has gained significant mainstream attention throughout 2023, prompting Novo Nordisk to increase funding to enhance production capacity. On December 12, 2023, Novo Nordisk released a statement,

addressing the shortage of specifically the Wegovy 1.7 mg dose in the United States, saying it expected to resume shipments in early January 2024.[13]

Despite these efforts, though, shortages are expected to persist into the next year, and new data highlighting the positive cardiovascular benefits of Wegovy adds complexity to the situation and raises concerns of continued or even worsened shortages. Looking ahead to 2024, Neeland and Weddle both expressed hope for changes to mitigate shortages and ensure the drugs reach those who need them the most.

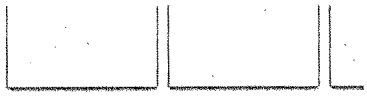
While manufacturer supply issues are being addressed, the broader supply chain—including shortages of pens—remains a challenge. Weddle noted that medium and large employers are more likely to cover these medications, and the hope is that increased market competition will eventually lead to lower prices. Encouragingly, the potential for primary care physicians to receive training in obesity management was highlighted as a crucial aspect. Having more clinicians trained in prescribing these medications appropriately is essential to ensure they are used correctly, ultimately reducing the risk of shortages and promoting successful outcomes for patients.

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United States

US files first-ever charges against Chinese fentanyl manufacturers

By **Sarah N. Lynch** and **Luc Cohen**

REUTERS

My View Following Saved



Plastic bags of Fentanyl are displayed on a table at the U.S. Customs and Border Protection area at the International Mail Facility at O'Hare International Airport in Chicago, Illinois, U.S....
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WASHINGTON/NEW YORK, June 23 (Reuters) - The U.S. Justice Department on Friday filed criminal charges against four Chinese chemical manufacturing companies and eight individuals over allegations they illegally trafficked the chemicals used to make fentanyl - a highly addictive painkiller that has fueled the opioid crisis in the United States.

The indictments mark the first time the U.S. has sought to prosecute any of the Chinese companies responsible for manufacturing precursor chemicals used to make the painkiller.

China's foreign ministry on Saturday urged the U.S. to stop using what it said were fentanyl-related pretexts to sanction and prosecute Chinese companies and citizens, and demanded the immediate release of those who were "illegally arrested".

"China urges the U.S. side to stop dumping blame and to stop smear attacks on China," the ministry said in a statement.

Earlier, the Chinese embassy spokesperson Liu Pengyu said such "long-arm jurisdiction" would create more obstacles for China-U.S. counter-narcotics cooperation.

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The move came after Antony Blinken made the first visit to China by a U.S. Secretary of State in five years and said he had made clear that Washington needs much greater Chinese cooperation to stem the flow of fentanyl.

During his visit, the two sides agreed to stabilize their intense rivalry so that it did not veer into conflict, but failed to produce any breakthrough and the mood quickly soured again after U.S. President Joe Biden on Tuesday referred to Chinese leader Xi Jinping as a dictator.

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The companies at the heart of the three separate indictments are accused of selling precursor chemicals to the Sinaloa Cartel in Mexico, which has flooded the U.S. with the drug.

Federal prosecutors in Manhattan announced the unsealing of an indictment against the China-based Hubei Amarvel Biotech, along with its executives Qingzhou Wang, 35, Yiyi Chen, 31, and Fnu Lnu, also known as Er Yang, with fentanyl trafficking, precursor chemical importation, and money laundering offenses.

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In the Eastern District of New York, prosecutors announced the unsealing of two more indictments against three other Chinese companies and individuals accused of conspiring to manufacture and distribute fentanyl.

Prosecutors said the companies - including one called Hebei Sinaloa Trading Co - advertised precursor chemicals on social media in Mexico and the U.S., and used false customs forms and mislabeled packages to ship the chemicals by boat and air.

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Two months earlier, the Justice Department charged leaders of the Sinaloa cartel with running a fentanyl trafficking operation fueled by Chinese chemical companies, including three sons of Joaquin "El Chapo" Guzman, the onetime cartel leader now imprisoned in the U.S.

Deputy Attorney General Lisa Monaco said the cases "break new ground by attacking the fentanyl supply chain at its origin."

"Fentanyl poses a singular threat, not only because the smallest doses can be lethal, but because fentanyl does not occur in nature. It is entirely man-made."

Also on Friday, Blinken announced he would convene a virtual ministerial meeting on July 7 of dozens of countries and international organizations, to launch a Global Coalition to Address Synthetic Drug Threats.

The aim would be to unite countries "in a concerted effort to prevent the illicit manufacture and trafficking of synthetic drugs, identify emerging drug trends, and respond effectively to their public health impacts," he said in a statement.

The Justice Department said undercover Drug Enforcement Administration (DEA) sources posing as fentanyl manufacturers met with Wang and Chen earlier this year and agreed to buy 210 kg of fentanyl precursors in exchange for payment in cryptocurrency. The DEA retrieved the chemicals from a Los Angeles warehouse in May.

Wang and Chen were arrested by DEA agents on June 8 and ordered detained in Honolulu, Hawaii until they can be transported to New York to appear before the judge handling the case. Yang remains at large.

Reporting by Sarah N. Lynch in Washington and Luc Cohen in New York; additional reporting by David Brunnstrom in Washington and Shanghai Newsroom; Editing by Chizu Nomiyama, Angus MacSwan and Alistair Bell

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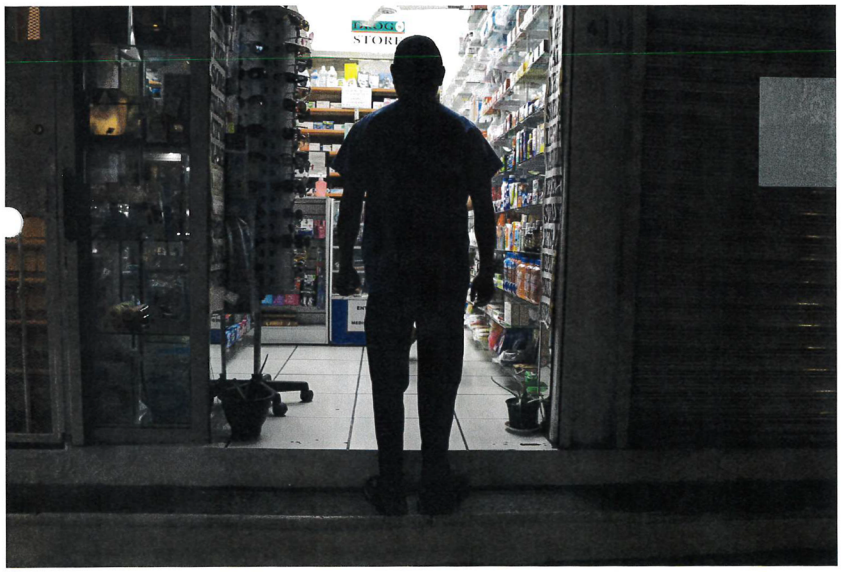
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Sarah N. Lynch is the lead reporter for Reuters covering the U.S. Justice Department out of Washington, D.C. During her time on the beat, she has covered everything from the Mueller report and the use of federal

WORLD & NATION

Hidden panels, counterfeit bottles, fentanyl: A year of buying drugs in Mexican pharmacies



Despite crackdowns on Mexican pharmacies since the Times' investigation began in January 2023, counterfeit medications are still available, and often harder to detect. (Wally Skalij / Los Angeles Times)

BY KERI BLAKINGER, BRITTNY MEJIA, CONNOR SHEETS

DEC. 30, 2023 3 AM PT

PUERTO VALLARTA, Mexico — The tag on her white lab coat read "professional pharmacist," and the framed health and safety certificates lining the walls behind her gave the drugstore an air of legitimacy.

That pretense faded seconds later, when she was asked for controlled medications — and got on her hands and knees to pop open a hidden panel under the counter. She rooted around for a minute and emerged with two sealed bottles.

"These are from licensed laboratories," she said. "The problem is when you're buying from a laboratory that's not certified."

One of those bottles — sold as Adderall — tested positive for methamphetamine.

In pharmacy after pharmacy in this Mexican resort city, workers offered similar assurances, but time and again the pills proved to be fakes. There were oxycodone pills that tested positive for heroin and over-the-counter cough medicine, and Vicodin tablets that turned out to be fentanyl. Pills sold as Adderall were sometimes methamphetamine or caffeine, and sometimes simply an appetite suppressant.

When confronted about the counterfeits, pharmacy workers often blamed suppliers, whose names they said they didn't know or couldn't remember. Others denied ever selling medications they had in fact sold just minutes or hours earlier.



Many pharmacies in Puerto Vallarta and other tourist-friendly parts of Mexico continue to sell fake medications to unsuspecting foreigners. (Wally Skalij / Los Angeles Times)

Last month, reporters visited dozens of drugstores in Mexico to interview pharmacy workers and piece together a fuller picture of the counterfeit medication problem The Times has been investigating for nearly a year.

The image that emerged is one of a troubling practice that seems remarkably resistant to change.

Despite pharmacy raids by Mexican authorities and a warning from the U.S. State Department, the latest round of testing found that fake medications appear even more plentiful at independent drugstores and regional chains in tourist hot spots and border towns now than earlier this year.

Some of the counterfeits are now more sophisticated, and lab testing found a wider array of substances in them than previously documented. And the latest reporting in Puerto Vallarta and Cabo San Lucas found that workers at small chains and individual pharmacies alike often went to great lengths to convince potential customers of the safety and efficacy of their counterfeit wares.

The Times is not naming independent pharmacies or workers due to safety concerns, including the threat of violence.

Dr. David Goodman-Meza, a UCLA assistant professor who studies drug use, said the results of The Times' investigation show a much larger problem than was initially apparent.

"This is a systematic effort to taint the supply," he said. "It involves many levels, and the endpoint is the pharmacy. There's likely other players making and distributing these counterfeit products — we just don't know who those players are."

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Reporters visited 10 vacation spots and border towns across Mexico this year and bought controlled prescription medications from pharmacies. Tests showed many pills were tainted with powerful drugs including fentanyl, heroin, meth and MDMA. (Wally Skalij / Los Angeles Times)

After visiting 10 vacation spots and border towns across Mexico this year, reporters used drug-testing strips and later lab testingto show that travelers who shop at pharmacies there risk unwittingly buying pills tainted with powerful drugs, including fentanyl, heroin, meth and MDMA — also known as ecstasy.

In February, The Times reported that some drugstores in Tijuana and the Los Cabos area were selling loose pills over the counter, passing off tablets containing fentanyl and meth as expensive brand-name medications, including Percocet and Adderall.

A team of UCLA researchers, including Goodman-Meza, reported similar findings in four unnamed cities in northwestern Mexico around the same time.

But U.S. authorities didn't take public steps to address the issue until March, after The Times reported that both the Drug Enforcement Administration and the State Department had known for years that U.S. travelers were dying after purchasing counterfeit pills containing fentanyl from Mexican pharmacies.

The State Department issued a travel advisory later that month, warning Americans to "exercise caution" when buying medications from pharmacies south of the border.



In the Yucatán Peninsula city of Playa del Carmen, pharmacies in the tourist zone welcome foreigners. (Connor Sheets / Los Angeles Times)

After several more trips to Mexico, The Times published an investigation in June that documented the presence of counterfeit medications at drugstores in cities from the Yucatán Peninsula in southeastern Mexico to the Pacific coast to the country's northern border.

Later, reporters showed that several stores and at least a few regional chains had begun selling tainted medications by the bottle, in elaborate packaging that was

sometimes indistinguishable from the real thing.

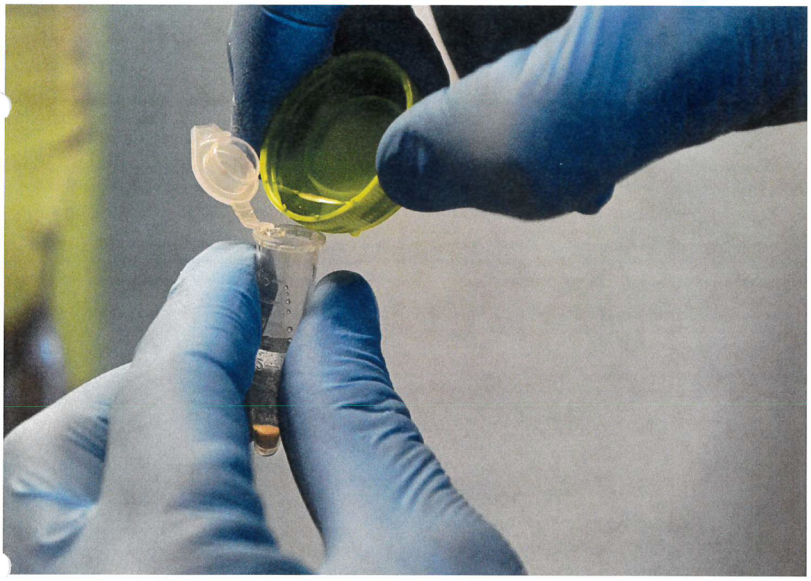
71 of 114

Of the 114 narcotic medications purchased over the course of the year, 62% were fake. Just over 71% of the stimulant medications used to treat attention deficit/hyperactivity disorder — such as Adderall and Vyvanse — were counterfeit, as were nearly 61% of the supposed opioid painkillers.

A few medications were consistently legitimate, including the opioid painkiller tramadol and the ADHD pill methylphenidate, best known as Ritalin. But some medications were almost always counterfeit.

Testing showed that 9 in 10 pills sold as Adderall, six in 10 pills sold as oxycodone, and 7 in 10 pills sold as hydrocodone were fake. Overall, 26 samples contained methamphetamine and 29 contained fentanyl.

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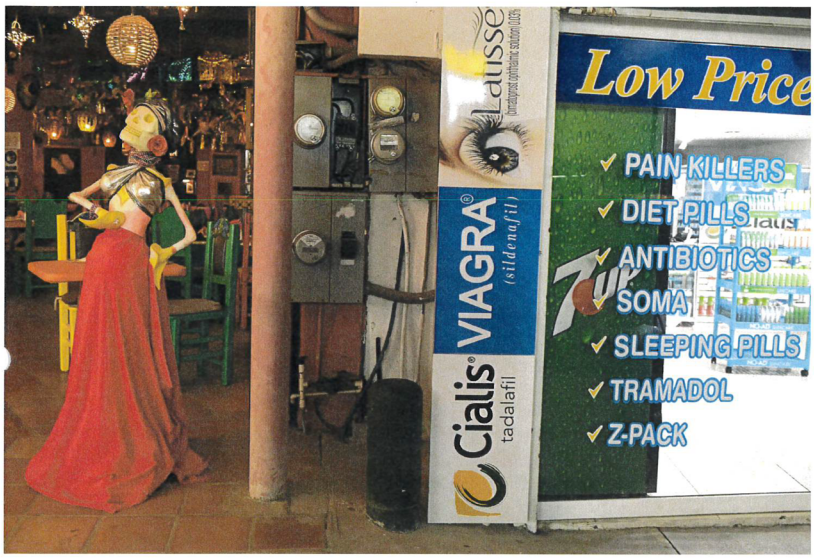
Many pills purchased by reporters in Mexico this year were lab-tested to confirm the initial findings from testing strips. (Wally Skalij / Los Angeles Times)

In March, authorities in Mexico inspected more than 100 pharmacies in Los Cabos and nearby La Paz, closing nine in Los Cabos for a variety of violations. In June, another series of pharmacy raids in Los Cabos resulted in four arrests and the seizure of cash and nearly 25,000 pills.

One worker said that during the second round of sweeps, authorities came to his Cabo pharmacy "looking for loose pills." The officials also reviewed financial records, and ultimately decided the store passed inspection.

"Everything we have, we have permission and invoices from where we bought them," the worker said in November. "Everything comes from a laboratory. Everything is safe here; that's why we're still operating."

But less than 24 hours earlier, the same store had sold three loose pills — purported to be Percocet, Vicodin and Adderall — and one bottle labeled as Adderall. Laboratory testing showed both painkillers were fentanyl, the tablet sold as Adderall was methamphetamine, and the bottle of supposed Adderall contained capsules of an appetite suppressant called clobenzorex.



A pharmacy in Cabo San Lucas advertises its wares to English-speaking visitors. Many also sell controlled medications — or counterfeit versions of them — upon request. (Wally Skalij / Los Angeles Times)

The news reports and resulting law enforcement activity "caused a lot of problems" for the families of closed drugstores' owners and employees, according to one worker at another Cabo pharmacy.

"All you're doing is affecting tourism," she said the day after selling reporters one bottle that was labeled "oxycodone and acetaminophen" but contained guaifenesin —

a cold medication — and another that was labeled as Adderall but contained clobenzorex.

Two months after the Los Cabos arrests, federal health officials in Mexico announced that authorities had closed 23 pharmacies in the Yucatán Peninsula after finding potential counterfeit medications and other irregularities during a series of raids.

Finally, authorities shut down 31 pharmacies and seized more than 4,681 boxes of medication during recent raids in Ensenada, where officials said some of the pills probably contained fentanyl.

At a Puerto Vallarta pharmacy near bustling Playa de los Muertos last month, a clerk said she had no controlled substances for sale before offering a warning.

"In no place in Puerto Vallarta are they going to sell you actual Adderall," she said. "Be very careful in what you buy."

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It's unclear why raids have failed to curb these illicit activities. But several pharmacy workers said authorities didn't confiscate any of their pills or take away samples for testing. Others said they stopped offering controlled medications immediately after the sweeps, but soon resumed sales.

Workers at two chain drugstores in Cabo San Lucas that sold reporters counterfeit pills said authorities hadn't inspected them at all in 2023.



In Puerto Vallarta, several pharmacies were raided by Mexican authorities in recent months, drugstore employees say. Officials would not elaborate on or confirm their accounts. (Wally Skalij / Los Angeles Times)

At several drugstores in Puerto Vallarta's lively tourist districts, employees said in November that pharmacies there had been raided a few months earlier. The Times could not independently verify their claims, and officials did not respond to requests for comment.

At a small drugstore on one of the city's main streets, an employee working the register said drug regulators had searched the store — even inspecting the bathroom and going through employees' bags. But they didn't find anything worth confiscating.

There were no opioid painkillers in stock, but reporters bought a bottle of supposed Adderall. The drug had been unavailable for about two months after the raids "all because of fentanyl," the worker said.

"We weren't selling any medication like this because they were checking," she said, referring to the authorities who carried out the raids. "They don't want us selling fentanyl or oxycodone or things like that."

The alleged Adderall tested positive for methamphetamine.

Aside from the glut of willing sellers and suppliers, another roadblock to reining in the sale of counterfeit pills in Mexico is the constant demand — often from Americans looking for medications that may be cheaper or easier to get than in the U.S., where opioid painkillers are tightly controlled and ADHD medications are scarce due to a years-long shortage. In recent months, several people prescribed ADHD drugs told The Times they'd purchased or considered purchasing their medications in Mexico.

One of those was Andrés Muñoz. Earlier this year, he took a few days off from his consulting job in Chicago for a family trip to Cancún. Muñoz was 30 and in Mexico for the first time, and he decided to stop in at a drugstore for ibuprofen.

He had recently been prescribed Adderall in the U.S., and was surprised to see that the drug was available without a prescription. He said he almost bought at least one $200 bottle of the pills, even though he knew that fentanyl-tainted counterfeits were a concern in Mexico.

"Honestly, I didn't even consider the dangers of it," Muñoz said, adding that uneven access to affordable, quality health insurance leaves many Americans with few good options. "So of course you're gonna go try to find a solution. The system we have in place doesn't offer a solution."

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Shopping for narcotic medications in pharmacies in Mexico often means listening to workers explain that bottles stashed in hidden compartments and loose pills kept in

unlabeled plastic bags contain legitimate medications.

At one pharmacy in Cabo San Lucas, a worker warned that "a lot of people sell fake medication" — and even offered reporters advice on how to spot it.

"Those are real," she said, pointing to a box of medication with a code on the side. "If they don't have that number, they're not."

But the painkillers purchased from that pharmacy tested positive for fentanyl, and the supposed ADHD medications were made of methamphetamine.

At a Puerto Vallarta outpost of a drugstore chain that sold reporters fake medications, Ed Sheeran was crooning through tinny speakers about having faith in what he sees.

The clerk claimed the pharmacy did not stock counterfeit pills. But the worker said some stores in another regional pharmacy chain had been "making irregular medications that had fentanyl" and selling them to unsuspecting travelers.

On two separate trips to Puerto Vallarta, reporters visited several stores in that same regional chain, and repeatedly purchased pills sold as Adderall that tested positive for methamphetamine.

One of those purchases was the bottle the "professional pharmacist" had pulled out of a secret panel behind the counter. Another was a bottle that a young worker pulled from a locked hiding spot.



A Mexican pharmacy offers a wide array of powerful medications over the counter. (Connor Sheets / Los Angeles Times)

She said the medication was hidden from view for safekeeping because it was pricey — $300 per bottle.

"We can't have expensive medications out like that," she said. "We mostly sell sunblock."

The chain did not respond to requests for comment.

In addition to concealing illicit wares and offering empty assurances about safety, pharmacy workers seemed choosy about their customers.

Several residents said the stores would sell narcotic medications over the counter only to foreign tourists. At one drugstore, when a reporter started speaking Spanish, the clerk grew suspicious.

At a Puerto Vallarta location of the prominent national chain Farmacias Similares, a worker said only customers with prescriptions could buy controlled medications. Other pharmacies, she said, would sell them without a prescription — depending on who you are.

"If I go, as a Mexican, and I ask them, they're not going to tell me" whether they have the medications, she said. "Because it's not something they're supposed to [sell]. Only to foreigners."

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Organized crime experts say that Mexican drug cartels are almost certainly involved in making the sophisticated counterfeit medications. But it is unclear exactly how the pills end up on pharmacy shelves or in hidden compartments behind the counter.



Earlier in 2023, drugstores in Mexico tended to sell counterfeits of controlled medications as loose pills — but the fakes are increasingly sold by the bottle in convincing packaging. (Connor Sheets / Los Angeles Times)

Vanda Felbab-Brown, a senior fellow at the Brookings Institution who studies criminal organizations, told The Times earlier this year that the tainted pills "must be coming from the Mexican criminal groups." But she said it was unclear whether the pharmacy owners were seeking out the fake medications or selling them under threat of violence.

"It would be fascinating to know whether they have any clue what they're selling," she said.

The Times' recent reporting found that many store workers know there are fentanyl-tainted fakes on the market, and that some drugstores sell them. As one worker at a pharmacy that would not sell controlled medication without a prescription put it: "Where else are you going to get that medication that easily?"

When asked about the source of their medications, some workers shifted blame to the stores' owners.

"Our boss gives them to us," said a clerk at a pharmacy in Cabo. "They come from laboratories — you should focus on them."

But when asked for contact information for the store's distributor, the worker said that was "private."

At another drugstore, an employee said she couldn't remember the name of the store's supplier, but that it was a big distributor in Guadalajara. Workers at other stores suggested their pills came from California, but also could not name a supplier.

This month, after getting back results from lab testing, reporters called and messaged more than a dozen pharmacies they'd visited in November. Most did not respond to repeated messages inquiring about the counterfeit goods or the suppliers who provided them.

One worker who did respond said he knew the Cabo pharmacy where he worked did not sell opioid painkillers because he was one of only two people who worked there. When a reporter explained that the store had sold fentanyl-tainted pills weeks earlier, his tone shifted.

"Perhaps you have the pharmacy confused," he said.

Instead of denial, some responded with fear. A few weeks after selling reporters fentanyl- and methamphetamine-laced pills, a worker at a different pharmacy in Cabo refused to answer questions about such a "delicate topic."

He said he was embarrassed and wouldn't disclose where the drugs came from.

"I can't give you any information," he said in a telephone interview. "It's scary to even talk about these kinds of things."

When asked what he was scared of, he hung up.

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Dec. 21, 2023

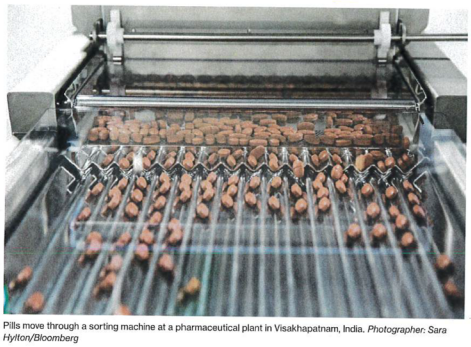


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Industries + Politics

US Leans on India's Pharma Industry to Snub China. There's Just One Catch

- Report reveals close ties between companies in India and China
- Large generic drugmaker gets 55% of raw materials from China



Pills move through a sorting machine at a pharmaceutical plant in Visakhapatnam, India. *Photographer: Sara Hylton/Bloomberg*

By Anna Edney
February 5, 2024 at 6:00 AM EST

The Biden administration embraced a plan from India's government last year to edge China out of its position as a leader in making ingredients for generic pharmaceuticals sold in the US. But a new report shows that much of those ingredients are likely still coming from China anyway.

America's reliance on China for drug ingredients has raised alarm bells in Congress. House committees will hold two hearings Tuesday on drug shortages and the US Food and Drug Administration's foreign inspection program, which has seen a large drop in visits to Chinese factories over the last few years, due in large part to the Covid pandemic.

The report put together ahead of the hearings by the Coalition for a Prosperous America, a trade organization pushing for tax breaks for domestic manufacturing, showed India-based Aurobindo Pharma Ltd. gets about 55% of its raw materials for ingredients from China. Aurobindo is a bellwether for the industry: It supplies the most generic drugs by volume to the US, and its $3.1 billion in 2023 revenue was second-highest among Indian drugmakers, according to data compiled by Bloomberg. The company's 2022-2023 annual report said it has "a high dependence on the China market" for materials and ingredients used to make drugs.

"We did suspect they had ties to China, we just didn't know how much," said Nick Iacovella, a spokesman for the coalition. "This is really a red flag."

Read More About Contaminated Drugs:

- The Pentagon Is Skeptical of Cheap, FDA-Approved Generic Drugs
- Tiny Lab Finds Danger in Dry Shampoos, Zantac While FDA Trails
- New Contaminant in Popular Drugs Could Cost Big Pharma Millions
- Popular Diabetes Drug Found to Contain Potential Carcinogen
- Carcinogens Still Vex Drug Industry Years After Recalls Began

President Joe Biden's administration has focused its efforts on deepening its collaboration with India, where US relations are good in comparison with China. As tensions with the Asian superpower grow, so do concerns over how the US and the rest of the world count on the country for many pharmaceuticals, particularly the key ingredients used to make drugs.

Security Threat

U.S. military officials have gone so far as to call vulnerabilities in the drug supply chain a national security threat, and the Defense Department has begun an effort to test generic drugs for safety and effectiveness. Meanwhile, the supply chain has never felt more tenuous: Drug shortages in the US peaked at 309 last year, the highest number in almost a decade.

With their low labor costs and lax environmental standards, China and India dominate generic drug manufacturing. Yet companies in those countries operate largely outside of FDA view. While the agency can easily make surprise inspections at US plants, they're often announced ahead of the time in the two countries.

The report also shows Aurobindo is doing business with suppliers that have ties to China's military industry, questionable track records on safety and are based in Xinjiang, where the US government has warned there is "evidence of widespread use of forced labor."

Aurobindo didn't respond to a request for comment, including a question about whether they use materials from the Chinese suppliers in drugs made for the US market.

The coalition worked with experts and research analysts examining import and export data.

Suppliers' Ties

One of Aurobindo's suppliers in China last year was Zhejiang Huahai Pharmaceutical Co., according to the report. The document said Aurobindo ordered valsartan, a blood pressure medication, from Huahai.

The drug went into shortage five years ago when a probable carcinogen, N-Nitrosodimethylamine, or NDMA, was found in ingredients used to make it that were supplied by Huahai. FDA inspectors found that the China-based company had ignored evidence that the ingredient was contaminated.

Aurobindo does business with at least four suppliers that have ties to organizations under US sanctions for their connections to China's military industry, the report said. One of the suppliers referred to in the report, Henan Topfond Pharmaceutical Co., Ltd., is controlled by China Meheco Group Co. Ltd. One of that company's top shareholders is China Aerospace Science and Industry Corp., which the US government has determined "to be acting contrary to the national security or foreign policy interests of the United States."

India's companies have their own quality issues to contend with, making the FDA's efforts to oversee drug safety a game of whack-a-mole that the agency is far from winning. Inspectors have documented a host of issues at companies in India that haven't improved over the last decade, including factories with unsanitary conditions, ignored contamination and made-up test results.

Warning Letter

The FDA sent Aurobindo a warning letter in 2022 after an inspection of one of its factories in India found it failed to ensure suppliers could provide materials "of intended quality and purity," according to an inspection document. Inspectors also found Aurobindo's protocol for testing samples of drug-making materials it received was not "scientifically sound and appropriate" to ensure the products met US standards.

Aurobindo said Friday it would halt production on some of its manufacturing lines at an Indian subsidiary, Eugia Pharma Specialities Ltd., after an FDA inspection. The company said it received an FDA report listing nine potential violations but didn't say what inspectors found.

"The company has already started working with the regulatory authority/third party consultants to accelerate the process and re-start production on those lines at the earliest," Aurobindo said in a statement. "At this point in time, we don't foresee any material impact on the business."

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Justice Department Announces Eight Indictments Against China Based Chemical Manufacturing Companies and Employees

October 03, 2023

DEA Administrator

Administrator Milgram Remarks As Delivered

Good Afternoon. Fentanyl is the greatest threat to Americans today. It is devastating families across our country and killing Americans from all walks of life. And it is the leading cause of death for Americans today between the ages of 18 and 45.

The Drug Enforcement Administration is actively targeting every single aspect of the global fentanyl supply chain — so that we can put an end to the most devastating drug crisis our country has ever seen.

The two drug cartels that are responsible for fentanyl coming into the United States are the Sinaloa and Jalisco Cartels. They work with chemical companies based in the People's Republic of China to get their raw materials, which are chemicals called



fentanyl precursors. Nearly all fentanyl precursors come from China. These precursors are then made into fentanyl.

But it doesn't stop there. Companies in China also manufacture other synthetic or man-made drugs — that make the fentanyl threat even more addictive and even more deadly. These drugs include xylazine and nitazenes, which are then mixed with fentanyl to extend the high and increase the cartels' profits.

DEA has taken the lead in these cases, investigating and holding accountable the companies and individuals in China and elsewhere who are responsible for these poisons. Today, we announce 8 indictments, charging 8 companies and 12 individuals, for importing into the United States fentanyl precursors, xylazine, and other man-made or synthetic chemicals.

We have seized more than 80 kilograms of synthetic chemicals in these investigations — enough, when mixed with other chemicals, to make more than 48 million deadly doses of fentanyl.

As I said before, precursor chemicals are turned into deadly fentanyl, and xylazine and nitazenes are then added to make that fentanyl even deadlier — killing Americans, both young and old.

Let's talk about xylazine. Xylazine is known on the street as "Tranq" and is a veterinary drug used to sedate animals, like horses and cattle. It has no legitimate use in humans. But drug traffickers mix xylazine with fentanyl because it extends the high and serves as filler. When it ends up in humans, it can cause human tissue to rot and lead to amputation. It also does not respond to Narcan, a drug used to prevent fentanyl poisoning and overdose. In other words — xylazine makes the deadliest drug threat, fentanyl, even deadlier.

DEA has seized xylazine-fentanyl mixtures in 48 of 50 states and in Washington, D.C. We know where this xylazine comes from—it comes as powder from China and as liquid diverted from veterinary supply chains.

In one of the cases being announced today, DEA agents seized more than 300 grams of xylazine shipped from a company in China to Miami, and paid for in Bitcoin. That same company shipped xylazine to a fentanyl trafficker in Philadelphia multiple times a month. When agents conducted a search of the trafficker's home, they found 1,500 counterfeit pills, two pill presses, a powder mixture of fentanyl and xylazine, and two bottles of liquid xylazine.

Despite all of this, xylazine is not yet a controlled substance. This is why it is so important for it to be scheduled.

We also found nitazenes in these cases. Nitazenes are dangerous synthetic opioids that can be as powerful, or even more powerful, than fentanyl. They have no legitimate use. In April 2022, based on the work of DEA chemists and agents, I signed an emergency scheduling order placing 7 nitazenes into Schedule I. In one of the cases announced today, companies and individuals in China are charged with shipping two of those nitazenes to Georgia and to South Florida.

In these cases, we also found fentanyl analogues, like fluorofentanyl. These analogues are a treacherous attempt to work around the law: every time we make one substance illegal, the drug cartels and their chemical suppliers switch to another that is slightly different at the molecular level but has the same impact. DEA is doing its part to schedule each fentanyl analogue it finds one at a time—but we need permanent class-wide scheduling of fentanyl related substances, and we stand ready to work with Congress to get this done.

Despite all of the different synthetic chemicals we found in these cases, a few things remained constant. The chemicals were cheap—a deadly dose cost mere cents. At prices like these, the amount of deadly drugs that can be made is limitless. The chemicals were sold online. On public websites and through encrypted applications like WhatsApp, WeChat, and Wickr. The chemicals were shipped through common carriers, by air and by ground—through the postal service, UPS, and FedEx. The chemicals were carefully packaged to deceive customs inspectors. And the chemicals were paid for in every way—Western Union, MoneyGram, Paypal, Alibaba, bank transfers, and most commonly Bitcoin and other cryptocurrencies, to make it harder for us to follow the money.

This is the unprecedented threat that we are dealing with. And it is the reason why 110,757 Americans died from drug poisonings in 2022 alone.

Today's indictments target the threat where it starts.

I want to thank this incredible team that is here and has assembled all of us working together have had an incredible impact in this investigation and I hope, and more work to come. I want to pay a particular tribute to DEA's Miami Field Division, our Counternarcotic Cyber Investigations Task Force, and our DEA Tampa District Office Chemical Express Group. I also am deeply indebted to our prosecution partners in the Southern and Middle Districts of Florida, specifically U.S. Attorneys Markenzy Lapointe and Roger Handberg, as well as the line prosecutors who all worked tirelessly with our agents and Intel analysts on these investigations.

Today's charges continue DEA's work to target the global fentanyl supply chain. We will not rest or relent, until this crisis ends. There is more to come. Thank you.

It is now my privilege to introduce my friend and partner, the lead Postal Inspector, Gary Barksdale.

DOJ Announces Eight Indictments

October 4, 2023

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BUSINESS

How troubles at a factory in India led to a U.S. cancer-drug shortage



By Daniel Gilbert

June 27, 2023 at 6:00 a.m. EDT

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The Intas Pharmaceuticals plant churned out medicine in a sprawling industrial park in western India, far from the minds of American cancer patients until its problems became theirs.

The factory accounted for about 50 percent of the U.S. supply of a widely used generic chemotherapy drug called cisplatin, a reality that few understood until the U.S. Food and Drug Administration inspected the site in November.

The inspectors found widespread problems, including freshly torn-up documents doused with acid, and a "cascade of failure" in quality assurance. Intas suspended production as it works to resolve the problems, triggering a shortage of cisplatin, according to supply-chain experts. Now, oncologists are scrambling to procure supplies or come up with alternative treatments, potentially affecting hundreds of thousands of patients.

It is the latest case of a generic drug that is suddenly hard to get in the United States, where consumers have also struggled over the past year to find everything from children's acetaminophen to antibiotics and medicines for treating attention-deficit/hyperactivity disorder. The reasons for the shortages vary, but together they are putting new focus on the dicey business of making generic drugs and the fragile network that delivers critical medications to Americans.

Generic drugs — cheaper copies of brand-name medications — help control health-care costs, making up more than 90 percent of prescriptions in the United States but less than 20 percent of spending on prescription medicines, according to the Association for Accessible Medicines, which represents generic drugmakers. Rising competition in the industry has flattened manufacturers' profits, giving them little incentive to upgrade aging plants often running near capacity that are vulnerable to breaking down, experts say.

In this fragile supply chain, a disruption at a single plant can trigger widespread shortages when other manufacturers can't make up the difference. In addition to Intas, four other companies that make cisplatin have reported a shortage to the FDA, citing a "demand increase." That shortage, in turn, has contributed to a shortage of carboplatin, a chemo drug that can be substituted for cisplatin and was also made at the same Intas plant.

William Dahut, chief scientific officer of the American Cancer Society, said patients can't simply wait for a chemotherapy drug to become available and risk having their cancer continue to grow. "You may just continue on with other drugs that might not be as effective," he said.

That very scenario added to Anne Ingebretsen's anxiety after she was diagnosed with ovarian cancer in April. The diagnosis itself was a blow for the 63-year-old, an elected official in Greenwood Village, Colo., who was initially prescribed carboplatin for chemotherapy. "Then you find out that actually you're not going to get the standard protocol, you're going to get the second-string protocol. That's another gut-punch," she said.

The National Comprehensive Cancer Network, an alliance of cancer centers, surveyed 27 of its members in May and found that between 70 and 93 percent had a shortage of cisplatin or carboplatin. The drugs are used to treat cancers of the lung, bladder, breast and prostate, among others.

"We are not aware of any past shortages of anti-cancer medications that approach the current scale seen with cisplatin and carboplatin," Robert Carlson, the network's chief executive, said in a statement. The drugs "are so widely used — and so effective — across so many cancer types that the impact is much bigger than past oncology medication shortages."

The FDA added drugs made at the Intas plant to an "import alert," under which they may not be allowed into the United States, but exempted ones that are in shortage. Intas and its U.S. subsidiary, Accord Healthcare, have worked with the agency to verify the quality of cancer drugs it has already produced and ship them to the United States.

"Intas is fully dedicated to continuing its heritage of supplying quality medicines," the company said in a statement.

The FDA has arranged to temporarily import cisplatin from a Chinese supplier and is exploring more such options. The agency has 14 cancer drugs on its shortage list.

"The FDA is doing everything possible to help mitigate these shortages," a spokesperson said.

But ending the nation's chronic drug shortages will require a fundamental shift in how generic drugs are made and bought, experts say. A report published Wednesday by the Brookings Institution's Hamilton Project argues that the U.S. government must intervene, with legislation and funding, to create incentives for manufacturers to invest in reliable equipment and for the purchasers of their drugs to pay a premium for quality.

That could cost up to $3 billion a year, the report estimates, but is cheap compared with the societal costs of drug shortages. An unpublished FDA analysis in 2018 calculated that a single shortage of norepinephrine — a blood pressure medication — led to higher mortality and a "social cost" of $13.7 billion.

'Pretty much nobody is making money'

In 2017, Teva Pharmaceuticals, the world's biggest generics manufacturer, reported its largest-ever annual loss. The culprit: its U.S. generics operation.

The business of making generic drugs is essentially to copy another company's innovation and, once the original drug loses patent protection, offer it to the public at a lower price. It's a formula that historically has netted manufacturers a tidy profit while lowering costs throughout the health-care system. But the viability of this model has come under pressure in recent years.

Hospital purchase groups, wholesalers and distributors that buy drugs from Teva and other drugmakers have consolidated, leaving a few large players with greater leverage to drive hard bargains. FDA regulations and policies have also led to increased competition for generic drugs, putting further pressure on manufacturers to offer ever-lower prices.

As Israel-based Teva analyzed the cash it expected to bring in from selling generics in the United States in 2017, it concluded that the business was worth $11 billion less than it had previously believed, leading it to post a huge loss.

Since then, Teva has dramatically cut back on its manufacturing footprint. As of May, the company operated 52 plants globally, down from 80 in 2018, and plans to close up to another dozen facilities, according to an investor presentation. It has reported a current shortage of nine cancer drugs that it makes.

Teva said its new strategy is a response to "recent years' radically shifted market dynamics," according to a spokesperson, and that it is "not currently planning any changes to drugs in short supply due to high demand." The company said that it has seen a "triple-digit demand hike" for cisplatin and carboplatin because of the Intas plant shutdown, and that it is "increasing efforts across its supply chain to meet our commitments to customers and find ways to address excess demand."

"Pretty much nobody is making money in the generics business in the U.S.," said Carlo de Notaristefani, who oversaw global operations at Teva until 2019. The lack of profits makes it hard for manufacturers to invest in upgrading older factories, he said, creating another risk for disruption along with shortages of raw materials and complying with regulations. "As plants get older, they are more susceptible to unexpected breakdowns."

Cancer drugs that are injected are particularly complex to make and handle because they go directly into a patient's bloodstream and must be produced in a sterile facility, leaving less margin for error than oral medications that go through the body's digestive system.

Supplies of such generic injectable drugs are also more vulnerable to disruption, with at least 15 percent having a single manufacturer, according to the new report from the Brookings Institution's Hamilton Project.

Because of the meager profits in the United States, "US plants continue to close, while an increased number of sites are being opened in India with Indian government support," the study says.

FDA inspections of foreign manufacturers plummeted during the covid-19 pandemic, according to agency data. 3efore the November inspection, the last time the Intas plant was inspected was in February of 2020, which uncovered problems but didn't result in regulatory action.

'That's how we end up with shortages'

On the day inspectors arrived at the Intas plant in India's Gujarat state, they noticed "a large black plastic bag that was [hidden] under the staircase" by a quality control area. Inside the bag were torn-up documents on the plant's manufacturing practices for drugs sold in the United States.

Initially, an Intas official explained that an employee had used the documents to clean up a spill on the floor. Later, a quality control officer admitted he had trashed the documents when he heard investigators were coming, dousing them with acid "in an attempt to destroy the evidence of the tests that he was working on that had issues," according to the heavily redacted inspection report.

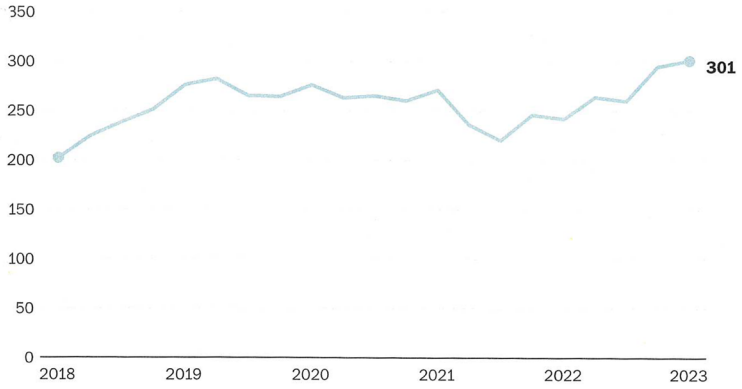
The FDA investigators also found a truck full of trash bags containing ripped-up documents that concerned quality tests, waiting for clearance to leave the manufacturing zone.

"We have determined the shredding of documents to be an isolated incident," Intas subsidiary Accord Healthcare said in a statement, adding that it has taken "appropriate corrective actions" and launched a "corporate-wide Culture of Quality initiative."

"I think if you're not being watched and you know it, then the temptation is there to cut corners," said Erin Fox, associate chief pharmacy officer at the University of Utah, which tracks shortages nationally. "I am worried that as FDA ramps up inspections, they're going to find more problems" that could lead to more shortages. The number of drugs in active shortage is the highest since 2014, according to the university's drug information service.

Sustained shortage

The number of drugs in short supply is on the rise, as new shortages are happening faster than existing ones are resolved.



Source: University of Utah Drug Information Service

DANIEL GILBERT / THE WASHINGTON POST

Some experts on drug shortages are voicing hope that the current crisis will get lawmakers to act on long-standing recommendations.

Marta Wosinska, a visiting fellow at the Brookings Institution and lead author of the Hamilton Project paper, proposes low-interest loans for manufacturers to upgrade their plants and funding for the government to stockpile key generic drugs. But the most critical reform, she says, is to create a system that rates the quality of manufacturers and steers demand to the most reliable ones — by financially rewarding hospitals that purchase from them.

"If we want resilience, we will need to pay for it," Wosinska said.

An industry white paper published Thursday made some similar recommendations, calling for incentives for hospitals, wholesalers and distributors to make long-term commitments to buy drugs at fixed prices. The notion of scoring manufacturers on reliability — a metric known as quality management maturity, or QMM — is still a matter of debate.

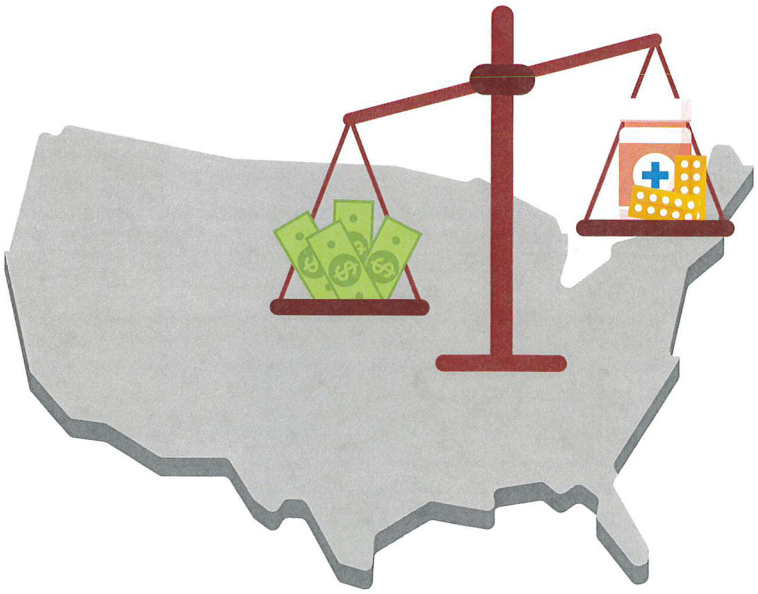
Brian McCormick, head of Teva's global regulatory policy, said at a Hamilton Project forum that he supports efforts to improve manufacturers' quality but worries that steering demand to the highest-quality plants could harm older facilities and lead to a less-diverse supply chain.

"I want a facility with a low QMM score on the U.S. marketplace because I want as many adequate suppliers available to us," he said.

"That's right," Wosinska replied, "but ... what I don't want is that facility to have 50 percent of the market share." She added, "That's how we end up with shortages."

U.S. Consumers Overpay for Generic Drugs

Policy solutions must address the intermediaries who benefit



Erin Trish, PhD
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USC Schaeffer
Leonard D. Schaeffer Center for Health Policy & Economics

Schaeffer Center White Paper Series

U.S. Consumers Overpay for Generic Drugs

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KEY TAKEAWAYS

- Generic prescription drugs save the U.S. healthcare system money overall.
- Growing evidence shows that U.S. consumers often overpay for generics as pharmacy benefit managers game opaque and arcane pricing practices to pad profits.
- Greater transparency across the generic prescription drug supply chain and policies to spur competition and deter anticompetitive practices can reduce generic drug costs for patients.

ABSTRACT

Growing evidence indicates U.S. consumers, employers and the government often overpay for generics as pharmacy benefit managers (PBMs) and their affiliated insurer companies game opaque and arcane pricing practices to pad profits. PBMs played an essential early role in driving U.S. uptake of generics. However, PBMs' current practices—coupled with market distortions within the pharmaceutical supply chain—have inflated retail generic prices. Commercial tactics such as spread pricing, copay clawbacks and formularies that advantage branded drugs over less expensive generics have funneled the savings from low-cost generics into intermediaries' pockets, rather than the pockets of patients. Greater transparency across the generic supply chain and policies to spur competition within the generic industry can help ensure that patients continue benefiting, both clinically and financially, from generics.

INTRODUCTION

Over the last 50 years, innovative drugs have delivered enormous health benefits, especially for people with chronic conditions like diabetes and heart disease—even reducing other healthcare spending in some cases.[1] But new branded drugs are costly to develop and expensive to purchase, especially in the United States. Nearly four decades ago, Congress crafted a compromise designed to spur drug discoveries and speed lower-cost generics to market by enacting the Drug Price Competition and Patent Term Restoration Act, known as Hatch-Waxman. The 1984 law jump-started production of therapeutically equivalent but lower-cost generics and set the stage for a rare cost-containment success story in U.S. healthcare: The United States leads the developed world today in using generic prescription medications.[2]

At the time, California Democratic Congressman Henry Waxman, working with Utah Republican Senator Orrin Hatch, brought branded and generic industry leadership together to develop the compromise agreement that gave the branded industry longer monopolies while the generic industry got an abbreviated drug approval process.[3] For generics, the goal was to create a viable market that could drive prices down to competitive levels—close to marginal production costs—after a branded drug's patent expiration. Following the law's enactment, manufacturers rapidly introduced generic drugs into the U.S. market, extending the societal benefits of less expensive versions of essential medicines in perpetuity.

HATCH-WAXMAN ACT

A 1984 federal law that set the stage for making low-cost generic drugs widely available.

90%

OF ALL PRESCRIPTIONS DISPENSED IN THE U.S. ARE FOR GENERIC DRUGS.

GENERICS: AN AMERICAN SUCCESS STORY

Generics have made high-value and lifesaving medications more affordable and accessible and overall continue to save the U.S. health system money. The rapid and deep embrace of generic prescription drugs in the U.S. ticked all the elusive healthcare value boxes: lower costs and increased patient access while maintaining quality. In the U.S., generics are dispensed 97% of the time when available, growing from 78% of all dispensed prescriptions in 2010 to 90% in 2020.[4] Generics account for only a slice—about 18%—of overall U.S. retail prescription drug expenditures, which reached nearly $350 billion in 2020.[5,6] Nonetheless, by one estimate, U.S. use of generic and biosimilar drugs in place of branded drugs in 2020 saved $338 billion, with 10-year estimated savings from generics of nearly $2.4 trillion.[7]

AS DRUGS PLAY BIGGER ROLE IN CARE, THEIR INSURANCE BECOMES KEY

Hatch-Waxman's passage coincided with a particularly productive era in scientific discoveries that led to new medicines to treat many chronic conditions, including high cholesterol, high blood pressure, diabetes, depression and gastric reflux. Fueled by such blockbusters as Zoloft, Lipitor, Zantac and Nexium, sales of branded drugs jumped more than tenfold between 1984 and 2009, from $20 billion to $250 billion.[8]

As these groundbreaking but expensive therapies came to market, insurance coverage became increasingly important in enabling millions of patients to afford prescription drugs. Employers, eager to recruit and retain workers with a new benefit, expanded coverage of prescription drugs. By 1994, more than 50% of dispensed prescription drugs were covered by insurance.[9] The 2006 Medicare expansion of Part D outpatient drug coverage further increased prescription drug use.[10] Starting in the 1990s, insurers and PBMs introduced tiered drug formularies, with patient cost-sharing amounts tied to a drug's tier. Low-cost drugs with equal or superior efficacy and safety—often generics—were placed on preferred tiers, where patients could get the best deals using their insurance benefits with minimal out-of-pocket cost. Higher-priced branded drugs had greater patient cost sharing.[11]

But insurance coverage can introduce drawbacks as well. When a third party pays for any product or service, the end consumer faces little or no incentive to seek the best price, and sellers respond accordingly by raising prices and increasing profits. Consider car insurance: A typical auto insurance plan does not cover oil changes, a routine service that is readily available at mechanics and express oil shops throughout America. In addition to being more price sensitive to the cost of oil changes because they bear it fully, consumers are unlikely

3
LARGEST
PBMS

> ***Vertical integration and consolidation enable practices that prevent consumers from seeing the full benefits of generic savings.***
>
> ***The three largest PBMs—which process nearly 80% of all retail prescription claims—all operate under the umbrella of large insurers.***

to overpay for oil changes because they have many providers to choose from and can easily compare prices. In turn, oil change providers have every incentive to attract more business by competing on price. However, when getting auto body repairs after a covered accident, consumers pay little attention to the cost because, after paying their deductible, insurance pays the rest. The same is true for covered medicines. Most insured people rarely know the price of their prescriptions—they know what they spent at the pharmacy but not what their insurance paid. A lack of transparency about the actual cost of generic medicines—by one estimate, generic versions of many critical medicines can be profitably produced at a 99% discount from the price of the brand drug[12]—leads to widely varying generic prices across insurers, PBMs and pharmacies. Yet insured patients have few incentives to shop around to find the lowest price if it only saves their insurer money.

BRAND AND GENERIC DRUG MAKERS INITIALLY PROSPER

The branded drug industry flourished in the wake of Hatch-Waxman, with U.S. per capita prescription spending increasing an inflation-adjusted estimated 138% between 1984 and 2019.[13] As blockbuster branded drugs used by millions began losing patent protections—Zoloft, for example, in 2006—and became available as generics, branded drug manufacturers raised prices on their remaining patented drugs to make up for lost revenue from the so-called patent cliff.[14] However, more recently, spending growth has been driven by the introduction of new branded drugs and the increased volume of branded prescriptions rather than price increases.[15]

The generics industry also prospered initially after Hatch-Waxman, competing vigorously to bring the large backlog of older off-patent medications to market at lower prices. But in recent years, as PBMs, insurers, wholesalers, pharmacies and the government pressed generic manufacturers for lower prices, the industry consolidated, resulting in fewer companies making certain generics.[16] Reduced competition led to higher prices,[17] and manufacturing problems that shutter production, even for a short time at one company, can now spark shortages of important drugs.[18] Responding to these issues, high prices and shortages, groups ranging from a nonprofit like Civica Rx to a public-benefit corporation started by billionaire Mark Cuban have launched initiatives to manufacture generics that had been subject to shortages and price gouging.[19]

INTERMEDIARIES PREVENT CONSUMERS FROM SEEING THE FULL BENEFITS OF GENERIC SAVINGS

Despite generic entry driving down prices relative to branded drugs,[20] consumers are not benefitting fully from the lower prices because middlemen—PBMs and insurers—are reaping the financial benefits rather than passing the full savings to consumers. Among privately insured beneficiaries, a 2021 study concluded that generic drug price declines between 2007 and 2016 were not fully passed through to consumers.

Researchers found that direct out-of-pocket payments by insured consumers to pharmacies for generic prescription drugs declined by about 50% during that time, while the total price—out-of-pocket consumer payment plus the price paid to the pharmacy by the insurer—fell by nearly 80% during the same period.[21]

A growing body of research shows that the federal government and Medicare beneficiaries are also overpaying for generic prescription medications. An analysis by Schaeffer Center researchers, for example, found that Medicare Part D standalone drug plans paid $2.6 billion more in 2018 for 184 common generic medications compared with prices for the same drugs available to cash-paying Costco members.[22] The researchers also found such overpayments in a convenience sample of commercial claims, although they were slightly less common than in Medicare claims.

The three largest PBMs—CVS Caremark, Express Scripts and OptumRx—operate respectively under the umbrella of large insurers Aetna CVS Health, Cigna and UnitedHealth Group.[23] Such vertical integration and consolidation contributes to opaque and inflated generic drug prices. PBM and insurer practices such as copay clawbacks, spread pricing and profit-oriented formulary design enable overpayment on generic drugs.

Copay Clawbacks

A 2018 Schaeffer Center study found that commercially insured patients' copayments for a generic prescription exceeded the total cost of the medicine more than a quarter of the time (28%), with an average overpayment of $7.32.[24] Total overpayments in the commercial claims studied amounted to $10.51 per member per year. Known as a copayment "clawback," the practice was abetted by "gag clauses" in PBM/insurer contracts that prevented pharmacists from telling consumers they could save money by paying the cash price; Congress outlawed such gag clauses in 2018.[25] However, PBM contracts commonly require pharmacies to give the PBM their lowest price when accepting reimbursement for a prescription.[26] As a result, pharmacies are careful to set cash prices higher than their negotiated PBM rates. Without prohibition of such anticompetitive contract clauses, pharmacies will not offer competitive cash prices for fear of triggering these best-price clauses.

Spread Pricing

Many PBM contracts enable intermediaries to collect large margins on transactions through a practice known as spread pricing. In such arrangements, when a beneficiary fills a prescription, the PBM reimburses the pharmacy one price while charging health plans a higher price and pockets the difference or "spread." Because neither the health plan nor the pharmacy knows what the other side was paid or charged, the practice hides the PBM's margins from scrutiny. In 2018, Ohio's auditor of state conducted an audit of PBM services to the state's managed Medicaid plans, finding that the average spread on generic prescriptions filled by Medicaid managed care beneficiaries was 31.4%, costing state taxpayers $208 million in one year.[27] As a result, Ohio mandated that its Medicaid managed care plans renegotiate all PBM contracts from spread pricing to "pass-through" models in which PBMs charge plans only the amount paid to pharmacies plus a fixed fee per transaction.

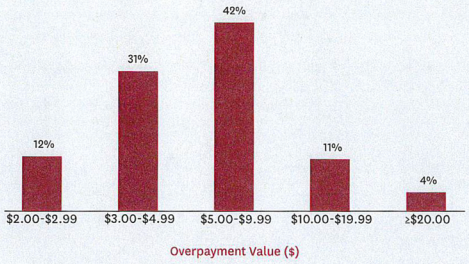
OVERPAID
$2.6
BILLION

> ***Medicare Part D standalone plans paid $2.6 billion more in 2018 for 184 common generic medications compared with prices for the same drugs available to cash-paying Costco members.***

28%

of patients' copayments for generic prescriptions exceeded the total cost of the medicine.

Distribution of Overpayments for Generic Drugs, By Overpayment Value



Source: Van Nuys, K., G. Joyce, R. Ribero and D. Goldman (2018). Overpaying for Prescription Drugs: The Copay Clawback Phenomenon. *USC Schaeffer Center for Health Policy & Economics.*

Profit-Oriented Formulary Designs

Many formularies, as currently constructed, do not prioritize lower-priced medicines. Instead, they favor the use of branded medications that bring in lucrative manufacturer rebates but not necessarily lower prices for consumers, employers or the government. Rebates are a form of price concession paid by a pharmaceutical manufacturer to the insurer or PBM. Pharmaceutical companies rebate back a percentage of the price to the insurer or PBM in return for coverage of the medicine. Rebate amounts vary based on coverage tier, administrative restriction (e.g., prior authorization), market competition and market share. PBMs keep a share of these rebates, increasing their bottom lines, and pass the remainder to insurers. As a result, both commercial and Medicare drug plans often are slow to put new generics, which typically do not pay rebates, on the formulary.[28] Another study of Medicare prescription drug plan formularies found that plans regularly place branded drugs on lower tiers than their lower-cost generic competitors, with 72% of Medicare Part D formularies on at least one occasion assigning a lower cost-sharing tier for branded products compared to multisource generic medicines.[29] This may be due to the perverse incentives created by rebates: Plans may prefer the higher-priced branded version of a drug because it offers a large rebate, rather than its generic equivalent that offers no rebate. Beyond rebates, PBMs often charge manufacturers administrative fees that are calculated as a percent of a drug's list price, providing additional incentives for PBMs to prefer higher-cost drugs over lower-cost alternatives.

Such practices lead to significant distortions when higher-priced, rebated medicines are favored over cheaper alternatives such as authorized or multisource generics. Among the PBMs that typically set and oversee such formulary practices, the top three control nearly 80% of retail prescription claims in the U.S.[30] Such market power, coupled with a lack of transparency about the actual costs of producing generics, gives PBMs significant pricing clout.

IMPLICATIONS AND POTENTIAL SOLUTIONS

Overall, generic medications continue to save the U.S. health system money—an estimated $330 billion annually—but growing evidence shows U.S. consumers and employers, as well as the government, often overpay for generics as the big PBMs and their affiliated insurer companies game opaque and arcane pricing practices to increase their profits.

Generics accounted for 90% of U.S. prescriptions but only 18% of drug expenditures—and about 3% of all U.S. healthcare spending in 2020.[31] While generics represent a relatively small share of U.S. healthcare spending, market distortions and business practices that prioritize higher intermediary profits over lower system costs result in patients paying billions of dollars in higher out-of-pocket costs for generics as purchasers essentially sanction and pay inflated prices that may be 13% to 20% too high, according to a recent analysis of Medicare claims for the most common generic drugs.[32] The bottom line is that many patients are simply overpaying for generic drugs as middlemen profit from lack of price transparency and supply chain inefficiencies.

Current PBM and insurer practices also may contribute to quality issues and care fragmentation. Cash-only pharmacies like Blueberry Pharmacy and Mark Cuban's Cost Plus Drug Company that cut out middlemen, and entities like GoodRx that offer discounted prices, enable patients to save money by paying cash rather than using their insurance to fill generic prescriptions. While just 4% of U.S. prescriptions filled in 2020 were paid in cash, 97% of these were for generic drugs.[33] Patients who pay cash generate no claims data, threatening an important information source for care coordination.

The Hatch-Waxman bargain struck nearly 40 years ago was predicated on the widespread availability of low-cost generics once branded patents expire. Importantly, removing inefficiencies and lowering prices in generic markets will not affect returns on investment in developing new drugs because the savings will come from downstream middlemen rather than drug innovators. Thus, future innovation will likely be unaffected.

Policymakers and purchasers should consider how to foster greater price transparency across the generic supply chain and how to spur generic industry competition and deter anticompetitive practices so that patients can continue benefiting both clinically and financially from generics.

GENERICS ACCOUNT FOR:

90%	18%	3%
OF U.S. PRESCRIPTIONS	OF DRUG EXPENDITURES	OF ALL U.S. HEALTHCARE SPENDING

But many patients are overpaying for generic drugs as intermediaries profit from lack of price transparency and supply chain inefficiencies.

POSSIBLE POLICY APPROACHES FALL INTO TWO CATEGORIES:

1. Policies to Regulate PBM Commercial Practices

- **Restrict rebate contracting** to remove financial incentives for a PBM/insurer to cover a branded medicine instead of its less expensive generic version.
- **Require formulary tier placement of generics to reflect total cost to the health system.** Such an approach would make formularies do what they were originally intended to do—steer patients toward lower-cost alternatives, rather than steering them toward higher-profit alternatives.
- **Require transparent PBM reporting** that enables regulators and others outside the industry to see where the money flows in generic drug transactions.
- **Require PBM contracts to use fixed fees per transaction** rather than calculate fees as a share of drug costs, which creates incentives for PBMs to prefer higher-cost drugs.

2. Policies to Improve the PBM Market

- **Reexamine the PBM market from an antitrust perspective.** Consider breaking up dominant players and reducing concentration in horizontal market segments and in self-dealing vertically integrated corporate structures.
- **Impose fiduciary requirements on PBMs and insurers,** forcing them to act in the best interests of patients and clients rather than solely in the interests of their shareholders.
- **Provide audit rights for employer and government purchasers** to determine actual prices paid by PBMs and insurers to pharmacies.
- **Encourage transparent pass-through PBM models that operate with a commitment to cost transparency.** Instead of using tactics such as spread pricing, rebate retention and clawbacks that are designed to obfuscate a PBM's actual costs, transparent PBMs disclose their actual costs to clients.[34] A transparent PBM commits to passing through all discounts and rebates received to the health insurance carrier and earns its revenue by charging straightforward administrative fees to the carrier, often structured as a flat fee per prescription.
- **Encourage a transparent, competitive cash market for low-cost generic drugs, and let consumers decide whether to fill their prescriptions using insurance or cash.** The economic case for insurance is strongest for large, unpredictable expenditures. Most generic drugs are low cost, and many treat chronic conditions, so their usage is highly predictable, meaning there is little economic rationale for insuring them. A robust, competitive cash market would require that pharmacies be protected against retaliation from PBMs so that posted cash prices reflect their true, competitive costs. It would also require implementing alternative systems to track patient adherence, drug interactions and other elements of care coordination for patients who pay with cash. If a competitive cash market were available, some health plans could even decide to eliminate low-cost generic drugs from coverage altogether. The savings could be used to fund accounts from which beneficiaries could pay for prescriptions purchased with cash. The costs of most such prescriptions in a competitive cash market would be modest: Among the 184 most commonly prescribed generic drugs in Medicare Part D in 2018, 90% could be purchased at Costco for less than $20 for a 30-day supply.

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The Biopharma Patent Cliff: 9 Drugs Losing Exclusivity by the End of 2023

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Pictured: Series of outcroppings with steep cliffs down to the ocean/iStock, ***honster***
The biopharma industry has been creeping over a **patent cliff** for months, with several drugs losing their primary patents and more patents expected to expire in the next seven years. This opens the door for new generics to enter the market, lowering drug prices and therefore reducing how much manufacturers can rake in from brand name products.
Maria Whitman, global head of ZS Associates' pharmaceutical and biotech practice, **previously told** *BioSpace* that drugs going off-patent could impact between up to 79% of a company's revenues. Drug prices go down any time a new generic becomes available, but the impact may be more pronounced around patent cliffs. One **analysis** found that the steepest price declines for brand name drugs between 2008 and 2014 occurred when the first three generics were introduced.
Not every company will experience this decline in the same way. For example, Eraxis, an antifungal drug owned by Pfizer, is expected to lose its exclusivity in September. But loss of exclusivity probably won't have a major impact on the company, said S. Sean Tu, a law professor at West Virginia University and affiliated faculty at Harvard Medical School's Program on Regulation, Therapeutics and Law.

"Even if a lot of generics [for Eraxis] went on the market tomorrow, I don't think it would hurt Pfizer's bottom line. They have a pretty diverse portfolio," Tu told *BioSpace*.
Smaller companies like Eiger Pharmaceuticals may have more to lose. The company has one commercial product, Zokinvy, that will start losing exclusivity soon. In **SEC filings**, Eiger warns investors that it may never be profitable.
Just because the primary patent for a drug expires, it doesn't automatically mean other companies are free to start marketing generics. For example, AbbVie **filed hundreds of patents** for its biologic drug Humira, preventing other companies from producing generic adalimumab. It was only after a 2017 **settlement** that Amgen was able to start marketing biosimilars overseas, and eventually in the U.S. in January of this year. Then, last month, a flood of new Humira biosimilars **hit the market**.
Owning multiple patents for a single drug, what's known as **patent thickets**, help drug companies make up for lost time and costs during the FDA approval process, according to Tu. However, more companies are relying on them to limit competition. A **research letter** authored by Tu and others found that recently approved drugs have more patents filed and more patents litigated compared to older drugs, leading to delays in generics entering the market.
Here are some drugs that may see generic versions enter the market soon.

1. **Takeda's Vyvanse, Aug. 24**

Vyvanse (lisdexamfetamine dimesylate) is an oral amphetamine used for attention-deficit hyperactive disorder. New River Pharmaceuticals filed a provisional application for the drug **in 2003** and the patent was issued in 2007. It was eventually **acquired** by Shire and **later** Takeda, bringing in **$2.52 billion** for the Japanese company between March 2021 and 2022. The patents covering adult indications of Vyvanse **expired** on Feb. 24, and those for the pediatric indications are due to expire Aug. 24. As of July 31, there were 12 tentative approvals for Vyvanse generics, with some issued as early as **2014** and others as recently as **June 14, 2023**. Companies looking to market these generics include Teva, Mylan and Sandoz.
Tu predicted that the breadth of Takeda's portfolio would minimize the impact of the loss. Indeed, a **financial forecast** filed by the company July 27 says that growth and launch of new products are "largely offsetting" the impact of losing Vyvanse's exclusivity.

Saxenda brought in **$1.5 billion** in 2022, and the weight loss drug's main patent **expired** in February of this year. Novo sued **Orbicular Pharmaceutical Technologies** and **Sun Pharma** in 2022 for attempting to market generic versions of the drug.

Novo still maintains a stronghold in the diabetes drug industry with Ozempic, which has also **lost patents** but likely won't see generics until 2031. Ozempic sales will likely offset any losses from Victoza and Saxenda; the former **brought in** $2.9 billion in the first quarter of 2023, compared to $415 million for Victoza and $483 million for Saxenda.

Mr. SCHWEIKERT. Thank you, Mr. Chairman.

This is an area that we have been actually very interested in in our office and have spent a couple of years looking on. I am going to run through a couple policy things, and I have a fascination with Civica. I have actually done a couple of floor speeches about your model and some of the things you are doing.

One of the things I want to walk through is, Mr. Chairman,—I am going to submit a series of articles here that make it very clear that many of the small molecules, combination molecules, precursors could not actually right now get permitted to manufacture in the United States because they produce really, really toxic byproducts.

A series of articles talking about why certain chemotherapies were coming out of India. The fact of the matter is we almost don't have a disposal mechanism from the toxic byproducts. So this may be something the left and the right could actually talk about is, if you care about the shortage of these supplies, we need to understand why you don't make them here. And they produce some really nasty stuff, and we need to understand that.

Mr. Chairman and Ranking Member, a couple of the other things also in here is there is a revolution going on out there in pharmaceutical manufacturing. And I am going to submit some articles about everything from three—high-speed 3D printing now making certain small molecule drugs, making it so you no longer need a very, very expensive clean room, you can do the cartridges; discussions about new ways to make insulin.

There also are the economic models. And our friend from Civica here, you are now making, what is it, eight types of generic insulin?

Mr. COUKELL. Thank you, sir. We are developing the 3 types of insulin that account for about 80 percent of use in the U.S.

Mr. SCHWEIKERT. And one of the articles I had was saying eight.

Mr. COUKELL. It is three. It is insulin, glargine, Aspart and Lyspro, and we will make those available in both vials and prefilled pens.

Mr. SCHWEIKERT. So, if I come to you and buy five vials, my price is what?

Mr. COUKELL. What we have said is it will be available to the consumer, including all of the supply chain and dispensing costs, for not more than $30 a vial.

Mr. SCHWEIKERT. And 55 for the——

Mr. COUKELL. Fifty-five dollars for five pens.

Mr. SCHWEIKERT. So that is actually cheaper. And this is the point I wanted to make, because I did this as a floor speech. We, right now, as a government, we give $16 billion a year to Big Pharma to buy down the price of insulin. This was a Democrat bill, $16 billion to Big Pharma to buy down insulin when they are going to do it cheaper than a subsidized price. Maybe we need to really think about this co-op model, these new manufacturing methods, and the ability to do it better, faster, cheaper.

Sorry, there are just so many things here on the supply chain.

Would actually Civica ever consider going into something such as the chemotherapies, which actually do have other real complica-

tions, particularly you would probably have to find some way to have a high-temperature incinerator for the throw-off chemicals. Is that something you would consider?

Mr. COUKELL. Absolutely, and thank you for the question. So let me answer it in two parts, and I will be quick.

One is all of the elements of our model now in terms of carrying a buffer stock, vetting our manufacturing partners, having long-term purchase and supply contracts could equally be applied to cancer drugs. And we are actually looking at that now. If we were to manufacture them in our own bricks-and-mortar facility, you would need a dedicated facility for that because the cytotoxic drugs do require special procedures and air handling, and so on. So that would take an additional capital investment over and above, you know, what we have invested in the current facility.

But it may be in the long run that we say in the U.S. these drugs are too important not to have such a facility.

Mr. SCHWEIKERT. Thank you. You actually got—you stole my punchline from me.

Mr. Chairman and fellow members, if I came to you right now and said in the United States off-patent, generic drugs, are they more expensive or less expensive than the rest of the industrialized world—I have a paper here that says they are 16 percent less expensive in the United States. So you actually have this interesting thing, where we actually have a fairly competitive model. The non-patented—the non-labeled were actually less expensive here.

If we could actually work together to deal with the difficulties in the manufacturing side and also embrace the fact that there is a revolution coming in even the manufacturing process, maybe you could actually create a new renaissance where the discussion of a shortage and pricing just never comes up again.

And, with that, I yield back, Mr. Chairman.

Chairman SMITH. Mr. Blumenauer.

Mr. BLUMENAUER. Thank you, Mr. Chairman. I find this hearing fascinating, and I want to follow up on my colleague from Arizona's conversation about Civica.

I was struck by how you outlined a proposal that—specifically to address the Generic Sterile Injectable drugs, non-profit, non-stock, founded by U.S. health systems and philanthropists.

I am curious as to what the problems are for a broader application of this model. It seems to me that there are huge costs that we are incurring now in terms of disruption of treatment, misallocation of costs that seem to benefit nobody. Can you describe what the limitations would be to expand your non-profit, holistic, long-term approach to this supply problem?

Mr. COUKELL. Thank you for that question, sir. We certainly aim to continue expanding our model, adding hospitals, adding drugs, and so on. Whether we are doing these—I will call them Civica-like practices, buffer inventory, supplier qualification, and so on—inside a non-profit model or inside a for-profit model by some of the existing supply chain stakeholders, I think the friction is the same, which is right now the system is driving towards one thing which is not valuing sort of resiliency of the supply chain.

So we have to switch those incentives. And I think that will allow the Civica model to expand and grow, but also allow other supply chain entities to step in and have similar practices.

Mr. BLUMENAUER. Well, I am curious about what the limitations are to expanding it. It seems to me that the long-term costs are ultimately higher by having the inefficiencies that we have described. Is there some reason we can't employ this through CMS or other Federal agencies to be able to take your model to scale?

Mr. COUKELL. No, I think we absolutely can and should, and I think—I am not an economist, but an economist might say that the stakeholders right now aren't putting a value on those long-term indirect costs. And so, essentially, what we have to say is we are willing to pay a bit more not to have those indirect costs associated with shortages.

Mr. BLUMENAUER. Mr. Chairman, the American consumer pays the highest prescription drug prices in the world. Most of the manufacturing is in China or India. The profits are booked to Ireland, and the taxpayer doesn't get the benefit.

But Americans are the largest market for this, and it seems to me we are missing the bet if we do not rigorously approach efforts that are modeled on a non-profit, longer-term initiative and consider the totality of costs.

In the long run, we are going to end up paying an inordinate price for the inefficiencies, the misplaced profits, and the problems for treatment, which can have disastrous consequences. And I would hope that there is an opportunity for us to take a step back and look at this model, which appears to be delivering results in a way that we all should embrace and think about ways to expand the sweep of it, rather than what we are doing now, where the American consumer ends up paying more, less overall benefit at a time when we desperately need to get more out of the system.

I appreciate this hearing. It was fascinating, looking at some of these models and thinking about the costs and consequences, and I hope we will get to a point where we can look at the overall approach and be able to determine better quality of service, lower overall costs, and better performance for American patients.

Thank you, and I yield back.

Chairman SMITH. Thank you.

Mr. LaHood.

Mr. LAHOOD. Well, thank you, Mr. Chairman, for having this hearing today. I want to thank the witnesses for your valuable testimony here today.

The title of today's hearing, "Examining Chronic Drug Shortages in the United States," is real and it is acute. And, like many of my colleagues, I have heard directly from my constituents on the issues of persistent drug shortages and the ramifications and challenges that affect them and their loved ones.

I have a district that has a lot of rural territory, and timely access to lifesaving medications is essential to safeguarding patient health.

During my time in Congress, I have had the great pleasure of working with an organization in my district, Illinois CancerCare, ILC, which is a foundation with locations throughout most of the rural parts of my district and specializes in the treatment of pa-

tients with cancer and blood disorders. ILC is currently having an incredibly difficult time locating a supply of Rydapt, which—they have three patients suffering from acute leukemia requiring this medication. ILC is spending countless hours calling specialty pharmacists to ask about their supply chain, and the frustrations with coordinating with the patient's prescription insurance to allow for out-of-network overrides has been significant, and ensuring timely shipment to avoid potential delays. These patient stories showcase why reducing drug shortages is of paramount importance.

I have a question for Dr. Schleicher. As I mentioned, cancer patients are being forced to possibly delay treatment because the drugs they need are in short supply. Are there potential disparities between patients being treated for cancer at a facility in a rural area, compared to a more urban area?

Dr. SCHLEICHER. Thank you very much for the question, Congressman.

My concern is potentially yes, especially with some of the suggestions about really emphasizing hospitals having these drugs. Obviously, there is an importance for hospitals, but also a lot of these community oncology practices like the one you are mentioning in rural America are not part of a hospital.

And, where we practice, Tennessee Oncology is very similar to the practice in Illinois. We have 35 clinics. Most of them are rural. We help cover hospitals, but we are not part of a hospital system. So we deliver the treatment in our treatment rooms where patients live. And, if hospitals get a drug, then that means we will not if there is a limited supply. So, to that point, we need to make sure that any solutions don't further exacerbate disparities based on where patients live.

Or, in our case, we take all the uninsured patients in the state. One of our large hospital systems, which is actually a 340B, doesn't see uninsured or even Medicaid patients in the outpatient. So, if we were not able to have those drugs, patients would, one, not be able to get them close to home; and two, certain patients, either without ability to pay or insurance status, would be unable to get them, as well.

Mr. LAHOOD. Thank you for that answer. I am going to pivot now to another focus, which is supply chains and the dependency on foreign countries.

Between this committee and the Select Committee on China, which I also serve on, we regularly discuss our global economy and the geopolitical challenges we face, and it is important for this committee to explore proactive measures to address the underlying causes of drug shortages and strengthen medication supply chains that are imperative to ensuring continuity of care and promote overall health care resilience.

It is no secret that the U.S. drug supply is heavily dependent on foreign suppliers. I share the concerns of many of my colleagues as it pertains to the CCP, Chinese Communist Party, and allowing them to operate under a different set of rules and standards, which they do. Our allies around the globe are craving U.S. leadership in this space. It is important that we step up to the plate and find ways to support American businesses looking to prioritize more domestic drug manufacturing.

I have been proud to work—I am proud of the work that we have done with this Congress to identify instances of malign activities and practices by foreign countries like China that leave the U.S. more vulnerable, but we need to do more and do it quickly.

I will now turn to Dr. Schondelmeyer. Can you provide an example of unfair trade practices that foreign countries, particularly China, use to undercut American drug manufacturing?

Mr. SCHONDELMEYER. Thank you for that question.

China, over time, has developed policies as a government about sectors of the pharmaceutical market that they want to enter and, in fact, dominate. They subsidize the companies that are involved, they develop the infrastructure hubs, or they have whole areas larger than the D.C. area that are manufacturing products. So they subsidize them.

Then they at times engage in predatory pricing or even dumping of product in the market to drive other players out of the market. And one category of drugs that particularly China dominates is the fermentation antibiotics. About 80 percent of the antibiotics in the world are produced in China. And so, if they went out of the market, or if there was a nuclear power plant in the middle of the three or four companies that make those antibiotics and we had a Chernobyl incident, we wouldn't have antibiotics, and it would—yes, Civica and others could make antibiotics, but they can't do it tomorrow, they can't do it next year. We are talking years down the line to develop the capacity to replace that.

So China has used a number of tactics, clear strategy, investing in infrastructure, predatory pricing, and dumping in the market.

Mr. LAHOOD. Thank you for that.

I yield back.

Chairman SMITH. Mr. Pascrell.

Mr. PASCRELL. Good morning, Mr. Chairman.

Chairman SMITH. Good morning.

Mr. PASCRELL. To our witnesses, a great group of witnesses this morning. I can think of few subjects that are more important than easing access to lifesaving medicines.

Americans received terrific news last week that the Medicare has begun its historic negotiation to lower the price of 10 popular drugs. And that will go on each year. Starting September the first, our seniors will see price cuts for those drugs. Similarly, the cost of insulin is now capped at $35 for millions of Americans, thanks to the action that we took.

We want to bring safe, plentiful, and less expensive prescription drugs to Americans. I think that is all of our goal. Congress has a big role in protecting these medicines, and that includes addressing the shortages, which we spent a lot of time on this morning.

The testimony today should upset a lot of us, that science, research, and industry has come so far to create lifesaving medicines, yet gravely ill patients might be denied access because of shortages. And that is just unacceptable, I hope, to all of us.

In the wake of the COVID pandemic, we recognized the dire need for America to fix our supply chains. And we did it. We have a lot more to do. For too long, our nation has been relying on other countries for raw materials, big and small. Domestic manufacturing is a key to unlocking our supply chain challenges. We have made im-

portant changes. We have brought jobs and technical capacity back home. That is a little progress. But we are running out of cancer medicines. We just simply are. And we have not made enough progress here on our home front. And when we still rely on China for so much, we have a lot of work to do.

So Mr. Ballreich, thank you for your work at Johns Hopkins. Your written testimony is very instructive to me. I could speak for myself. You cited a cancer drug manufacturer who relied on a plant in India that was red-flagged by the FDA. It sends me back to 15 years ago, when we debated here, when we debated the question about drugs from Canada being properly researched, studied to see if they were pure. A lot of folks from the Midwest bought those drugs quickly because they were cheaper. But we did not know, really, the quality. Do you remember that? I remember it like it happened yesterday.

So how much should Americans be concerned about the quality of the medicine coming from overseas right now?

Mr. BALLREICH. Great question. I think the Americans should not necessarily be concerned. We have an excellent FDA.

That being said, medicines being sourced overseas, it does represent a susceptibility to supply chain. The FDA is under tremendous stress to make sure all of the parts of the supply chain are thoroughly inspected. You know, using FDA's own inspection citation research database, it is a little scary to actually see how many facilities are cited, how many facilities have inspections. And this is part of the whole transparency aspect.

As a researcher, I rely on data to understand the situation. There is a lack of transparency. More transparency will give us better information.

Mr. PASCRELL. I want to get in one more question before it is time out.

Mr. BALLREICH. Ah, yes, please.

Mr. PASCRELL. You argue that most of the—this is what you say in your testimony, that most of the shortages are the product of manufacturers themselves. Well, can you expand on that? What does that mean?

Mr. BALLREICH. Yes.

Mr. PASCRELL. What are you trying to tell us?

Mr. BALLREICH. So most are quality issues. Companies are not necessarily incentivized to invest in their supply chain, to invest in their quality. As it has been noted, generics, they compete on price. You know, companies that procure generics generally want to find the generic at the cheapest cost. That does not incentivize that generic company to invest in additional capacity. It does not incentivize that generic company to have thorough oversight of their quality.

So, if you are just competing on price, lower cost means you have a better market position.

Mr. PASCRELL. Thank you.

Thank you, Mr. Speaker.

Chairman SMITH. Thank you.

Dr. Wenstrup.

Dr. WENSTRUP. Thank you, Mr. Chairman, Ranking Member Neal, and all those that are here today. I appreciate you being here

to examine this problem that we are experiencing in the United States of America. This has been an issue for me for probably five years, and certainly the pandemic has highlighted and exacerbated this tremendously. So I really appreciate the testimonies here today.

These drug shortages, these vulnerabilities in our supply chain, they put our national security at risk. They put our national health security at risk. I am a soldier. I served in Iraq. If you would have told me that my protective equipment and my pharmaceuticals relied on an adversary, China, I would say, "How in the heck did we get here? How did our military get here?"

This is a huge problem, and I think it is underestimated, and we are late to the game in discussing it, but I am glad that we are. Right now in the United States, there are 252 drugs in shortage, lifesaving drugs: albuterol for asthma, chemotherapy drugs. This is serious, serious stuff for the United States of America, and our vulnerability is huge right now.

And the bottom line up front is we have an over-reliance on foreign manufacturers. That is the bottom line. And in many ways, we have regulated our way there.

I would tend to disagree with what was just said about our FDA. I am not trying to slam them, but, if they are not in those labs in China, and especially since the pandemic, it is a problem, you know, and so we will talk about not only the quantity of medications available that is the problem, but the quality of medications available.

I have served in the Reserves for 25 years, I just retired last year. And, before I retired, I was in uniform and in my administrative position. I was clinical at Walter Reed. My administrative position I had the opportunity to work with the defense logistics medical supply chain counsel, working to reduce or eliminate our supply chain challenges, what they are, how severe the risk is, why there is a risk, and how they can start to do it. But they can't do it without us. We cannot turn this around unless we make some changes here in the United States, whether it has to do with regulation or not. But the risk is there. And these are essential medical products.

So it is not only domestic, but it is geographic. Puerto Rico does a tremendous job in supplying many of our medical supplies. They have two hurricanes, we can't get saline here. That is a problem. So it is not only the ability to have the capabilities and opportunities to do it here, we can't just have it in one place. We have to have a diverse supply chain.

And working with our allies is fine with me too, but certainly not relying on an adversary. Because the problem is it is just like that in a darker day, they cut us off. And as the CEO of a generic manufacturer in Europe said, "If China cuts us off, our supply chain—our shelves are empty in two months." That is a quote.

So today, I plan to release a discussion draft of legislation I have been working on for years. And I want to start with our critical battlefield medicines, and provide new, powerful incentives to locate manufacturing of these medical products in the United States, all the way down to the Active Pharmaceutical Ingredients. And I look forward to officially introducing this bill. I hope my colleagues

on this committee will join me. Take a look at it, offer any advice you may have to it, and I hope it serves as a template to go across the board to serve all maladies, not just in the battlefield.

Dr. Schondelmeyer, can you describe as best you can the degree to which our supply chain for drugs is dependent on foreign sources, both quantity and quality?

You know, I would like to remind people it wasn't maybe 15 years ago we had 250 Americans die from tainted heparin. Right? And the opportunity for sabotage is there. There are all types of things we need to be concerned about as we go forward.

Mr. SCHONDELMEYER. I have commented several times about the quantity; quality is an important issue. And as you pointed out, the heparin, more recently we have had eyedrops come out of India that were contaminated and caused people to lose their eyes or even die because of that. We have had baby formula contaminated with bacteria that caused some deaths of babies using baby formula. I think quality is a major concern.

And remember, I said that India is responsible for 45, 50 percent of all the generics that come to the U.S. India does not participate in the International Council on Harmonization of Drug Regulation. The US does, Canada does, Mexico, Europe, most major westernized countries participate in that group. India does not. We, as a country, should not continue buying product from India. We should leverage them to participate in that conference that will improve the quality of their products. And that is one example of ways of leveraging them. So we need to be concerned about quality.

Second, we have had several people comment about we are going to have to pay more for generics. I agree with that. But you don't indiscriminately pay more for all generics, because some companies will continue to free-ride on that and take the higher price and keep cutting the cost.

So we need quality measures that are specific, that are product-specific, producer-specific, and reliable, and then we can pay more for the companies who meet those criteria.

Dr. WENSTRUP. Thank you, and I yield back.

Chairman SMITH. Thank you.

Mr. Kustoff.

Mr. KUSTOFF. Thank you, Mr. Chairman. Mr. Chairman, I seek unanimous consent to enter into the record Saint Jude Children's Research Hospital's statement on their perspective on the impact that chronic drug shortages have on the treatment of pediatric cancers.

Chairman SMITH. Without objection.

[The information follows:]

Statement for the Record of

St. Jude Children's Research Hospital

for the

Committee on Ways and Means

U.S. House of Representatives

"Examining Chronic Drug Shortages in the United States"

February 6, 2024

St. Jude Children's Hospital (St. Jude) submits this Statement for the Record to share its perspective on the impact that chronic drug shortages has on the treatment of pediatric cancers. As one of the largest pediatric cancer research hospitals in the world, St. Jude is leading the way the world understands, treats and defeats childhood cancer and other life-threatening diseases. Treatments developed at St. Jude have helped push the overall survival rate for childhood cancer from 20 percent when the hospital opened in 1962 to more than 80 percent today. Consistent with the vision of our founder, Danny Thomas, no child is denied treatment based on race, religion or a family's ability to pay.

St. Jude writes to share our sentiments on the ongoing childhood cancer drug shortages, especially generic sterile injectables. While the childhood cancer community has been experiencing oncology drug shortages for more than a decade, today's shortages may be the worst we have seen. These shortages are caused by an array of factors, including quality issues, manufacturer business decisions, disruptions to raw ingredients and excipient supplies, and natural disasters and other emergencies that take place in countries that house critical drug manufacturing facilities.

Like other hospitals, St. Jude pharmacists and other clinicians can often mitigate the patient care impact of shortages, such as identifying alternatives or compounding medications if the formulation we need is not available. Over the last several years, these mitigation activities have become increasingly more challenging leading to an increased risk of medication errors and patient harm. However, curing children with cancer represents a different challenge. Elaborate chemotherapy regimens that cure children have been developed based on decades of evidence from clinical trials. Some of the serious shortages over the last year, such as methotrexate and cisplatin, are essential curative chemotherapies for children with cancer. Unfortunately, these chemotherapy agents do not have effective alternatives.

Resilience in the generic sterile injectable drug supply must be developed. Because generic sterile injectable shortages occur for many reasons, multiple policy interventions will be needed so hospitals like St. Jude can focus their efforts on caring for patients instead of procuring drugs in short supply.

Thank you for your leadership on behalf of children with cancer. St. Jude welcomes the opportunity to further discuss the unique challenges of childhood cancer drug development and research. Should you have any questions or need additional information, please contact Dr. James Hoffman, Senior Vice President – Quality and Safety and faculty member in Pharmacy and Pharmaceutical Sciences.

Mr. KUSTOFF. Saint Jude Hospital, which is located in Memphis, Tennessee, is one of the world's largest pediatric cancer research hospitals in the world. The statement they are submitting into the record discusses the current childhood cancer drug shortages, especially the Generic Sterile Injectables.

Saint Jude believes that resilience in Generic Sterile Injectable drug supply must be developed to ensure that they can continue to focus on their efforts to care for and treat their patients, rather than procure drugs in short supply. Thank you, Mr. Chairman.

If I could, Dr. Schleicher, thank you. Thank you to all the witnesses for appearing today. Dr. Schleicher, I represent part of Memphis, Tennessee, in west Tennessee to the west of you. And, if I could, I would like to read a portion of a column written by Dr. Sylvia Richey. You may know her. She is the chief medical officer for the West Cancer Clinic that is in Memphis or Germantown, Tennessee. This is a column, or part of it, that she wrote on May 28, 2023, in the Daily Memphian. And I do this because you gave us similar stories about your patients.

She says, in part, "Cancer patients throughout the country are dependent on chemotherapy drugs for their lives. And now there is a nationwide shortage of two drugs that are the backbone of many cancer treatments. Many of these treatments are for cancers that are curable," what you said, "and we don't want to miss those opportunities. This shortage is causing oncologists to make difficult decisions." That is similar to what you talked about. "Treatments are being skipped and delayed, doses are being reduced. Treatment plans are being changed and sequences of usual treatments are being altered. Doctors should never have to put their patients in these situations. Oncologists are literally rationing chemotherapy."

You know, you gave the story about the two patients from your clinic. Where we are today, February of 2024, is it any different or any better than during the height of COVID?

Dr. SCHLEICHER. Yes, thank you very much, Congressman Kustoff, and I know Dr. Richey well.

So it is different drugs now, but it is not over. Cisplatin and carboplatin were the big ones that hit us last summer. I know seven patients at our group in the last, you know, few months with CNS lymphoma for which their treatment was delayed, awaiting another generic injectable, methotrexate.

Vinblastine is commonly used in Hodgkin's lymphoma, which is very curable. We thought we were going to run completely out about three weeks ago, and then ended up getting a supply. And again, in hindsight, we got a supply, but week by week we actually thought we were going to run out and have to figure out a plan.

I heard just last week sandostatin, another drug used for carcinoid tumors, is running out right now, as well. So the carboplatin and cisplatin were so common and they are in so many regimens that that was a big hit, and it was the first that I have ever experienced.

But it is not over. Still, three drugs just in the last few months we are still having problems with.

Mr. KUSTOFF. Thank you, Doctor.

Dr. Schondelmeyer, if I could with you, thank you for appearing today. Dr. Richey, in her column that I just cited a moment ago,

I think this is her closing line and I wanted to ask you about it because we have been talking about solutions. You all have suggested solutions. You have talked about the different countries that we are relying on, and maybe ways that Congress can alleviate.

But let me ask you about the last statement in Dr. Richey's column: "We need the FDA and the White House to focus on reliable manufacturing of generic drugs, and making sure the American people have access to the treatments that they need when they need them." So my question to you is, in the very short term, are there things that the FDA and the White House could do today?

Mr. SCHONDELMEYER. Yes, I think there are.

First, though, I would remind us that we need to look at what has FDA been authorized to do and appropriated to do by Congress. And, to the best of my knowledge, their authorizations don't include looking at economics or the market for pharmaceuticals. And we may want to delegate that to other agencies other than the FDA, and that could be done.

There are some things that have already been done, not necessarily by FDA, but by various administrations, both the current and previous administrations. They funded Flow Pharmaceuticals to make API for 25 critical drugs needed in the U.S., and they are working on that. They are making, I don't know how many, 7 or 8 so far, and they will make 25, and that has been supplemented by funding from the state of Virginia.

Civica, of course, we have heard about, and that was by hospitals and players from the market who came up to provide drugs.

And then in Missouri, there is an API innovation center that was funded by the State of Missouri for development, to develop an industry to produce API in the State of Missouri, and to do just what we have been talking about, reshoring.

So there are—we could continue, but we need more than just Flow and API and Civica. We need 4 or 5 or 10 of each of those, not just one of each of those.

Mr. KUSTOFF. Thank you, Doctor.

Mr. Chairman, I yield back.

Chairman SMITH. Thank you.

Mr. Davis.

Mr. DAVIS. Thank you, Mr. Chairman, and let me thank you for this hearing. I also want to thank all of our witnesses.

Your expressions and answers have been so informative. And, as I listened to Dr. Wenstrup a moment ago, it just reminded me that this is Black History Month, and I am reminded of a song that a woman named Billie Holiday used to sing. The lyrics went sort of like this. "Them that has got shall get. Them that has not shall lose. So the Bible says, and that still is the rule. Mama may have, Papa may have, but God bless the child that has got his own."

And, given the impact and the influence that China, India, perhaps even other countries may have on the production, control, and distribution of what we need, I am ready to join with Dr. Wenstrup with the legislation that you have got ready to go, because all of the other things that we discussed and talk about, are they really solutions or are they the solutions that we need?

And I am convinced that no matter how long it takes, how much it costs, that we need to be in the business of producing more of what we need.

But, Dr. Coukell, one of the solutions that people are talking about now and that are being proposed by stakeholders is a buffer stockpile, where manufacturers of—and hospitals would maintain a six-month supply of a product and receive some type of add-on payment or other incentive for maintaining stockpile. So it is stockpiling. What do you think of that as a possibility, or a way of alleviating some of the problems?

Mr. COUKELL. Thank you for that question, sir. I think we need a stockpile, and I will tell you why.

Even if we have got four companies making versions of the same drug, if one of them drops out of the market by choice, or because they have a quality problem, it takes the rest time to increase their production and generate additional batches. And, if we don't have a buffer stock, we will have a shortage. And so having that additional stockpile buffers and allows the market to respond so we have continuity of supply through that.

I don't think it should sit at the hospital level. I think it should sit upstream at a wholesaler or at a manufacturer, and that allows for much more efficient allocation. And the provider, you know, is not set up to manage a six-month inventory, but that exact approach, I think, would take us a long way towards resilience.

Mr. DAVIS. Thank you—yes.

Dr. SCHLEICHER. Just to add to that comment, and thank you for the question, I similarly would be concerned if hospitals were stockpiling, only because that could worsen shortages at non-hospitals if it is at the provider level. And, at least in our market, we are usually the provider in rural America, and that would hurt access for our patients.

And I mentioned some of the insurance issues beforehand.

Mr. DAVIS. Thank you very much. I was thinking specifically of rural America and the challenges and difficulties in those areas.

Thank you very much, Mr. Chairman, I yield back.

Mr. SMITH of Nebraska [presiding]. Thank you. I will next recognize Dr. Ferguson for five minutes.

Dr. FERGUSON. Thank you, Mr. Chairman, and thank all of you all for being here today. It is a shame on topics like this we only get just a few minutes to delve into it.

But it seems that we have—and I say we, America—has three major failures in what we are talking about today: one of them is a regulatory failure; the other one is a trade failure; and the other one is a marketplace failure. Okay?

So, as I go through this, I want to touch on each of those in the beginning, but I also want to do it with the notion that, no matter what we do as a nation, when we decide to fix something we generally can find a way to do it. We may not always agree specifically. But let's look at the threat that we had to America with semiconductor production, and this body voted to spend a lot of money to make sure that we had access to chip production. And I would think that we might want to consider that in the same vein as it relates to the production of the most basic pharmaceutical products.

But as I go through this, I want to ask each of—you know, a couple of you some specific questions as it relates to the regulatory failure.

Mr. Coukell, if you were going to look at the regulatory environment, give me two things real quickly that if we could change dramatically would have an impact on manufacturing here in the U.S.

Mr. COUKELL. Thank you for that question, sir.

You know, we see the FDA as a key part of ensuring quality across the system. We look to them to identify poor-quality facilities, and we look to their guidance on how to ensure good quality. But they are not often in—especially these overseas facilities—as often as we would like them to be. And so we may have a situation where domestic facilities are getting inspected on a regular basis, but we are not having the insights that we might need on the overseas facilities.

Dr. FERGUSON. Okay. You did not mention the—you mentioned the FDA. What about the EPA? Isn't there an environmental component that, as my colleague from Arizona pointed out, in many cases we can't make some of the very basic things here in America because of the EPA. Shouldn't we be investing in not only the production of that, but technologies that allow us to meet our own regulatory rules here so that we can produce it here in America?

Mr. COUKELL. So we are a manufacturer of finished dosage drugs, so nothing comes out of our facilities except finished dosage drugs. There are no waste products.

Dr. FERGUSON. Yes.

Mr. COUKELL. But, if you are making API, that is essentially a chemical plant, and there are waste products. And several witnesses and members today have talked about continuous manufacturing of API, which is a newer technology for API which produces much less waste.

Dr. FERGUSON. Yes, all right——

Mr. COUKELL. And so in terms of bringing it back, that may be the future for the U.S.

Dr. FERGUSON. So there is a regulatory component.

I mentioned a trade component. Dr. Schondelmeyer, two things. With trade, can you speak to how important it is that we protect our intellectual property here in the U.S. and that we create a level playing field with countries that have unfair practices?

Mr. SCHONDELMEYER. Well, certainly, intellectual property is a valuable asset and needs to be protected. By and large, the drug shortage issue isn't centered around intellectual property issues, however. It may be an issue on the brand name product sides and products like Ozempic, Wegovy, and Zepbound.

But on the drug shortages, remember, those are largely generic and sterile injectables. So intellectual property isn't the major issue in that component.

Dr. FERGUSON. Okay.

Mr. SCHONDELMEYER. But there are plenty of trade issues that do affect drug shortages.

Dr. FERGUSON. All right. You know, we are going to have to come up with some short-term solutions.

Mr. SCHONDELMEYER. Right.

Dr. FERGUSON. And we are going to have to come up with long-term solutions that are going to require investment.

Mr. SCHONDELMEYER. Yes.

Dr. FERGUSON. You know, we have talked about antibiotics. AMR is very important. We have we—you know, the next pandemic could be bacterial—and not viral—in nature. And we have been working in a both a bipartisan and bicameral way to address that with the PASTEUR Act that fixes a marketplace problem, where we are not able to pull drugs into the marketplace. We do the basic research, we do the basic investment, but these are usually done by startups that are strapped for cash, and we don't have a stable marketplace. And the PASTEUR Act fixes that because it is a pull incentive to get it into the market.

Doctor, do you believe that that would be helpful in the near term in developing new antibiotics to fight resistant bacteria?

Mr. SCHONDELMEYER. Yes. Antibiotics are a concern anyway, because we have resistance and issues, and the ones—the antibiotics we have that do work, many of them are made in China and we are in trouble if they put a trade barrier in place, anyway.

So, yes, we must focus on antibiotics, and that does involve intellectual property and stimulation of production in the U.S.

Dr. FERGUSON. Thank you, Doctor. Thank you all of you for your time and expertise.

I yield back.

Mr. SMITH of Nebraska. Thank you. I now recognize Mr. Hern for five minutes.

Mr. HERN. Thank you, Mr. Chairman, for holding this hearing today, and I want to thank the witnesses for being here today to help us better understand the issue we have at hand.

For the past year, I have been getting calls and written messages from distraught constituents that weren't able to get their prescription drugs they needed, everything from ADHD medications to chemotherapy treatments. I can only imagine the distress patients feel when they hear that their treatments could be paused today because of the supply chain issue. As we all know, lapses in treatment can be devastating for patients' health outcomes.

I have also heard from hospitals in my district about the effect drug shortages have had on them. In Oklahoma specifically, they have been dealing with the shortages of clindamycin, one of the few effective drugs against MRSA, and they now have to restrict the use of this injectable. Physicians are having to switch orders to other oral antibiotics, even if it is not ideal for their patient. Not only does this affect daily patient care; physicians now worry about how the overuse of these broad spectrum antibiotics will contribute to antimicrobial resistance. This is a clear example of how having a stable supply of drugs is a public safety issue.

In addition, there is a real concern from hospitals that, if cancer drug shortages continue, they will need to consider triaging patients and no longer treating palliative care patients. What a sad and grim thought that is.

The COVID pandemic exposed how fragile our supply chains really are, and it is clear to me that the drug supply chain is no different. It is extremely concerning that, even as the pandemic ended, drug shortages still do not subside.

As you all have highlighted today, the drug supply chain is complicated, with many different factors able to cause a disruption. We have heard today how drug shortages affect patients, health systems, and the negative effects they have on public health and safety.

I am also curious as to how the drug shortages not only affect those we have mentioned today, but the drug market as a whole.

Dr. Gralow, it is interesting to me how you brought up the topic of clinical trials in the context of drug shortages. How do you think drug shortages affect clinical trials, particularly combination drug trials?

Dr. GRALOW. Thank you for that question.

Well, an example I gave was of a clinical trial that supplied both a standard of care, which was the drug that they were looking for, as well as comparing it to an experimental arm, where we tested would it be better or not. What we found during these drug shortages was most clinical trials didn't cover the standard of care arm, so that option of being able to go in a clinical trial and get the standard of care as one of two choices wasn't available for most.

You asked about combinations. A lot of new agents that we test are built on the backbone of old drugs. So you would test maybe the standard drug plus or minus the new drug. And, if you don't have the standard drug, that trial just gets shut down, you know, because that is covered by standard of care.

So our clinical trials were affected by these drug shortages, paused. Many of them couldn't continue for a while.

Mr. HERN. So these—you know, these could affect—these affect delays, new treatments being brought to the market. And how will this ultimately affect patients who are waiting for these treatments that are so badly needed?

Dr. GRALOW. We need to speed up our trials. We need to get our promising new therapies tested and, if they are effective, out to the patients as soon as possible.

So in these cases, the drug shortages can delay the evidence that is required to determine if a drug should be approved and if it is better than something prior. So it is also holding back research.

Mr. HERN. Thank you for your thoughtfulness.

And Mr. Chairman, I yield back.

Mr. SMITH of Nebraska. Thank you, Mr. Hern. I now recognize Ms. Sánchez for five minutes.

Ms. SÁNCHEZ. Thank you. I want to thank the chairman and Ranking Member Neal for holding this hearing on a very important issue today, and I want to thank our witnesses for their thoughtful testimony.

A stable, affordable drug supply is critical to our nation's public health and its infrastructure. And patients who experience drug shortages report increased out-of-pocket costs, increased rates of drug errors, sometimes adverse health effects, and even increased mortality. So we do need to get our hands around this issue.

I just want folks to know that the Biden Administration is aware of those gaps, and I want to talk about a few things that we have done in response.

In November, President Biden announced additional investment in our domestic production of materials for injectable medicines

through the Defense Production Act. And Democrats have also worked to improve access and reduce the cost of care through the Inflation Reduction Act. We put money back in millions of Medicare recipients' pockets and capped out-of-pocket prescription costs and insulin costs at $35 a month, and that has very real impacts. I hear about that from my constituents.

But we are here today to talk about additional solutions to the related and growing problem that affects every American and, disproportionately, unfortunately, impacts disadvantaged communities more. Over 80 percent of drugs reported in shortage are generics or branded generics, and the FDA reported that in 2023 that pain management and cardiovascular diseases were the top disease areas with drug shortages and, sadly, two diseases—these are two diseases that disproportionately affect Black and Latino patients more. Medicaid enrollees are also more likely to be affected by those drug shortages.

Dr. Gralow, can you expand on how drug shortages exacerbate existing health gaps in access, care, and quality?

Dr. GRALOW. Thanks for that question. It is always the underserved who, when the system is stressed, become more underserved. So the inequities just get exacerbated.

Whether it is racial and ethnic minorities, whether it is the rural communities, whether it is older populations, the ability to get access to these drugs in the cancer drug shortages is limited. You don't have as many options if you have to drive farther, take more time off work, et cetera, et cetera. You just have less options. So sadly, it was very clear that these drug shortages just exacerbated the already existing inequities in access to care.

Ms. SÁNCHEZ. Thank you. And how has that impacted providers' ability to practice medicine?

Dr. GRALOW. I think we have talked about some heart-wrenching examples of how do you make these choices? We are calling them impossible choices. How do you decide who gets a potentially lifesaving or life-prolonging drug?

We have, you know, had our members have to make decisions about taking patients who have metastatic disease that might not be curable, but they are being held in—it is being held in check, and they are still living a productive life, and removing them from treatment so a newly diagnosed patient with a curable disease could get the drug. I mean, how do you make that kind of decision? How do you explain that to the patient, to the family? It is impossible.

Ms. SÁNCHEZ. Thank you for your testimony, Dr. Gralow.

Quality deficiencies in our supply chains cause those devastating drug shortages, and the Biden Administration created the Council on Supply Chain Resilience to try to address this. HHS is also working to designate a new supply chain resilience and shortage coordinator to build on that work.

Dr. Schondelmeyer, you also discussed the need to shift drug manufacturing for Active Pharmaceutical Ingredients from the Asian Pacific region to the Western Hemisphere. What are some of the potential barriers for reshoring our API supply chains to Mexico, Canada, or other countries in the Americas?

Mr. SCHONDELMEYER. Thanks for that question. We have heard people address this around the edges. That is, the reason products have gone to Asia rather than the West is they have lower environmental regulation, lower labor costs, and other government policies that encourage them to work there. So we need to begin to do the same things, evaluate can we develop technologies that make this possible within the U.S. or within Mexico or Canada and the Western—in terms of environmental conditions.

How can we help lower the cost? This investment in continuous manufacturing that people have talked about, this is like—remember Henry Ford, when he started making cars on the assembly line? That was a continuous flow process. Before, we made cars one at a time. We are still making drugs one batch at a time like one batch of cookies at a time. We need a continuous flow process. It is leaner, greener, more effective, more efficient in a lot of ways. And so—but we need to invest and help the industry in America and in Mexico and Canada and the West develop the capital costs and capital equipment to produce drugs efficiently.

And then finally, I think we tie this with increased transparency and disclosure. The Government of New Zealand has a database called Medsafe, and they require in New Zealand every product that is approved to be on the market to disclose their supply chain. What is the name of the company who makes the API, and where is the factory located, and the street address, and what is the company that makes the finished dosage form and address, street address? And you can actually go to the Medsafe New Zealand website and look up any drug product in their market and tell what its supply chain is.

Ms. SANCHEZ. We do that——

Mr. SCHONDELMEYER. We need a——

Ms. SANCHEZ. We do that with our defense contracting that way.

Mr. SCHONDELMEYER. Yes, and we need a similar database in the U.S.

Ms. SANCHEZ. Yes. Thank you so much for your testimony. I thank all of you.

And I yield back.

Mr. SMITH of Nebraska. Thank you. I now recognize Mr. Estes for five minutes.

Mr. ESTES. Well, thank you, Mr. Chairman, and I appreciate the opportunity to talk about this important topic today. And thank you to all our panelists for joining us today to go through this important issue.

Americans depend on a robust health care system in the United States, and we are grateful to the countless doctors and nurses who care for us in times of sickness and great difficulty. We have come to expect that when we are facing a health care crisis, health care providers will be ready to assist us.

Unfortunately, many Americans are now facing a drug shortage crisis, causing delays in treatment that produces unnecessary hardships and cost. This can be especially devastating to folks living in rural parts of our country. In my district in Kansas, a large part of our population lives outside of a major metropolitan area, relying on community and critical access hospitals for care. When the med-

ical supply chain breaks down, too often it is the rural Kansans I represent who are at the end of the line and are impacted the most.

Unfortunately, the problems don't just stem from one part of our system. An over-reliance on foreign countries like China and India, complex supply chains and distribution processes, and unsustainable Medicare reimbursements aren't just hurting many drug manufacturers, they are hurting Americans who rely on those medicines.

A particular area of concern, as we have talked about before, is the amount of Active Pharmaceutical Ingredients, or API, that is produced in China. Kansans have rightfully shared their concerns with me about relying so heavily on China to produce these critical medicines that we rely on every day. And it is not just specialty drugs or uncommon medicines, it is products like ibuprofen, hydrocortisone, and acetaminophen. When Americans are reaching for a common, over-the-counter medicine to relieve a headache or a backache, they are more likely opening a pill bottle with drugs from China.

While this has been a growing problem for a while, the COVID–19 pandemic highlighted the awareness and exposed the potential pitfalls of ceding our critical medical manufacturing processes overseas. Now, with drug shortages throughout the country, we are reaping the detriments of depending on China and others for our pharmaceuticals.

Dr. Schondelmeyer, you talked a lot earlier, and I wanted to follow up on a couple of things that you had mentioned. You know, typically or historically, how much finished product and API has been produced domestically, kind of as a percentage or component versus internationally?

Mr. SCHONDELMEYER. Well, 30 years ago, the majority of API was made in the U.S. and finished dosage forms were made in the U.S. But over the last 30 years or so, that has moved to the Asian market, just like almost all consumer goods.

You know, if you listen to Mr. Wonderful on Shark Tank, he will say, "I am going to take that product and I am going to move it to Asia and decrease your cost of production." That has happened in pharmaceuticals, too, but we haven't paid attention to the quality and other ramifications of that, and now we are paying the price for that, that we haven't kept the quality up when we did that.

Mr. ESTES. And how open or how available is it for the FDA to test and inspect and make sure that there is good quality, safe—in that development in a country like China or India or someplace else?

Mr. SCHONDELMEYER. Well, the first thing that I am sure you, as, you know, Members of Congress, realize is that when we send a person from the FDA, an official representative of our government to China, we have to notify China ahead of time that they are coming and the purpose of their visit. And so suddenly, the factory gets whitewashed, and all of the problems they might have get cleaned up, and you don't find many problems when you go inspect it.

And, secondly, just the cost in time and budget to—for FDA to inspect these facilities exceeds the resources that they have, anyway.

So we really can't regulate factories in China like we would factories in Canada or Mexico or the U.S. because of time and cost and because of the government helping those companies hide things they don't want people to see.

Mr. ESTES. Yes, and I am just so glad that you all have been here talking through this at this hearing. It is—it really became exposed during COVID–19, the risk that we are at for the country. And we saw countries, as mentioned earlier, India threatened to not release pharmaceuticals and drugs to help us, and we saw the similar comments coming out of China, more for some of the equipment and manufacturing that they made there. So it highlights how important it is to bring that back to the United States.

So thank you, and I yield back, Mr. Chairman.

Mr. SMITH of Nebraska. Thank you. I now recognize Ms. Sewell for five minutes.

Ms. SEWELL. First I would like to thank all of our witnesses for being here today.

Chronic drug shortages are having a detrimental effect on the health of patients and providers across the country. Access and affordability are the key components of health equity, yet 84 percent of generic drugs experience shortages. These shortages have had a disproportionate impact on the most vulnerable in our communities.

In the spring of my very first year in Congress, nine Alabamians died in one of the worst known cases of drug shortage-related deaths at the time. Their deaths were attributed to bacterial contamination of a hand-mixed batch of liquid nitrogen because the pre-mixed liquid wasn't available.

Mr. Chairman, I would like to enter into the committee record this article by CBS highlighting the 2011 public health crisis created by drug shortages in my home state of Alabama.

Mr. SMITH of Nebraska. Without objection, so ordered.

[The information follows:]

THE EARLY SHOW

Drug shortages blamed in at least 15 deaths

September 23, 2011 / 8:55 AM EDT / AP

TRENTON, N.J. -- A severe drug shortage is endangering patients and forcing hospitals to buy life-saving medications from secondary suppliers at huge markups because they can't get them any other way.

An Associated Press review of industry reports and interviews with nearly two dozen experts found at least 15 deaths in the past 15 months blamed on the shortages, either because the right drug wasn't available or because of dosing errors or other problems in administering or preparing alternative medications.

The shortages, mainly involving widely-used generic injected drugs that ordinarily are cheap, have been delaying surgeries and cancer treatments, leaving patients in unnecessary pain and forcing hospitals to give less effective treatments. That's resulted in complications and longer hospital stays.

Just over half of the 549 U.S. hospitals responding to a survey this summer by the Institute for Safe Medication Practices, a patient safety group, said they had purchased one or more prescription drugs from so-called "gray market vendors"- companies other than their normal wholesalers. Most also said they've had to do so more often of late, and 7 percent reported side effects or other problems.

Hospital pharmacists "are really looking at this as a crisis. They are scrambling to find drugs," said Joseph Hill of the American Society of Health-System Pharmacists.

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President Biden holds campaign rally in Las Vegas ahead of Nevada's primary election

A hearing on the issue was set for Friday before the health subcommittee of the House Energy and Commerce Committee. The Food and Drug Administration is holding a meeting Monday with medical and consumer groups, researchers and industry representatives to discuss the shortages and strategies to fight them.

The FDA says the primary cause of the shortages is production shutdowns because of manufacturing problems, such as contamination and metal particles that get into medicine.

Other reasons:

– Companies abandoning the injected generic drug market because the profit margins are slim. Producing these sterile medicines is far more complicated and expensive than stamping out pills, and it can take about three weeks to produce a batch. Making things worse, companies don't have to notify customers or the FDA that they've stopped making a medicine. That means neither FDA nor competitors can try to fill the gap.

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– Only a half-dozen companies make the vast majority of injected generics. Even if other companies wanted to begin making a generic drug in short supply, they're discouraged by the lengthy, expensive process of setting up new manufacturing lines and getting FDA approval.

– Theft of prescription drugs from warehouses or during shipment.

– Secondary, "gray market" vendors who buy scarce drugs from small regional wholesalers, pharmacies or other sources and then market them to hospitals, often at many times the normal price. These sellers may not be licensed, authorized distributors.

Hospitals that buy scarce medicines from the "gray market" are taking a gamble.

The drugs may be stolen and hospitals can't always tell whether a medicine was properly refrigerated – as required for many injectable drugs – or whether it's past the expiration date, said Michael R. Cohen, a pharmacist and president of the institute. Either way, the active ingredient might have degraded and the drug might not work well or could harm the patient, he said.

Cohen attributes at least 15 recent deaths to drug shortages based on reports by medical personnel, but says many deaths and injuries go unreported.

In the worst known case, Alabama's public health department this spring reported nine deaths and 10 patients harmed due to bacterial contamination of a hand-mixed batch of liquid nutrition given via feeding tubes because the sterile pre-mixed liquid wasn't available.

So far this year, 210 drugs have been added to the list of drugs in short supply, one less than the total for all of last year, according to the University of Utah Drug Information Service, which tracks the shortages. That's triple the roughly 70 a year from 2003 to 2006, when shortages began to climb steadily.

"The shortages aren't resolving. They're piling up on top of existing ones," said Erin Fox, a pharmacist who manages the service. She said at least 55 drugs from shortages before this year are still unavailable or scarce.

The average price markup on drugs sold by secondary distributors was 650 percent, according to an Aug. 16 report by the Premier Healthcare Alliance, a group that helps U.S. hospitals and other health providers improve their patient care and finances. The report is based on an analysis of 636 unsolicited sales offers that were faxed and emailed to hospitals from secondary distributors in April and May.

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price, the survey found. The drugs with the highest markups
r medicines for surgery or for emergency care, cancer,

rug for dangerously high blood pressure, normally priced at

t they'll soon have to start passing them on to insurers and
n.

Hospitals sometimes have to cave in to save patients, according to Cohen and several hospital pharmacy directors.

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The FDA says it must uphold quality standards but also works hard to prevent shortages.

"When FDA detects a contaminant, whether it be shards of glass or metal particles or an infectious agent, we have to take action to protect the public," said Dr. Peter Lurie, a senior adviser in the FDA commissioner's office.

When the agency orders a production shutdown, it urges other manufacturers to boost their output and expedites any approvals needed, said Valerie Jensen, associate director of FDA's drug shortage program. When raw materials used to make drugs are in short supply, the FDA tries to find new sources.

The agency averted 38 shortages last year, Jensen added.

Legislation pending in the House and Senate would increase penalties for drug thefts from warehouses and tractor-trailers. Another proposal, which has bipartisan support, would require drug manufacturers anticipating a shortage to immediately notify the FDA.

Sen. Amy Klobuchar, D.-Minn., the primary sponsor of the Senate version of the notification bill, said other solutions being considered include better tracking of medicine shipments, mandatory accreditation of distributors, stockpiling of key drugs and allowing routine imports of prescription drugs from countries such as Canada.

Distributors that supply about 90 percent of prescription drugs to hospitals buy direct from drug manufacturers and deliver only to customers with appropriate licenses, said John Parker, a spokesman for the Healthcare Distribution Management Association. He said HDMA members don't participate in the "gray market" but would not comment further.

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s generally say they have small batches of specific drugs that are
roller coaster ride' of pharmaceutical shortages? ... I utilize over 60 vendors to locate and procure needed pharmaceuticals to assist when you have shortage needs," one reads.

Several distributors who sent hospitals solicitations for scarce drugs didn't return calls from the AP. One representative said he wasn't authorized to discuss the issue.

Watch CBS News

One company, Novis Pharmaceuticals, defended the higher prices, saying secondary distributors have to charge far more because they don't get the big rebates manufacturers give primary distributors. They also have high costs to locate and transport batches of scarce drugs, although the company, which mainly distributes blood plasma, would not disclose its profit margin.

It's illegal for companies to create a monopoly or collude to create a medicine shortage and raise prices, and there's no evidence of that. There's no federal law against price-gouging on prescription drugs, according to the FDA, but it does urge pharmacists to report cases to its Office of Criminal Investigation. An agency spokeswoman said she could not discuss whether any cases are being investigated.

The top three wholesalers say they try to alleviate problems by working with drug manufacturers, updating hospitals on shortages and rationing scarce supplies by giving their regular hospital customers a portion of their normal order. McKesson Corp. and Cardinal Health Inc. say they halt sales to any smaller distributors found to be diverting drugs or otherwise breaking rules. AmerisourceBergen Corp. does background checks on customers.

The hospital association and other groups urge hospitals not to buy from unaccredited vendors, to insist on documentation of the drug's source if they must, and to report price gouging to state authorities. But only three states – Kentucky, Maine and Texas – have price-gouging laws that specifically cover medicines.

"Something has to be done here," said pharmacist Michael O'Neal, head of drug procurement for Vanderbilt University Medical Center in Nashville, which has had to purchase medicines from secondary suppliers about 70 times the past two years.

"This is unethical," he said. "We're talking about people's lives."

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Ms. SEWELL. Now, over a decade later, drug shortages continue to compromise patient care and threaten lives. As a representative of a constituency with high rates of chronic illness, I am particularly concerned about these shortages. My citizens, the citizens in my district, have historically struggled to afford their medication and access to basic health care. Drug shortages only exacerbate these challenges.

There is a story of Gary. Gary is a constituent of mine from Marengo County, Alabama. He is a veteran who is prescribed a monthly pain medication for PTSD-induced pain. Just this past week Gary drove from his rural home to the nearest city, two hours away, only to be told that his pain medication was not in stock. Unbeknownst to him, pain medication across the country is experiencing one of the highest rates of drug shortages. Gary was sent home not knowing when he would be able to receive this medication which was already two weeks overdue. Though he has now gotten his prescription filled, he is already wondering if he will be able to fill his prescription next month. No one, especially our veterans, should have to experience the anxiety associated with not knowing whether or not you will be able to have the medication that you rely on.

Since joining Ways and Means seven years ago, I focused my attention on policies that remove barriers to health care for rural and underserved communities like the one I represent. This is why I have sponsored the Nancy Gardner Sewell Multi-Care [sic] Multi-Cancer Early Detection Screening Act, along with my colleague, Congressman Jodey Arrington. If enacted, our legislation will create access to the first-of-its-kind multi-cancer screening technology. These screenings will be in vain if patients cannot access lifesaving therapies due to drug shortages.

Generic drugs are often a part of the foundational cancer treatment. Due to shortages, many cancer patients go without these lifesaving drugs. In many cases, doctors must choose which patients will receive available cancer treatments, putting the most vulnerable patients at risk. As a matter of fact, Medicaid cancer patients are more likely to be affected by cancer drug shortages than anything else.

To add insult to injury, small rural hospitals are unable to gain the preferential access to scarce drugs that larger counterparts enjoy. We cannot continue to have a health care industry that does not prioritize health equity. We must do all that we can to ensure that quality drugs are both affordable and available and public.

I would like to thank all of our oncology experts who are testifying at the hearing today. In particular, I would like to ask a question of Dr. Gralow.

Could you speak to how the oncologists within the American Society of Clinical Oncology servicing in rural and underserved communities, have been impacted by the drug shortages?

Dr. GRALOW. The rural communities have been impacted even more than those in the rural—in the big cities. They are frequently small practices. They don't have the ability to stockpile, if you will. Most sites that do have a drug that might be nearby are not willing to send the supply over, so those patients would have to travel a greater distance to get it. We talked earlier about——

Ms. SEWELL. Like my constituent, Gary.

Dr. GRALOW. Like your constituent.

Ms. SEWELL. Yes.

Dr. GRALOW. And then you get into the insurance issue of out of network. So, even if they could find drugs somewhere two hours away, then they deal with the insurance company that says, no, we won't pay for an out-of-network provider. So the rural communities were tremendously impacted.

Ms. SEWELL. Thank you.

I yield back the rest of my time.

Mr. SMITH of Nebraska. Thank you. I now recognize Dr. Murphy for five minutes.

Dr. MURPHY. Thank you, Mr. Chairman.

Thank you all for coming today. I am actually still in this fray and have faced, especially over the last five or six years, when I ask for a drug and all of a sudden the hospital or whatever says it is not available.

I was just looking at the drug list of ones that are not available, generic. It is 238 names long, 238: Tylenol suppositories; acyclovir; BCG, which I use a lot for bladder cancer patients. It is unconscionable. I mean, we can't even get injectable epinephrine. So now we have to mix it with other, you know, anesthetics to do something like that. So I guess it really comes down—it is cost, it is higher regulation, and it is the environment.

And Dr. Schondelmeyer, you made a good comment about New Zealand. It just makes me think how we could, in one way, fix this. We ask our pharmaceutical companies—I have a real thing about direct-to-consumer advertising—that we take some of those costs, that we actually turn it into generic manufacturing for our people. You know, it is funny because you said New Zealand. The United States and New Zealand are the only two countries on Earth that allow generic—I mean allow direct-to-consumer advertising. It is a real bee in my bonnet. We don't need it, it is an added expense.

So with Dr. Ferguson, I would just agree that we could go on, I could go on for minutes, for a long time.

Predatory pricing. I wonder if you could accent this a little bit about this. Was this most exacerbated during the pandemic, and what was done about it?

Mr. SCHONDELMEYER. Actually, the examples I am aware of were with respect to antibiotics about a decade before in the late 2000s, although there has been predatory pricing of medical equipment, you know, masks and other things, coming out of the U.S. and out of China during the COVID epidemic. And we saw some products offered on eBay or online or other places for five, tenfold, as much as a hundredfold what their true cost was. That is——

Dr. MURPHY. That is one of the things, actually, that our government does very poorly.

Mr. SCHONDELMEYER. Yes.

Dr. MURPHY. It doesn't allow us to—and everything has to be done in a particular market, taken from a particular place——

Mr. SCHONDELMEYER. Yes.

Dr. MURPHY [continuing]. Rather than some of these individuals.

Mr. SCHONDELMEYER. Yes.

Dr. MURPHY. Why the FDA today is not going over and looking at India, which does not have the stringent policy, is my understanding, that China does, and looking in those labs is beyond me. Why we allow eyedrops to cause bacterial infections or fungal infections is just ridiculous.

Well, this is for Dr. Schleicher and Dr. Gralow specifically with oncology, because I still deal with a lot of oncology patients. You know, when cisplatin was an issue, carboplatin was an issue—have there been studies now within journals to look at reduction of dose, and how this has affected?

Because, you know, I know when BCG was given—was predicted for six doses, that literally was picked because that was what the packaging has. So, you know, truth be told, have there been any studies to look at reduction of dose, whether that is doing anything with survival, whether it has done anything in that regard?

Dr. SCHLEICHER. So thank you very much for the question.

So I don't know of any—and you might, Dr. Gralow—any large studies yet, just because there probably hasn't been enough time.

So I know hundreds of patients who did not get the full dose from this study, as you mentioned. So we are actually missing doses. And for ours, it wasn't just delay, because we were up against potential months so people actually did not get the doses they needed——

Dr. MURPHY. It is going to be extremely hard to randomize people to say——

Dr. SCHLEICHER. A hundred percent.

Dr. MURPHY [continuing]. You are going to get a full dose, you are going to get half a dose.

Dr. SCHLEICHER. So I don't know doses. I can tell you my patients who didn't get that, if their cancer comes back, they are always going to wonder.

Dr. MURPHY. Sure, that was——

Dr. SCHLEICHER. The palliative side, when patients did not get it—because we did have to ration—if they died sooner, the family always wondered.

So without data it still——

Dr. MURPHY. It is going to be up here, anyway.

Dr. SCHLEICHER. It still has a huge impact.

Dr. GRALOW. I don't think that there are any new studies I am aware of to define this.

But with carboplatin, for example, the various trials in different disease types, ranged doses—so we use an area under the curve as the dose for carboplatin. And so recommendations for treating ovarian cancer could be you use an AUC of four to six and give it every three to four weeks because we have never head-on compared those, and different trials showed that those were better than alternatives.

So during this crisis and shortage, [inaudible] recommended use the lower dose since we don't have proof that the higher dose is better since we recommend this range——

Dr. MURPHY. Right.

Dr. GRALOW [continuing]. And use the longer interval. We haven't head-on compared those, and I don't think we ever will.

Dr. MURPHY. You know, I personally think—and we—you know, to your point, Dr. Schondelmeyer, about the fact that we did this 10 years ago or 15 years ago, and we offshored so much, it is labor costs, it is supply chain. And the fact that we don't onshore these things or nearshore—and I am talking about Central America, where the big border crisis occurred, this was an absolute opportunity when they opened the southern border—is to say if we are going to look for "root causes," why are we not using Central America?

You know, I have done plenty of work. I have worked in Nicaragua, probably been there 20 times. There are people begging for jobs. And why are we putting those in India, China, rather than Nicaragua and El Salvador, et cetera?

Mr. SCHONDELMEYER. You are exactly right. If we nearshored these in Central America, it would provide better economy, jobs, keep those people from marching to the U.S. saying, hey, we want in, you know, take care of us. It would help with the economy of these countries around us. It would help with the border issues and other things.

Dr. MURPHY. It——

Mr. SCHONDELMEYER. It won't solve all of them, but it will help.

Dr. MURPHY. It is a win-win for everybody.

Mr. SCHONDELMEYER. Yes.

Dr. MURPHY. Why have we have not explored that in the politic of the last two-and-a-half years and for the decade prior?

Mr. SCHONDELMEYER. Yes.

Dr. MURPHY. It is unbelievable to me. I have visited Nicaragua a bunch of times, worked there, and there is so much that is done there. But gosh, so much more.

Thank you, Mr. Chairman, I will yield back.

Mr. SMITH of Nebraska. Thank you. I now recognize Mr. Fitzpatrick for five minutes.

Mr. FITZPATRICK. Thank you, Mr. Chairman, and thank you to our witnesses for being here today to provide your insight on the chronic drug shortages that are facing our nation. I am the co-chair of the bipartisan Cancer Caucus. This issue is at the very, very top of our list of priorities.

There are currently over 250 drugs that are in shortage in the United States. And it has also been reported by 86 percent of surveyed cancer centers that they themselves are experiencing drug shortages. Through conversations with constituents and doctors in my home community back in Pennsylvania, I have heard the following story.

A doctor must deliver the news not only that their patient has cancer, but that they don't have the lifesaving cancer drugs available to help cure them because it is in shortage. And to further compound this issue, the rate of cancer incidences across America, including in our communities, is increasing for certain types of cancers. Therefore, the fact that chemotherapy drugs are in shortage has to be at the top of all of our priorities.

Mr. Schleicher, first question for you. In your testimony, you noted that there was an interval of over 10 days during which you did not receive any shipments of two generic injectable

chemotherapies. In your experience as a chief medical officer, can you speak about how this changed the decision-making process for oncologists treating patients, and what other options were available to patients during that 10-day period?

Dr. SCHLEICHER. Thank you very much for the question. Yes, it was terrible, and that was just the worst, where we had 10 days before that. And it is in the written testimony, there is a huge graph of declines before that where we already had to start thinking about what diseases we could treat, and then a slow pick-up.

So we actually had to sit and make the decision. Are we going to prioritize palliative, which means not curable yet still very important to extend quality of life and extend life for patients with families? Are we going to do it where there are diseases where there might be a substitution, even if it is not randomized data to show it is adequate? Or are we going to pick small diseases, where, hey, at least we can do one group of patients, then divide up patients with curative cancer—curative breast cancer, and half get, half don't?

So it was hard. And, at one point in my email that I had to send to the group last June, at the worst we were only able to use carboplatin for curative chemo radiation with lung cancer, which means that every patient who needed it for breast cancer, metastatic lung cancer, tons of women's health cancers like gynecologic malignancies were unable to get it for a period of time.

Mr. FITZPATRICK. Thank you.

Dr. Gralow, obviously, this issue extends not just to adult, but to pediatric cancers, as well. Could you shed some light on how shortages affect the treatment of pediatric cancers and the unique challenges faced in providing care to this vulnerable population, and what can Congress do to address this?

Dr. GRALOW. Pediatric cancers were actually where it came on ASCO's radar back in 2011, 2012. We actually had a pediatric oncologist who was our president at the time. But this is where we really started to see several pediatric oncology drugs that were critical for high cure rates in these diseases start to go into shortage.

Now, the amount of drug that is made, you know, they—it rebounded. It goes up and down. One drug goes out, another drug goes out. It is a small amount compared to this recent big cisplatin, carboplatin shortage. But these pediatric drug shortages have never really stopped. It is just they wax and wane. A new drug goes in or out. Right now we have shortages of several drugs that are critical to pediatric cancer. And, without them, we really impact the survival. So this is a big problem in pediatric oncology.

What can we do about it? I think all the things we are talking about for adult oncology drugs, too, you know, bringing, you know, quality manufacturing into the U.S., you know, having earlier insight and transparency into what is happening so that companies like Civica, that model, that they can jump in well before the drug isn't on the shelf anymore.

Mr. FITZPATRICK. Thank you, Dr. Gralow, thank you to all of our witnesses for being here.

Mr. Chairman, I yield back.

Mr. SMITH of Nebraska. Thank you. I now recognize Ms. Chu for five minutes.

Ms. CHU. Thank you to all the witnesses for providing your testimony today. I have heard from so many constituents, patients, and providers across my field who have all been negatively affected by the strain of drug shortages. It is shocking that there is so little concrete information on why they occur. There are no standardized shortage reporting codes, and manufacturers are not obligated to give detailed information on the cause of the shortage. And, shockingly, more than half of drug shortages as of June 2023 did not have a declared cause.

It is clear that increasing transparency over the supply chains is necessary to address the root cause of shortages, and ultimately solve this crisis. It is important to note where our drugs and their ingredients are being made so that when a drug shortage or other supply interruptions happen, FDA manufacturers can respond appropriately. And we must ensure that the FDA knows at the earliest possible time when a surge in demand for a drug is likely to cause a shortage.

So, Dr. Ballreich, under current law there are no requirements for reporting shortages caused by increases in demand. How can early notification by manufacturers help the FDA address drug shortages?

Are there ways we can better align the supply chain to allow for more accurate predictive modeling and give us earlier warnings for drugs in danger of going into shortage?

Mr. BALLREICH. Excellent question. Generally, more information is better. If we had information about anticipated changes in demand, anticipated changes to circumstance, to manufacturers regarding, you know, shortages or regarding access to APIs, it could allow additional players in the supply chain to think about additional sources, think about remediation of that, just identifying the risk.

You know, we could have a situation if there are 5 generic manufacturers or 10 generic manufacturers where you might think, oh, that sounds fairly resilient. But, if they are all sourcing from the same single API, like what happened with the chemotherapy drugs and sourcing it from Intas, the manufacturer in India, that exposes a significant supply chain threat.

So more information, more transparency is obviously, I think, going to make it a lot better, and it is going to be a better option.

Ms. CHU. Thank you so much.

Dr. Coukell, drug shortages are intertwined with the problem of high prescription drug costs. That is why Democrats worked through the Inflation Reduction Act to negotiate the price of prescription drugs. It is so important.

But there are other solutions that can help address both shortages and high costs. For example, my home state of California launched the Cal Rx program in 2020 to empower the state to develop, produce, and distribute generic drugs, and sell them at a low cost. And, in March of last year, they announced the program's first project, called the Cal Rx Biosimilar Insulin Initiative, to support the development of a generic version of the three most popular insulin medications.

So, Dr. Coukell, how might more partnerships like the one between Cal Rx and Civica Rx help to alleviate generic drug shortages, while also lowering drug prices for consumers?

Mr. COUKELL. Thank you for that question.

You know, first of all, I think when we are talking about these issues, sometimes we have to hold two problems in our minds simultaneously. And so sometimes cost is a barrier to access, and we have to address that. When we are talking about drug shortage, though, as we have said, we are really talking about extremely low-cost drugs for the most part, where the problem is the margins are so low that companies are not investing and not staying in the market.

But to your question, Civica is developing affordable insulin, the three insulins that are used most commonly in the U.S. Even for a biosimilar, insulin, that is a very expensive undertaking. And so we are happy to have a partnership with the State of California, which has contributed a substantial sum towards the cost of bringing those products to market.

Ms. CHU. Thank you.

Dr. Ballreich, we have heard people say that some shortages are due to the results of prices being too low, but I am concerned that Republican proposals to address the root cause of this would give free rein to raise prices on consumers. So, Dr. Ballreich, what should be done to make sure that that raising prices won't cause harm to products and patients?

Mr. BALLREICH. Yes, excellent. I think any change to reimbursement should be tied to some meaningful change to supply chain resiliency.

You know, in my testimony, I suggested a scorecard type approach. You know, we—Congressman Kelly talked about car parts. You know, we—when we look at other consumer products, we know where they are from, we know brands, we know the quality of that product. In generic drugs, we don't. And right now, in the generic drug market, we are—it is solely based on price. Everything is trying to drive down the price, which is great for patients. But if that price is not tied to some sort of meaningful investment into the supply chain, then it doesn't really help patients if they can't get access to that drug.

So I think any change to reimbursement should be tied to some sort of meaningful aspect that either incentivizes investment or some sort of tie to the quality of that product.

Ms. CHU. Thank you.

I yield back.

Mr. SMITH of Nebraska. Thank you. I now recognize Mr. Steube for five minutes.

Mr. STEUBE. Thank you, Mr. Chairman.

The Hatch-Waxman Act, formerly known as the Drug Price Competition and Patent Term Restoration Act of 1984, was originally designed to create more competition in the generic drug market. Congress sought to balance the need to incentivize drug research and development with a desire to increase competition and make drug prices more affordable. The law made several key changes that initially helped foster competition in the drug manufacturing space and drove down the cost of essential medicines.

A loophole in the legislation, however, led to the hollowing out of America's public health industrial base. While the law rolled back some regulatory barriers in order to make it easier for new companies to enter the market, the law's original intent was never to create a race to the bottom that forced companies to cut corners in order to manufacture drugs for less than the price of a cup of coffee in order to remain competitive.

China and India both provide significant subsidies to generic manufacturers. China's Made in China 2025 plan openly states Beijing's goal of having their top 20 national champion manufacturers of essential drugs control at least 80 percent of the global market for those goods. As part of the Chinese Communist Party's strategy to accomplish this, China imposes a 5.5 to 6.5 percent tariff on most drug imports, in addition to a 17 percent value added tax on all imported goods, which works similarly to an additional tariff. By contrast, the United States imposes no costs on imports.

India offers an even larger incentive program with over 24 separate subsidy programs funding its generic pharmaceutical manufacturers. Indian generics are refunded on everything from FDA user fees to 100 percent expensing in some cases. Combine this with India's purchasing of cheap Russian oil and low-cost Chinese imports. The Indian producers are at a significant advantage. And it is apparent from recent reports that these subsidies have directly resulted in the offshoring of America's generic pharmaceutical manufacturing industry, and today they place U.S. firms at a significant disadvantage.

That is why I am honored to cosponsor Representative Tenney's PILLS Act to restore the U.S. generic drug supply chain through production-based tax and investment tax credits. This bill is comprehensive to cover all materials, testing, and packaging involved at every step of the manufacturing process.

The byproduct of this hearing must be policy solutions to solve our drug shortage, including countering China and India's presence in this space by reshoring our domestic drug making capabilities.

Dr. Stephen Schondelmeyer—did I say that right?

Mr. SCHONDELMEYER. Yes.

Mr. STEUBE. Can you recommend some changes to the tax code to promote Made in America investments and onshoring?

Mr. SCHONDELMEYER. I probably could. I can't off the top of my head in terms of tax code, but I think there are issues.

We need to look—most of the companies that we call manufacturers in the U.S. that are the sponsors at the FDA don't really manufacture the drug. They contract with someone else to make it. And so, often the product might be made somewhere else, and even the revenue may be booked somewhere else, like Ireland or in other countries. So we need to look at, for the products used in America and the profits made by selling those in America, are we capturing those in our tax code?

Mr. STEUBE. What trade barriers currently exist that would affect the supply of generic drugs?

Mr. SCHONDELMEYER. Well, as I said, we saw emerge some bans on exporting of drugs to the U.S. And I think we need to look carefully at what Florida is trying to do by importing drugs from Canada——

Mr. STEUBE. Yes.

Mr. SCHONDELMEYER [continuing]. And Canada now saying we don't want to export them. We need to work through that with a trusted trade partner, Canada, and figure out how can we make this work for both of us?

Mr. STEUBE. Mr. Cavacini, am I pronouncing that correctly?

Mr. CAVACINI. Yes, sir.

Mr. STEUBE. Can you describe how wholesalers make decisions on which manufacturers to purchase drugs from?

Mr. CAVACINI. Thank you for the question.

Our sourcing strategy really is centered around three pillars: the first is consistent supply; the second is clinical importance; and the third would be price and cost. And when we think about those three pillars, they might flex in priority based on what is happening with that specific molecule.

When we think about consistent supply, we are looking at manufacturers' historical performance, their financial strength to the extent that we can find out where the raw materials come from and how the products are made.

And then clinical importance, are—these primary agents, are they curative? Are there other alternatives available?

And, in places where we have really strong supply and performance and a lot of alternatives, we might prioritize price. If that is not the case, where there are few options, high concentration, and risky, we would enter into long-term contracts and potentially pay more to make sure that we have the supply that we need.

Mr. STEUBE. Can wholesalers predict drug shortages?

And how do they mitigate that?

Mr. SCHONDELMEYER. I think predicting is difficult, based on the information we have. There are clear indicators of higher-risk products, and we have talked a lot about those today. Those medications that have been around a while are often very inexpensive, have complex manufacturing processes, and could be made in riskier places based to geopolitical or weather or other environments. Those are high-risk for a drug shortage.

The way that we mitigate is really a couple-fold. You know, first is that we invest and hold inventory in our 30 distribution centers that are positioned across the United States, close to patient populations that we can deliver to within hours. We might have days to months on hand based on the supply. And then we also use allocation strategies to make sure equitable and fair distribution of the products that are in the supply chain, especially those that are vulnerable.

Mr. STEUBE. Thank you guys for being here today.

I yield back.

Mr. SMITH of Nebraska. Thank you. I now recognize Ms. Moore for five minutes.

Ms. MOORE of Wisconsin. Let me just thank this distinguished panel and the ranking member and the chair for convening this important meeting that, really, all of our constituents are facing.

I guess I want to direct my questions—maybe first with you—with Dr. Gralow and Mr. Coukell. I am trying to understand better the drug shortage prevention strategies that you have.

And I am wondering, you are saying we—and I have heard others—I heard you telling others that we need a database. The FDA has a drug shortage database. But what am I missing here? Is it stockpiling and hoarding?

I am thinking about my own situation in Milwaukee, Wisconsin, where we have, for over a year, been having a problem with amoxicillin. Now, amoxicillin is just—it is like an everyday drug. I mean, you can anticipate with all of the RSV and flu and stuff. I don't understand why that drug, as an example, is facing a shortage. And, using that as an example, can you please explain to me how this database strategy, for example, would stop that problem?

Pick and choose, Dr. Coukell or Dr. Gralow, okay.

Mr. COUKELL. Thank you for that question. What I highlighted in my testimony are, I think, three kind of pillars that would move us towards a resilient supply. One is holding a buffer stock of roughly six months' inventory. Another is ensuring that, when we choose suppliers, we have a process to validate their quality maturity, and that we are choosing not just based on price but based on the likelihood of a shortfall of supply. And the third is entering long-term purchase and supply contracts that bring stability to the market. If we move in that direction, I think that we will address a lot of the shortages that we are facing right now.

I haven't called for a database in my testimony, and certainly you can always make, you know, better decisions with more information. But the biggest predictor of a future shortage is a past shortage. So we are actually quite good at predicting what drugs are going into shortage in the future.

Ms. MOORE of Wisconsin. Okay. Can I ask Mr. Cavacini?

As you know, mifepristone is an important medication in women's health care. And it has been in the market for over 20 years. The FDA has done thorough, evidence-based research to determine that it is safe. And it is so safe for women that it is sort of the number-one method for an abortion strategy. And it is sold over the counter.

So I am asking you, as a prescription distributor, how—and McKesson, of course, is one of the key components in ensuring that women have access to this safe and effective medication. Can you just give us a status update and how you are working with pharmacies to make this happen? And when will distribution begin?

Mr. CAVACINI. Well, thank you for the question. As you mentioned, McKesson's role as a distributor is centered around the principle of making sure that FDA-approved, appropriate medications are available for prescribers and patients where and when they need them.

At the current time, we are not an authorized distributor of mifepristone. The manufacturer of those products has set up a limited distribution network with another company in the supply chain.

Ms. MOORE of Wisconsin. Okay, well, that is good to know.

I have 41 seconds. Great. So Dr. Gralow, let me come back to you. Mr. Hern mentioned how decisions are being made with regard to alternative treatments. And in the case of amoxicillin, the drug stores were doing the compounding themselves, getting the powders. Does that compromise the quality of these drugs, or is

that actually a solution for making sure that there aren't shortages?

Dr. GRALOW. I think that is a great question. I am an expert in oncology, not antibiotics and amoxicillin, and we don't usually compound our drugs either. So I would defer to a colleague on the panel, if you——

Ms. MOORE of Wisconsin. Thank you.

Mr. Chairman, with an indulgence, can somebody answer that? Is that a solution, or is that a quality—does that risk quality and contamination?

Mr. SCHONDELMEYER. Actually, I believe the antibiotics that are made in powders and then pharmacy simply adds sterile water to that and prepares it, and that makes the drug stable longer because, if you had it mixed in the water initially, the drug may not be stable for as long. So that probably does help in the process.

That is different, though, than compounding from raw ingredients a drug. And so it technically is a type of compounding, but it is really to help extend the shelf life of the drug, basically.

Ms. MOORE of Wisconsin. Okay. Well, thank you so much, and I yield back.

Mr. SMITH of Nebraska. Thank you. I now recognize Ms. Tenney for five minutes.

Ms. TENNEY. Thank you, Mr. Chairman and Ranking Member, for holding this important hearing. And thank you to all of you witnesses. This is really interesting work that you are doing, and your testimony is very insightful, so I appreciate the work you are doing.

And, obviously, as you know, for years our country has witnessed an increasing number of drug shortages, with patients and providers now seeking—seeing the largest spike in a decade. This has coincided as our nation has become increasingly reliant on nations such as China and India for Active Pharmaceutical Ingredients and the final forms of drugs, which you have all pointed out today.

Due to this offshoring to less regulated nations, these shortages have been especially noticed in injectable generics, which have justifiably much tighter regulatory tolerances than other medications, which many of you touched on today, as well. In my own district I have seen this, especially with oncology drugs, leaving doctors scrambling to track down the supplies of limited treatments or requiring patients to delay their lifesaving care for weeks. This is indeed not only devastating, it is life-threatening.

This is why I introduced the Producing Incentives for Long-Term Production of Lifesaving Supply Medicines, or the PILLS Act. I like to say the whole thing out there. I want to thank my colleagues who have cosponsored, Representatives Steube, Malliotakis, Miller, Murphy, and Representative Kelly, as well. This bill will provide pharmaceutical manufacturers incentives to reshore their production to the United States, shortening supply lines, and making access to these cures more reliable for American patients.

A cure does not really mean anything if you cannot get a hold of it when you need it, as you all know. I wanted to first just ask Mr. Cavacini a question.

And, in your remarks, you noted how McKesson works to diversify suppliers and incentivize higher quality manufacturing, but you do not expand as to how much and what incentives McKesson,

your company, uses in providing and encouraging near-shoring of the supply chains closer to home. Could you maybe explain how McKesson is willing to do that, or how you do that, if you do it at all?

Mr. CAVACINI. I think it is important to remember that McKesson's primary role is as a distributor and is making sure that products manufactured by manufacturers are available to providers and patients where and when they need them.

What I shared in my testimony is that in our sourcing strategies we try to source from reliable supply. As I think you shared in your comments, a cure if you can't get the drug doesn't do anybody any good. In our business, a great price, if I can't sell it to my provider partners, doesn't do anybody any good either. So we need to make sure that we secure a consistent, predictable supply. And that is a pillar of our sourcing strategy.

Ms. TENNEY. So is that—and so that means you would be willing to continue to invest to pay for pharmaceuticals from these reliable onshore—you do that already, then, with your company?

Mr. CAVACINI. We balance consistency of supply, clinical importance, and price. The focus on price is often driven by our provider partners. They are under intense reimbursement pressure. And absent of other incentives, the only metric that they lever on is price.

Ms. TENNEY. Well, let me ask you. What kind of incentives can you provide manufacturers who want to reshore their products? Say the critical active ingredients of pharmaceuticals, like—can you—are there other incentives you can give them to encourage them to make their products here, in the United States? Or, as you—we indicated earlier, in South America and other places closer to home, not China, not India.

Mr. CAVACINI. Well, as a distributor, I don't know that we could provide the incentives, but I think we support incentives in the system that would create the right environment for manufacturers to continue to invest in redundancy and quality manufacturing and their supply chain.

I think what we have heard from the panel today is that the economics of many of these products have been competed down to a point, that they are very inexpensive, and that does not support investment in redundancy. And there is no incentive because they are competing on price in the system that we have today.

Ms. TENNEY. You raise an interesting point. I just wanted to ask Dr. Schondelmeyer.

Did the Chinese and Indian Governments provide program incentives for API and API production to compete with us in that way? Did they provide similar incentives, those countries?

Mr. SCHONDELMEYER. Well, they provided incentives to the manufacturers in their country to make those products. That is different than reimbursement——

Ms. TENNEY. Would you——

Mr. SCHONDELMEYER [continuing]. Like we are talking about.

Ms. TENNEY. So would you describe them as incentives or subsidies, or both?

Mr. SCHONDELMEYER. Both.

Ms. TENNEY. Okay.

Mr. SCHONDELMEYER. We could find examples of both in India and China.

Ms. TENNEY. So what would—I mean, you are a professor. What would you say is the—I have just got a couple of seconds left. What would you say are the—the most effective way for us to do this? Would it be through incentives? Would it be through subsidies in the United States?

Mr. SCHONDELMEYER. I think, again, a mixture of both could be used effectively.

The most critical question, though, is which products are we going to incentivize. And there is where we do need a database to understand. I agree in the past we know past shortages might reoccur, but we are having new reasons of shortages. We had Acorn, a drug company, go bankrupt, and that—you couldn't have predicted that from past shortages. We have had companies go bankrupt because of the opioid crisis, and all of their products, even beyond their opioid drugs, have gone out of the market and caused shortages.

So we have other reasons for shortages beginning to show up in the market and new reasons. And, with databases we could predict where are we vulnerable, where do we have products that are critical in the U.S. market that are only made in one country in the world, and why don't we start making it here? Let's incentivize those. Let's subsidize those.

Ms. TENNEY. That is a great point. And diversification, definitely.

Mr. SCHONDELMEYER. Yes.

Ms. TENNEY. I appreciate your—thank you, everyone. My time has expired.

Chairman SMITH. Thank you. I now recognize Mrs. Fischbach for five minutes.

Mrs. FISCHBACH. Thank you very much, Mr. Chair.

And first of all, I would just like to say thank you to Dr. Schondelmeyer for coming from Minnesota, and it is always wonderful to have a Minnesotan on the panel. And I know that they have grilled you fairly well today, so I will probably stay away——

Mr. SCHONDELMEYER. Okay.

Mrs. FISCHBACH [continuing]. From asking you additional questions, but I did want to——

Mr. SCHONDELMEYER. I would just respond, "Yeah, you betcha."

Mrs. FISCHBACH. There you go, there you go. Okay, I appreciate that. Only I understood that in the room, though, so—but I want—I did want to ask Mr. Cavacini a couple of questions.

And first, I wanted to mention that on Monday it is going to be 37 in Minnesota, and it might snow in the afternoon, so bring a coat. I did tell him I would find the weather report for him because he is visiting Minnesota.

But in all seriousness, I do have a question. You know, can you describe how the drug shortages are not in the business interest of wholesalers?

Mr. CAVACINI. I think there are a couple things to consider there, and I appreciate the question. It is an important part of the discussion.

You know, our core business model is to make sure that providers and patients have access to the medications that they need. We often contract with hospitals and health systems, from large academic medical centers to small community rural hospitals, to health systems like the VA, pharmacies from national chains and household names to your mom-and-pop community pharmacy, as well as community practitioners and specialty like oncology. And our relationship with them is for all of their pharmaceutical needs. They look to McKesson to supply tens of thousands of products. They can order up until 8:00 or 9:00 the next day, and we deliver to their sites of care the following morning.

Our model is optimized when there is robust and ample supply, and we are filling orders in full to serve providers and patients.

Mrs. FISCHBACH. I appreciate that. And then, just changing a little bit, but do you feel that you have good quality indicators regarding the drugs you purchase from manufacturers?

And is it pretty standardized, or is it more difficult with different manufacturers to get that—information on that?

Mr. CAVACINI. Yes. Well, I think we have talked about quality a lot today.

Mrs. FISCHBACH. Yes.

Mr. CAVACINI. And I think it is important to highlight that, as I have mentioned quality, I am talking about quality of the supply chain and the infrastructure around those medications.

We only purchase FDA-approved medications. We, in our full-line wholesale distribution business, only purchased direct from the manufacturer, and we defer to the FDA and other agencies on the quality of the meds. But we do look really hard at the quality of the companies that we partner with. You know, what is their historical practice? What is any regulatory enforcement action, their financial stability, their diversification to the extent that we can find out where their plants are in the world and where do they source their materials.

But there are limitations. There is no obligation on manufacturers to share that information with us, and sometimes it is hard for us to make the best decision.

Mrs. FISCHBACH. All right. Well, thank you very much. And, given I have just—I have a little more time, what I am going to do is, since I am towards the end, is there anything that any of the panelists wanted to say but didn't have the opportunity to? I will give you a few minutes if there is anything you think.

You answered all the questions fully and you didn't have anything else to add? You have been here a long time, so I appreciate that.

But I do want to just say thank you all for being here, because it has been incredibly informative and very helpful. And the quality of the panel today is just exceptional. So thank you very much.

And with that I will yield back, Mr. Chairman.

Mr. SMITH of Nebraska. Thank you. I now recognize Mr. Kildee for five minutes.

Mr. KILDEE. Thank you, Mr. Chairman. And, to Chairman Smith and Ranking Member Neal, I appreciate the opportunity to participate in and listen to these really, really thoughtful witnesses on a subject that is, obviously, a really important one.

Last year—I am from the State of Michigan, so you can only imagine where I am going with this—last year in my state, as in other states, we saw this problem come home in really significant ways. The severe chemotherapy drug shortage caused people that I represent to reach out.

And, to hear their stories of having illness that could not be treated not because of the lack of the science, but just the lack of access to what science has proven to be effective was really hard to hear. Stories that we have talked about a bit today that Dr. Gralow, Dr. Schleicher, and others have shared about drug shortages preventing doctors from treating patients in the way that they know they should and, as a result, patient cancers progressing as a result.

Dr. Gralow, you mentioned an instance of head and neck cancer. It is a subject that is very close to me. It has only been a few months since I was diagnosed and treated for head and neck cancer. It has been a really difficult path, and I am not quite yet fully recovered. I am cancer free. But I only mention my own personal story because I know exactly how anxious I was when I first got that diagnosis, and how anxious I was to get on with it, to get treatment going. I was persistent, as you can only imagine. You know this, you deal with folks who go through this.

I could not even imagine if my physician, my oncologist told me that, you know, "We do have a treatment path for you that will likely be quite successful. That is the good news. The bad news is it is not available." I couldn't even imagine, as an anxious as I was in that moment, to hear those words. And I know that I represent people that have had to hear that.

So this is a subject, obviously, to the extent Congress can have an impact on this, we need to hear from you. And you have been very helpful in that to help us calculate what steps we ought to be taking to make sure we don't go through this again. Too many patients just are not getting access to the care that would be lifesaving and life-affirming for them. This is the richest country in the world. And as you have stated, it is unacceptable that we find ourselves in this particular situation.

What I am curious about is that I represent a group of older, industrial cities in the State of Michigan: Saginaw, Bay City, Flint, Michigan, all with great manufacturing capacity and a great manufacturing heritage. And I am curious. And, if I could start with Mr. Coukell, you noted that Civica Rx emphasizes sourcing in the United States wherever possible.

And I wonder if you might comment on what I think is a unique opportunity, and I think you did, as well, to reshore some of that manufacturing capacity in a way that not only does the very important work of providing access to these important therapies, but also helps communities that have a great manufacturing legacy, capacity, training programs, et cetera, to benefit from reshoring our manufacturing, and to see both a renaissance in terms of manufacturing capacity, but also securing a supply of necessary therapies in a way that is much more predictable. Could you comment on that possibility, and what you might suggest?

Mr. COUKELL. Yes, thank you for that question. I think, as you point out, there are multiple reasons to reshore the pharmaceutical

supply. Surety of supply is one. Protecting against, you know, geopolitical strategic risks is another. But these are also good-paying jobs in manufacturing communities that have lost them in the last decades. And so there is a lot of potential to bring those back.

And I think the kinds of things we have been talking about today are the kinds of policies that we need to look at. And it is not one size fits all. I think tax incentives, I think shifting the market towards preferring domestic or higher quality producers, but there are also places—and the example of penicillin and cephalosporin antibiotics is a good one. No U.S. manufacturer can invest right now, I think, in those products on a purely commercial basis, given the global price for those products. And so, if we want to make them here, it is going to take some government investment to bring those facilities back.

Mr. KILDEE. I really appreciate the panel. Thank you so much.

And again, I thank you for listening to my personal story. Members of the committee, I think, appreciated my recovery, but I think they especially appreciated that for a period of time after my very extensive surgery I completely lost my voice. Quite a number of you found me to be a much more reasonable person during that period of time. But I am back.

Thank you, I yield back.

Mr. SMITH of Nebraska. Thank you.

Dr. Ballreich, I understand you had some response to Mrs. Fischbach's——

Mr. BALLREICH. Yes.

Mr. SMITH of Nebraska [continuing]. In her extra time.

Mr. BALLREICH. Totally fine, yes. You asked about what has not really been said.

I think, first and foremost, there is no single solution. You know, there is a wide range of solutions because the problem is across the board in different medications. You know, it is totally different, talking about branded versus generic. It is different talking about mass market generic versus small market generic. It is different from, you know, small molecule generic versus a complex generic like a Generic Sterile Injectable, which requires a much more extensive manufacturing footprint. So I think we talk about a wide range of solutions, and just a recognition that there is not really one single one.

Also, I think there has been a lot of emphasis on improving the supply through tax incentives, tax subsidies. Also, we need to balance that with demand. There is no Made in the USA, you know, pill label. I think there is a lot of people, you know, Americans, who would want to know that the medications they are taking, it is U.S.-based.

So I just want to kind of highlight those two kind of facets of this problem that I think have—they have been mentioned, but maybe not articulated enough yet. Thank you.

Mr. SMITH of Nebraska. Thank you. I now recognize Mr. Moore for five minutes.

Mr. MOORE of Utah. Thank you, Chairman.

One of the last things patients should have to hear from their provider is that they can't get the best treatment for their illness because of a medicine shortage. We often talk about prices, and we

need to keep that focus on making sure things are affordable. But we are talking a medicine shortage.

Patients in Utah are being told this exact same thing far too often. And, according to the American Society of Health-System Pharmacists, there are currently over 250 drugs in shortage in the U.S. Unsurprisingly, the private sector, I believe, has stepped up to help solve this issue. I am proud to have a member of the Civica Rx community here. In 2018, Civica Rx, which is headquartered just south of my district in Lehi, Utah, was founded by several health systems to address ongoing drug shortages and make sure patients have access to the medications they need. We have made some improvements, but recent shortage spikes have shown that we must do better for our patients.

Mr. Coukell, again, I mentioned Civica Rx. You know, I have been excited to learn more about this. As I came onto the stage three years ago into this role, and particularly on the Health Subcommittee of Ways and Means, I appreciate the engagement and helping us understand and my team understand the complexities around this, but the efforts that you are trying to do with the patient in mind. And these things are important to do.

I would like to ask about incentives in the health—or in the Federal health programs, and how they affect the generic market. Do you think that certain Medicare reimbursement mechanisms encourage a sort of race-to-the-bottom pricing of generic drugs and contribute to shortages?

And are there any current policies that are particularly to blame?

Mr. COUKELL. Well, thank you for that, and we are proud to be in Lehi.

You know, I think the market dynamics we have been talking about today exist in the commercial market as it stands. But they drive a situation where we have got very low margins on some of these very low-cost drugs. So anything else that adds further erosion to those margins makes it that much harder for companies to keep producing these products. And so I think that goes to some of the programs you are talking about, yes.

Mr. MOORE of Utah. Any other solutions that Congress should look at that balance generic manufacturers' economic viability with the ability of health care providers to reliably obtain quality and affordable generic medicines?

I mean, that is the question, right? Like, how—what can we do or not do or try to avoid creating an environment where you all can better navigate the economic viability of this market?

Mr. COUKELL. Well, you know, I think not long ago the Center for Medicare proposed a bonus payment for, you know, additional buffer stock. And that is one example. And they decided not to move forward with that for a number of reasons. And there were some things that needed to be fixed there. But that is the kind of thing that sits in the jurisdiction of this committee, where you can say we can use our levers over providers and provider payment to shift purchasing towards much more resilient models.

Mr. MOORE of Utah. Yes, so I welcome Dr. Schleicher into this questioning, as well, Mr. Coukell.

Just speak to rural health care for a minute, and about how this affects rural health care, making sure that the, you know, physician practices in northern Utah particularly, or throughout the rest of rural America, how they are impacted by drug shortages. What can Congress do to make sure that we better address this need, Dr. Schleicher?

Dr. SCHLEICHER. Well, thank you very much for the question.

I think the—my main thought would be that, as people are thinking about solutions—and I don't know the magic solution—make sure that you are understanding the different sites of care where hospitals are and take care of patients, which is obviously a very important thing.

And then, often in rural America, where there aren't hospitals around and there might be a one-physician community practice, and make sure that, for instance, stockpiling doesn't influence one, and then the other actually has a shortage that might not have been there.

And just any solution, really make sure that we understand exactly who is going to get the benefit of that, and that we don't end up accidentally having patients in rural America or patients who might not be able to get in—or might be out of network for other sites of care get penalized for just where they live and their ability to pay.

Mr. MOORE of Utah. Mr. Coukell, anything to add for—to make sure that we have reliable access to affordable generic drugs in our rural markets?

Mr. COUKELL. You know, our model is set up to be equally accessible to any hospital of any size, and they all pay the same prices. And, I think, if we are up front creating a buffer stock, that not only benefits the entities that are providing, but it also creates a buffer that benefits everyone else because more stock anywhere in the system helps smooth out the effect of a supply interruption.

Mr. MOORE of Utah. Yes, thank you. Thank you to all of you for being here and sharing your perspective.

I yield back.

Mr. SMITH of Nebraska. Thank you. I now recognize Mrs. Steel.

Mrs. STEEL. Thank you, Mr. Chairman and Ranking Member Neal.

If the COVID–19 pandemic taught us anything, it is that we cannot trust the CCP as a reliable source for any part of our supply chains, especially vital medical supplies including drugs, PPE, and medical equipment. Unfortunately, drug shortages are still prevalent and are occurring more frequently, impacting patient care.

A recent Johns Hopkins University study found that over 90 percent of hospital systems across the country are now impacted by significant shortages of essential medicines to help treat patients. For a patient, this leaves them with unimaginable circumstances, delayed treatments, and delayed procedures. And, for an oncology or a pharmacist, it means rationing lifesaving drugs.

I believe promoting domestic manufacturing and building a trusted network of allied trading partners in the pharmaceutical sector will promote alternate sources for Active Pharmaceutical Ingredients and encourage resilience in pharmaceutical and medical goods supply chains, which is why I introduced the Medical Supply Chain

Resilience Act with Congressman Brad Schneider and Senator Tom Carper and Thom Tillis. This legislation will create strong supply chains for medical goods and services between the United States and key allies and partners around the world.

Having said that, you know, we asked so many different questions. And actually, we ended up asking double and triple, the same questions from these members. And I am one of the ending part of these members. So, instead of that, I am asking you any questions. If you can give any additional advice to this committee that what we can do, make sure that we can have enough drug supplies. And you tell us, because bottom line is we need to stop this shortage of medications and, you know, pharmaceutical supplies.

So whoever wants to tell us and give us more advice that you missed it, then I am just welcoming that.

Yes.

Dr. GRALOW. So I will start, just add a little information on a topic we haven't discussed in great detail. We have talked about these drug shortage lists that the FDA, that the American Society of Health-System Pharmacists put out, but, you know, right now, we have about 15 cancer drugs that are listed on these lists with very little additional data about why they are on the list. And I think it is a little bit of crying wolf.

You know, you have these drugs on, and in the clinic we are not seeing the problem. And so it is like, oh, yes, it is on this list, but it is not really in effect. If we understood why each one was on the list, I mean, you do know is it [sic] because one manufacturer went out of business, but what you don't know is, did they have 10 percent of the market or 90 percent of the market? You do know if there is a quality issue, but you don't know where, when, how long they expect it will be fixed. And, without knowing that, we just look at the list and say, ho hum, we will just see what happens when we don't get our orders placed.

So these lists are important, but this gets to—some of—it is the authority of the FDA to actually ask where you are getting your Active Pharmaceutical Ingredients, but what percentage you are getting from each place. They know they have to list all the places they might be getting it from because they are subject to having audits, but you don't know what percent they are getting from what. So I think more transparency around how drugs make it to the list, with explanation and estimated timeframes could be incredibly helpful.

It doesn't solve the economic and market problem, but it helps with the early detection.

Mrs. STEEL. I think Dr. Schondelmeyer was talking about that, too, that transparency, and then where these drugs came from, where they are manufacturing, and how they are making, right?

Mr. SCHONDELMEYER. Right. Just a quick comment on something that is happening in the marketplace.

There is public-private cooperation to address drug shortages. There is a group that has been formed, a non-profit called End Drug Shortages Alliance. McKesson is a member, Civica is a member, the University of Minnesota and others are members, and there are over 200 hospital systems in the country that are mem-

bers. And this group, as soon as we get any signal of a possible shortage, we try to dig and find out—we have a rapid response team that tries to find out the details of what is going on, everything we can, and then publish that so we can deal with the shortage more effectively.

I will say FDA has been somewhat cooperative, but FDA has said they can't officially share information with us or said on that rapid response team. And so, if you could find ways to authorize FDA to share with this public-private partnership to address shortages as they are happening, we could be much more effective in what we do.

Mrs. STEEL. Thank you so much. Actually, my time is up.

Thank you, I yield back.

Mr. SMITH of Nebraska. Thank you.

Mr. Beyer, you are recognized for five minutes.

Mr. BEYER. Mr. Chairman, thank you very much, and thank you all for being here.

Drug shortages are not a new problem. We saw the impact very clearly after Hurricane Maria hit Puerto Rico. We were able to see it more clearly during the pandemic, when demand for certain drugs like ADHD medicine surged. I have engaged with it many times. When children's Tylenol was scarce, Raul Grijalva and I led an inquiry to see if the administration could take action. And, on ADHD medicine, Abigail Spanberger has been leading the charge.

The key issue with drug shortages is understanding where in the supply chain is the issue. Constituents complain to us, thinking the issue often lies with the Drug Enforcement Administration, when, unfortunately, we have continually found that the issue lies with the drug manufacturers themselves.

I would like to submit a letter to the record on—from the DEA. This letter, dated November 1, 2023, states, "DEA does not manufacture drugs and cannot require a pharmaceutical company to make a drug, make more of a drug, or change the distribution of a drug." It also states, for amphetamine medications like Adderall, "Our data shows that in 2022 manufacturers did not produce the full amount that the limits permitted them to make, resulting in a shortfall of 1 billion doses that could have been produced, but were not shipped. And the data for 2023 has shown a similar trend." The letter then proceeds to indicate the actions DEA has taken, like requiring drug manufacturers to submit their anticipated production timelines.

U.S. Department of Justice
Drug Enforcement Administration

Office of the Administrator *Springfield, VA 22152*

November 1, 2023

Dear Americans:

On August 1, 2023, I wrote to you with FDA Commissioner Robert Califf to address the lack of availability of certain prescription stimulant medications. As we said then, the U.S. Food and Drug Administration (FDA) and the Drug Enforcement Administration (DEA) recognize the important role that prescription stimulants play in the treatment of conditions such as attention-deficit/hyperactivity disorder (ADHD), binge eating disorder, and narcolepsy. I am writing to you now to provide an update on actions DEA has taken, and is taking, to address shortages in prescription stimulant medications and prevent such shortages from occurring in the future.

As a reminder, DEA does not manufacture drugs and cannot require a pharmaceutical company to make a drug, make more of a drug, or change the distribution of a drug. That said, we regularly engage with manufacturers about their production of drugs, and we set limits (called quotas) for how much of these drugs can be produced.

For amphetamine medications, like Adderall, our data showed that in 2022, manufacturers did not produce the full amount that these limits permitted them to make—resulting in a shortfall of 1 billion doses that could have been produced but were not made or shipped—and the data for 2023 has shown a similar trend. DEA has been in communication with the relevant manufacturers, and 17 out of 18 manufacturers have informed us that they will use their allotted quota amounts and increase production of stimulant medications. Those manufacturers are currently in the process of providing us with information on how long it will take for those stimulant medications to hit pharmacy shelves.

DEA is also actively making changes to our quota allocation process. On August 28, 2023, we changed our quota regulations to reduce the amount of a drug that manufacturers must keep in inventory and to make it easier for manufacturers to voluntarily relinquish their quota allotments in case they are not able to produce a drug. Earlier today, we announced steps we will take to increase manufacturer transparency and receive better real-time data on the status of drug production going forward. These changes include:

- Requiring drug manufacturers to submit their anticipated production timelines for medications to DEA in advance of receiving their quota allotments;

- Requiring drug manufacturers to apply for quota allotments on a quarterly (instead of yearly) basis, so that we are able to provide quota allotments to manufacturers that have demonstrated they are using them to actually make and sell medications for current use;

- Requiring monthly, digital reporting from manufacturers and distributors on the amount of drugs being produced and shipped; and

- Specifying whether a manufacturer's quota allotment is for domestic production or export production, so that we can track how much of a drug is available to Americans.

These changes are designed to help us see shortages coming and adjust more quickly over the long run. We are also taking steps to reduce the burden on patients. On July 27, 2023, we revised DEA regulations to allow patients to transfer electronic prescriptions from one pharmacy to another without going back to their doctor.

As we said in our prior letter, there are still important issues that will need to be addressed through longer-term coordination by DEA, FDA, drug manufacturers, and other stakeholders to resolve these issues in the long term. DEA is committed to ensuring that patients who need stimulant medications have access to them and to ensuring that these drugs are being prescribed thoughtfully and responsibly, and we will continue working with our partners inside and outside of government to do so.

DEA remains committed to ensuring that all Americans can access appropriately prescribed medications. DEA will continue to do all we can to prevent drug shortages, limit their impact, and resolve them as quickly as possible.

Sincerely,

Anne Milgram
Administrator

U. S. Department of Justice
Drug Enforcement Administration
8701 Morrissette Drive
Springfield, Virginia 22152

www.dea.gov

Dear DEA Registered Manufacturer:

DEA is aware of concerns related to the availability of various mixed salt amphetamine products, such as Adderall, used in the management of attention-deficit/hyperactivity disorder (ADHD) and subsequent reports from patients who have been unable to fill prescriptions for these drugs.

DEA takes this issue very seriously and is committed to ensuring that all Americans can access appropriately-prescribed medications. We are working with our federal partners at the Food and Drug Administration as well as manufacturers and distributors throughout the supply chain to understand the causes of these shortages and work to solve them.

As part of these efforts, DEA has conducted an internal analysis of inventory, manufacturing, and sales data submitted by manufacturers through ARCOS and through reports submitted to DEA's Quota Management System. That analysis shows that dosage manufacturers have not utilized the full extent of their authorized quotas. In 2022, DEA authorized dosage manufacturers to generate 38,418 kg of amphetamine medications—which equates to approximately 3.3 billion amphetamine dosage units. But dosage manufacturers only shipped approximately 26,953 kg of amphetamine medications—which equates to approximately 2.3 billion amphetamine dosage units. In other words, approximately 1 billion dosage units were authorized but not shipped—that is approximately 30%.

Similarly, data submitted for 2023 suggest that current quotas are adequate to meet patients' needs, but dosage manufacturers have not utilized the full extent of those quotas. DEA's Diversion Control Division stands ready to expeditiously review and adjudicate individual applications under the current authorized quota levels for amphetamine, in accordance with DEA regulations.

Sincerely,

THOMAS PREVOZNIK
Digitally signed by THOMAS PREVOZNIK
Date: 2023.05.17 07:57:12 -04'00'

Thomas W. Prevoznik
Acting Assistant Administrator
DEA Diversion Control Division

I want to give credit to the Energy and Commerce Committee. This is where the leadership has been helpful. In addressing the black box of the pharmaceutical supply chain, Representative Anna Eshoo has been leading on this issue with several bills, including the Drug Origin Transparency Act, which, if this Congress is serious about this, should pass into law. We have also seen the importance of the need for more resilient supply chains.

So, Dr. Ballreich, in your testimony, you talk about how India and China produce most of the raw material for drugs. If one of those countries has an issue, be it a quality control issue, another virus, or a hurricane, we immediately see the impacts. Thanks to Congress appropriating money to BARDA, BCU and Flow were able to establish domestic manufacturing of vulnerable pharmaceutical ingredients.

Flow is also building the United States"s first strategic Active Pharmaceutical Ingredients Reserve, a long-term national stockpile to secure key ingredients used to manufacture the most essential medicines on U.S. soil, reducing America's dependency on foreign nations to supply its drug chain. Dr. Ballreich, can you speak to the importance of continuing such an effort?

Mr. BALLREICH. Absolutely, and a really great question.

This, you know, drug shortage, it is a national security issue, it is a health issue. So I think very direct efforts by government to support things such as Flow to develop an API stockpile, it is part of the solution package.

You know, we could talk about—and we have—the economics to increase incentives for companies to invest in their supply chain to build out resiliency. We talked about onshoring, manufacturing. All of that, I think, is also part of the solution. But having a stockpile—because inevitably, you know, look what happened in Puerto Rico. That is a U.S. territory. You know, we had a lot of concentration of manufacturing there, and we still experienced a shortage of several important medicines, including injectable azithromycin. So I think efforts to develop a stockpile is very important.

The buffer stocks—you know, CMS proposed a change to the inpatient prospective payment system that incentivized the build-up of buffer stocks, but they were only looking at three months. The average shortage is over 200 days long. So, if we really want to make sure we have our bases covered, I think we need to start thinking about six months, and we really need to prioritize essential medicines, you know.

Mr. BEYER. Thank you.

Very quickly, Dr. Gralow, the Biden Administration has taken numerous steps to address drug shortages: the supply chain coordinator, HHS, investments in BARDA, numerous actions at the FDA. Of the things they have done, which do you think are most promising, or what should be the next step?

Dr. GRALOW. I think, frankly, what is most promising is the attention that they have helped bring to the problem. Not one specific action, but, you know, this has been ongoing for over a decade. I think the depth of the problem, the Biden Administration's interest in cancer has now brought this to the forefront, where you are having hearings like this so that knowledge, that education, that discussion and dialogue is what I really think is the most impor-

tant thing that has happened, and that we will now maybe be able to fix a problem that has been going on for more than a decade.

Mr. BEYER. Okay, thank you very much.

Mr. Chairman, I yield back.

Mr. SMITH of Nebraska. Thank you. I now recognize Mr. Arrington for five minutes.

Mr. ARRINGTON. Well, thank you, Chairman. Thanks to the panelists.

It is quite stunning to read how many drugs are on the list of drug shortages for this—the greatest nation in human history. To think that for over 20 years we have had 50 drugs added to that—there were some good things that came out of COVID, one of them being the revelation of our dependance on China and other foreign countries like Taiwan with respect to computer chips. This supply chain dependency on materials, products that have tremendous import to the safety and security of the country is something I suspect both sides agree is alarming, and I don't think we have done enough. We are doing—we are digging into it now.

I mean, I am a free market guy. I think too often we think government is the solution, and I think all too often when we do, and create some government strategy, it can result in a worse scenario, or certainly more ill effects—unintended, but nevertheless more problems—than we started with.

I am shocked by the data that suggests that 86 percent of surveyed cancer centers report experiencing drug shortages. I am surprised that the pharmacists, the retail community pharmacists in west Texas, estimate that 40 to 50 percent of their daily calls are people from across west Texas asking about medication that they just don't have access to. Forty to fifty percent of the calls?

A pharmacist in Abilene, Texas recently informed my office that, of the 10 medications he dispenses, the most, 60 percent, were made in China. Furthermore, we were informed that over half the medications he carries in his pharmacy were made in China. This same pharmacist, who also compounds specialized medication for his patients, estimated that out of 100 pure ingredients on the shelves in their lab, 90 of them were made in China. And I could go on and on.

So I would hope there is no debate about the problem. Now, we have to figure out the solution. Let me orient around market forces and the—or the lack thereof that should provide best value to the customer, to our patients here in the country. I understand there are unfair trade practices that need to be addressed, but let's just talk about the dials that we have control over here with respect to tax regulations. And tell me, from—and other policy interventions that—tell me what the most—the central perverse incentives to the current system that yield this problem of drug shortages.

Again, I know it is bigger and broader, but what would you say are the top two, and just go down the list, perverse incentives that need to be addressed and adjusted so that we can maximize the competitive forces and the best value and reduce that shortage while giving folks, you know, the best value, low-cost access to drugs?

So just give me one or two—we control—perverse incentives to address, starting with the gentleman at this end of the table.

Mr. BALLREICH. Yes, absolutely. Right now, generics, they compete on low price. So, if you sell a pill for $0.10 a pill and a competitor comes in at $0.09 a pill, they are going to take your entire market share. There is no—you know, there is this drive for the lowest price.

And the result of that is, after 4 years of a generic company entering a specific market for that product, after 4 years, 50 percent of them will leave. You know, so it is—we are competing solely on price. We are not thinking about incentives for that company's supply chain. That company has a perverse incentive to cut corners, to try to drive down that lowest price. So it means moving your company, you know, your manufacturing facility to India or China, and——

Mr. ARRINGTON. Okay. With 10 seconds, since——

Mr. BALLREICH. Sorry, yes, sorry.

Mr. ARRINGTON. That is okay. I just—do you all agree, the rest of the panelists, that there is—you should just kind of shake your head yes or no. Do you agree?

Okay. Well, it seems like we ought to be able to focus on at least that together to address it. And we can talk about the solutions later. But I appreciate all that you guys are doing to give—lend your counsel and insight to us so we can have a more resilient supply chain and better and more secure future.

Thank you, Mr. Chairman.

Mr. SMITH of Nebraska. Thank you. I now recognize Mr. Smucker for five minutes.

Mr. SMUCKER. Thank you, Mr. Chairman, and thank you to our witnesses for being here today. I am glad that we are diving into this issue of drug shortages, which, as we have heard from you and have—we have heard from our constituents, really impact every community, certainly impact millions of patients across the country.

I can tell you in my congressional district—I represent a district in Pennsylvania—our hospitals are regularly telling me they are monitoring lists of critical drugs, comprehensive lists of critical drugs that are in shortage, and they are worried—there are new additions to that every single day. They are taking proactive steps to guard against this. One hospital system with a presence in my district has told me about instituting a weekly meeting in which its pharmacy team members are developing strategies to combat these shortages and mitigate the impact on patients.

And I think what one of the things I am hearing from you today—and I heard it from Mr. Arrington's questions now—drug shortages are largely a function of it being sort of an economic problem, certainly most prevalent, as you have said, among low-cost Generic Sterile Injectable drugs, mostly, or GSIs, which, of course, are a staple of hospital care.

And so I think what I have heard you say is we are seeing market pressures—reimbursement mechanisms, maybe more than anything—that are creating this environment, sort of cost-cutting environment which forces GSI manufacturers to produce the drugs. Maybe you could call it a race to the bottom. They are producing drugs at the thinnest margins possible, sometimes at a loss, which

creates a great deal of instability in the market, which—and to the detriment of patients, if that is true.

So we really should be pursuing policies that encourage market stabilization, encourage quality assurance. So I would just like to ask our witnesses a bit more on these topics.

Mr. Cavacini—and I don't know if I pronounced that correct, but we know, of course, the GSIs require very precise manufacturing, as they are injected directly into the bloodstream. And when there is very little return of—to reinvest in the quality of the facilities, we have seen problems that can occur. Recent FDA data shows that 62 percent of shortages can be attributed to quality issues, and I would like you to just talk about that a little bit.

Can you explain the difficulties of balancing contract demands geared towards lowest price with the need for quality when purchasing the drugs?

And how could we change—to the previous question, how could we change the system to drive the right incentives?

Mr. CAVACINI. Thank you for the question. I appreciate the opportunity, and I think we have talked a lot about today, you know, how we might be able to strengthen the system, bolster supply, and bring economic stability to markets. I think it is important. And you mentioned reimbursement opportunities. We have talked a little bit about today how we might incent, through differential reimbursement, providers to choose products on dynamics other than price.

I think there are also some barriers in the system that prevent generic markets from returning to normal economic forces. There are barriers that prevent generic manufacturers from raising prices. When things are in short supply, when their costs of input go up, when manufacturing costs change, they are often capped on if they can raise price. And, since they can't, they might choose to exit, which can cause a shortage.

So we have put forth a policy recommendation, and would ask the committee to consider, you know, where those barriers exist, maybe in the Medicare drug rebate cap or possibly in the Inflation Reduction Act, which does include some carve-out for drugs in shortage. But I think clarifying and codifying that in the regulation would be steps to consider.

Mr. SMUCKER. Thank you.

Mr. Coukell, you have talked about in your organization contracts are structured differently at times from a typical group purchasing organization. Is it more appropriate sometimes to structure a long-term contract versus short-term?

Mr. COUKELL. Thank you for that question. Yes, if we want a manufacturer to stick around, then we have to give them some reason to believe that there is a long term. And so, if you enter a contract but you don't know that tomorrow somebody is going to come along and say, "Sorry, somebody beat your price and we are shifting our volume," then you don't have much incentive to stay in there. Whereas, if you can enter a contract and know that I have got a predictable volume for five years, then you can make a commitment to stay in the market for that long. And so that is why we contract in that way.

Mr. SMUCKER. Thank you. I am out of time.

Thank you, Mr. Chairman.

Mr. CAREY [presiding]. The chair now recognizes Mr. Panetta. You are now recognized for five minutes.

Mr. PANETTA. Thank you, Mr. Chairman.

Mr. CAREY. And only five minutes.

Mr. PANETTA. Understood. Trust me, they want it less than five minutes, I get it.

But what I say by that is thank you to all the witnesses, for being here for such a long amount of time, but, more importantly, answering some very important questions.

Obviously, thanks to Chairman Smith and Ranking Member Neal for holding this hearing, which I think we can all agree, as we have heard today, is long overdue. And I say that based on the fact that my constituents in the 19th congressional district of California have been telling me for quite some time now about the shortage of cancer drugs.

And I think we can all agree that nobody, after receiving a cancer diagnosis, should then face the indignity of learning that our health system can't even provide the basic generic drugs to help them fight their disease. That is why I appreciate the bipartisan attention that this issue is receiving, that this hearing is attracting, and look forward to finding solutions for all of our constituents, not just in my district but across the country.

Now, in this committee, I have repeatedly raised the issue of the costs that are stretching the providers in my district, and the impact it is having on care. And, Dr. Schondelmeyer, you hit on this in your testimony when you talked about the measurable cost for everyone when providers face a drug shortage. You mentioned how some of the effects on our—some of the effects can be on our health systems, like having to hire and train more staff, patients who face new emergency room visits or even hospitalization. And you mentioned how the broader health system suffers. And, in some cases, patients may even need to switch from a generic to a much more expensive, brand-name drug.

I guess my question to you, Doctor, is in what ways is this the case in the current cancer drug shortage?

And then, two, what is the economic and opportunity cost for providers and patients when drug distribution breaks down?

Mr. SCHONDELMEYER. Well, thank you for that question, Mr. Panetta.

With cancer drugs, as there are with most drug shortages, there are costs clinically to the patient. They may not do as well with an alternative drug. Usually, the therapeutic protocols we use for cancer are carefully designed to use the optimum drug and the optimum doses. But when that is not available, then we have to look at alternatives. And we haven't necessarily done detailed studies on all of the alternatives and where they fit in, or we haven't constructed peer review panels to tell us what the optimal alternative therapy is. So patients suffer and providers have to make decisions with less information than they are used to.

But the health systems also—I am aware of a number of hospital systems around the country that have had to hire a pharmacist just to manage drug shortages, and that is an added cost that we

don't see covered anywhere. It is not covered by Medicare, it is not covered by Medicaid, but it is a cost to the health system.

So there are a number of costs, both clinically and economically, in the system that we aren't managing. But they are there, we are spending the money, we are just not getting good value for it.

Mr. PANETTA. Great. Thank you for that summary. Now, I want to kind of piggyback on what the chairman of the Budget Committee, my good friend, Mr. Arrington, talked about with kind of the global supply chain, especially when it comes to Active Pharmaceutical Ingredient supply issues.

Now, Mr. Cavacini, excuse my friend from Pennsylvania. But obviously, as an Italian heritage, I understand how to say your name. [Laughter.]

Mr. PANETTA. In your testimony, you talk about the steps that your company takes to oversee its supply chain and build redundancies, but that distributors—and I quote—"distributors have limited insight and even less control over upstream issues."

You also talked about the productive work between private companies and the Federal Government to increase supply chain oversight. So does your company support that type of supply chain transparency work, and what other tools can Congress consider when it comes to supply chain oversight?

Mr. CAVACINI. Thank you. Thank you for the question and the pronunciation. My grandfather will be proud.

Mr. PANETTA. So would mine.

Mr. CAVACINI. We do support, and we think access to information—good information to make good sourcing decisions and provide good information to our downstream partners. We heard the doctor talk about when he doesn't know when it is going to end, he doesn't know how to manage. So that visibility up and down is important.

We work with many manufacturer partners that share the same vision that we do and that are open and share their production facilities, their sources. But there are some that don't. And, quite candidly, I understand why those could be competitive reasons. But I think increasing that transparency and helping us all have visibility to where the drugs are made and the manufacturing to assess vulnerabilities can lead to better decisions.

But we need to be careful to not also incent additional potential bad behavior. The minute anybody finds out that something is at risk, their first reaction is to take care of themselves and their patients, and source additional supply that can further stress an already vulnerable supply chain. So making sure that our buffer stock programs are coordinated and centralized would be important considerations, as well.

Mr. PANETTA. Great. Thank you. Thanks to all the witnesses.

Mr. Chair, I yield back.

Mr. CAREY. I thank the gentleman. Mr. Feenstra, you are now recognized for five minutes.

Mr. FEENSTRA. Thank you, Mr. Chair, and I want to thank the witnesses for being here. This is a serious issue, and you guys all understand it, so I am very grateful.

So I am from rural Iowa, and the number-one issue that I hear in my 36-county tour is the concern about health care. Because in

my district, men and women families are traveling 50 to 75 miles for care. I mean, it is very significant. And the biggest issue that I am hearing is the shortage, ranging from IV fluids to seizure medications, chemotherapy drugs.

And it is such a delicate balance. You have the rural hospitals, you have your pharmacies, you have your federally-qualified health centers, your critical access hospitals. And so they all play this great role. So my question is in the critical access hospitals we are seeing that patients that are seeing their oncologists, they don't—they can't get the drug, or there is a waiting time for the drug. So they are spending days before that drug gets to them.

Dr. Schleicher, can you talk about this?

Obviously, you are from Tennessee. What is your perspective on this shortage in rural centers, and how can we remedy that?

Dr. SCHLEICHER. Yes, thank you. Thank you very much for the question.

I will say, too, a lot of rural hospitals like critical access hospitals aren't incentivized to even provide oncology services because they are kind of reimbursed cost plus one percent. So that is already an issue with hospitals in rural areas being able to deliver this care, which is a separate discussion.

A lot of the hospitals we are seeing deliver care, at least in our area, are the 340B hospitals, which are largely urban based.

Mr. FEENSTRA. That is right. And that is what mine are, right——

Dr. SCHLEICHER. So——

Mr. FEENSTRA [continuing]. 340B hospitals.

Dr. SCHLEICHER. Exactly. So leaving for—at least I can speak for Tennessee. Most rural care is done in small, community clinics, of which we provide about 50 percent across the state.

One of the large hospitals in urban Tennessee did not have near the same shortage we had. I will say they were great partners. We communicated, they helped us with recommendations. But our patients live an hour-and-a-half from Nashville and were not driving downtown.

Mr. FEENSTRA. That is right.

Dr. SCHLEICHER. And they couldn't really share a drug with us, either, because everybody wanted to hold on to their own. So there was a huge discrepancy of where the shortage was, based off the type of hospital and the size, leaving, at least in Tennessee, the big gaps in care in rural.

I will also add that, again, I had mentioned that some of the hospitals that had the most supply also were the ones that don't take a lot of insurances in the outpatient.

Mr. FEENSTRA. That is right.

Dr. SCHLEICHER. So we were seeing uninsured and local patients——

Mr. FEENSTRA. Yes.

Dr. SCHLEICHER [continuing]. And we were out of drug—way more severe than some of our hospital counterparts. Not their fault, of course, but it shows the system does have inherent discrepancies, and I think rural was effaced way heavier.

Mr. FEENSTRA. So do you have any solutions, or how do we address this gap?

I mean, do you have any—I am a solutions-oriented guy. I am trying to figure this out. What can we do?

Dr. SCHLEICHER. So, with this—at least what we dealt with, with cis and carboplatin, it was one amount of drug, period. We tried to stockpile ourselves because we saw it coming. And, even with months of as much as we could, we just simply ran out. So there was a net—just there wasn't enough supply.

And there were, obviously, issues in terms of where the supply went, which is why when people talk about stockpiling, maybe doing it more upstream, so with some transparency so we figure out patients who need it get it, versus just assuming some side of care needs it.

Mr. FEENSTRA. Got you.

Dr. SCHLEICHER. And then one other thing that is not this, but I can't help but mention, is the ability to ship drugs right now, which we are unable to do, really affects our rural patients who also live an hour away, and we are unable to ship drugs to their homes anymore.

Mr. FEENSTRA. Yes, thank you. And this is—so Congresswoman Beth Van Duyne is not here, and she has a McKesson facility in her—in north Texas, and so I wanted to ask Mr. Cavacini.

Her question is, is there a sufficient early warning signal to alert others to the potential of a potential drug shortage?

And is there a way that we have enough time, or a timely manner to do this in an appropriate way?

Mr. CAVACINI. Thank you. And I believe our U.S. headquarters is in Congresswoman Van Duyne's district.

Mr. FEENSTRA. That is what she said.

Mr. CAVACINI. Yes. As we heard from the panel today, there is not a centralized, standardized system or early warning system. There is a lot of information, public and private, and people are working to get at—the answers to the questions that you ask.

But, you know, drug shortages are unique. There are some that are very predictable, unfortunately, and there are others that aren't. So I think keeping an eye on multifaceted solutions to this complex problem is one that is important.

Mr. FEENSTRA. Good, thank you.

And, finally—and I don't have time for this, Dr. Schondelmeyer, but I am working on a study to analyze the supply chain when it comes to our drugs. And to me, this is very significant because a lot of the underlying ingredients come from China, especially when it comes to electronic devices and stuff.

I know you talked about this in your research, but I would love to get in contact with you. and work with you on a policy or legislation that we could address this.

Thank you, and I yield back.

Mr. CAREY. I thank the gentleman. Ms. Malliotakis, you are now recognized for five minutes.

Ms. MALLIOTAKIS. Thank you. Well, thank you guys so much for being—for this entire hearing. I know it is difficult to sit for a long period of time and answer all these questions from Members of Congress.

But I really appreciate you actually giving us a lot of insight and ideas of how we can address this issue, because I, like my col-

leagues, are very concerned with the fact that China and India provide the APIs that account for roughly 60 to 70 percent of our generic drugs here in the United States, and anything can happen at any time, as we saw with COVID, and that would leave our population very vulnerable if they are in need of medication they can't seem to reach.

And it seems almost illogical and odd and scary that a country like the United States would be in this position, where we are already seeing a shortage of roughly 250 drugs. I just had a couple of questions.

I assume China and India, they provide programs and they incentivize and they subsidize their API manufacturing. So how does the United States compete with countries that subsidize a large, significant—the production of these particular drugs?

Dr. Schondelmeyer, if you could, respond.

Mr. SCHONDELMEYER. Well, we may have to compete by subsidizing and incentivizing equivalently so we can bring manufacturers into the U.S. space or near-shored manufacturers that can do those same things. So we may have to compete by using the same techniques they do, but do it better.

Ms. MALLIOTAKIS. Okay. So how do we incentivize domestic generic drug manufacturing, though, without exacerbating existing drug shortages or creating disturbances in the supply chain?

Mr. SCHONDELMEYER. Well, I think that the Flow example, BARDA identified 25 critical acute drugs that—many of them are cancer drugs, and many of them are sterile injectables we have been talking about, and BARDA has funded them to develop API stockpiles of those drugs. So that will fill in some shortages that we might expect in the near future.

But we have to realize this is—that one act in 25 drugs doesn't solve the problem when there are 250 drugs, and there are new drugs all the time. So we can't just—this is not just a whack-a-mole process. We can keep whacking the moles, but we have got to do something to avoid whacking the moles, and get behind the problem, and solve it in a bigger scheme. With that, we could identify a broad spectrum, 400 or 500 drugs that need to be produced and available in the U.S. market.

Ms. MALLIOTAKIS. Yes.

Mr. COUKELL. This is actually an area where the current administration and the prior administration have issued very similar executive orders and directives, which is a good thing. There is at a high-level, I think, bipartisan agreement on where we need to go.

There is now, within the Administration for Strategic Preparedness and Response, ASPR, an office focused on industrial base manufacturing. And there is a presidential directive charging them with looking at domestic manufacturing and drug shortages. They have a lot of authorities now, but what they do need is some budget to be able to take steps.

Ms. MALLIOTAKIS. Yes, and, I mean, I think one interesting idea would be looking at areas like like Guam, for example, Puerto Rico, places that can certainly use that type of investment, and I think—we talk about near-shoring and friend-shoring. Why not do it in these U.S. areas? I mean, that would even be better, right?

Onshoring, I think, is the way to go. And do you—what changes to the tax code would you recommend to try to onshore some of this manufacturing?

And I was thinking possibly we can look at the opportunity zones as an area to kind of tie something together there that could perhaps allow for this and also create jobs in areas that need it in the process.

Mr. SCHONDELMEYER. Well, certainly, Puerto Rico has a large pharmaceutical industry that was created, like, three decades ago, and there are a lot of tax incentives and other things that helped support and create that. And it was very effective for a time.

Now many of those facilities are older, not necessarily up to date, need to be regenerated. But we could look at what we did in the past to create the Puerto Rican pharmaceutical industry and say, how can we, with modern techniques and with advanced manufacturing and continuous flow and other things, how can we redo that to bring them to Puerto Rico or Guam or to the American Samoas or, you know, other places?

And I would point out I support fully onshoring, but onshoring alone is not sufficient. We do need some redundancy in multiple places. Because remember, we also had the problem of Puerto Rico. When a hurricane hit the place, it wiped out a lot of our large volume parenteral production, and the U.S. had a shortage because we had it all concentrated in one place.

Ms. MALLIOTAKIS. Well, thank you very much. I mean, certainly we agree on that. But friend-shoring is an important one, right? I think relying on Communist China for a large portion of our APIs is not wise, particularly right now.

So thank you for your time.

Mr. CAREY. Okay. Mr. Gomez, you are now recognized for five minutes.

Mr. GOMEZ. Thank you so much.

First, it is great to be back on this committee. Ways and Means is not only just a prestigious committee, but it actively plays a role on so many issues that my district cares about, everything from, of course, drug pricing, but to child care, child tax credit, housing, you name it. So I am very excited to be back on the committee and to have an opportunity to ask our distinguished panel some questions.

And of course, this issue of drug prices, drug shortages is nothing new in the United States. But we often get—we often in this building and across the country like to be in the blame game. Who is at fault for the high drug prices? And we don't always have a holistic view of what we are dealing with. And it is very much, you know, if it is not the drug companies, it is the PBMs. If it is not the PBMs, it is the insurance companies. If it is not the insurance companies, right, it is the patient themselves. So a lot of folks like to place blame.

But—so I think this is a timely hearing to deal with this issue, and I am glad that this committee has taken some steps in the past when it came to, like, monthly—capping the monthly cost of insulin for Medicare beneficiaries, limit Part D out-of-pocket costs, and allow Medicare to negotiate drug prices for the first time ever.

And those were big accomplishments, but I know that there is a lot more to do.

I come from California, so I want to ask a specific California question. Mr. Coukell, your company is partnering with my state of California to manufacture low-cost insulin. Can you speak to how this agreement will address both shortages and the high cost of insulin facing patients?

Mr. COUKELL. Thank you for that question, sir.

Our focus on insulin is really focused on saving money for the consumer at the pharmacy counter, not so much on shortages, which tends—has not been a problem in this space so far. But we are developing three biosimilar insulins, the ones that account for about 80 percent of insulin use in the U.S., and we intend to make them available at the lowest sustainable cost and without all of the high-list prices and rebates that can distort the market. They will be available at a low and transparent price.

But it takes a substantial investment to bring those to market, and that is where the partnership with the State of California is extremely important, because California has—we have partnered with California, and they have contributed a substantial amount of funds towards developing these products and bringing them to market.

Mr. GOMEZ. Do you see that investments are sufficient enough to be able to have an impact on the market, or is it just the first step, is it just the beginning?

Mr. COUKELL. We will be able to supply a substantial share of the market, if needed. As a mission-driven non-profit, we always say, though, our goal is market impact, not market share. So we want everyone in the country to have access to affordable insulin if they need it.

Mr. GOMEZ. And can this agreement serve as a model for ensuring a steady supply of generic medications while bringing down costs?

Mr. COUKELL. I think it can. You know, it does—developing drugs, even generic drugs, is capital intensive. And so these kinds of partnerships can help us and other organizations do more and bring—make drugs available on a public interest basis.

Mr. GOMEZ. Well, I appreciate the testimony of this committee. I am going to have to run back and catch up on my votes.

One of the things about being the, I guess, the most junior member, I don't have a lot of time. So with that I yield back, Mr. Chairman.

Mr. CAREY. Okay, I thank the gentleman. I want to thank the chairman and the ranking member for this hearing. I would also like to thank our witnesses for appearing before us today.

Please be advised that members have two weeks to submit written questions to be answered later in writing, which I will be submitting to you since I have to run to vote. Those questions and your answers will be made part of the formal record.

With that, the committee now stands adjourned.

[Whereupon, at 2:04 p.m., the committee was adjourned.]

MEMBER QUESTIONS FOR THE RECORD

GWEN MOORE
4TH DISTRICT, WISCONSIN

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WAYS AND MEANS
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Questions for the Record
U.S. House Ways and Means Committee
Hearing: "Examining Chronic Drug Shortages in the United States"
Tuesday, February 6, 2024

Dear Mr. Cavacini:

As you know access to reproductive health care is a critical issue for women around the country and unfortunately, is under threat across America as extremist Republicans want to get between women and their doctors on these matters.

Mifepristone is an important medication in women's health care. It has been over 20 years now since the Food and Drug Administration has – through their evidence-based process determined this medicine is safe and effective for women – and over one year since FDA concluded that this drug could be safely offered through certified retail pharmacies. I understand that pharmacies are seeking to stock this medication and have been waiting for quite some time to do that.

McKesson is one of the key components in ensuring women have access to this safe and effective medication. During the hearing, you said that McKesson is not an authorized distributor of Mifepristone.

- What is the impact of McKesson not being a distributor on retail pharmacies that may have exclusive contacts with McKesson and want to carry Mifepristone?
- What is McKesson doing to ensure women have access to this critical, FDA-approved medication as quicky as possible?
- Can you give us a status update on how you are working with pharmacies to make this happen and when distribution will begin?
- What steps does McKesson take to ensure that its employees have access to Mifepristone?

Sincerely,

Gwen Moore
Member of Congress

McKESSON

March 6, 2024

The Honorable Gwen Moore
Member of Congress
2252 Rayburn House Office Building
Washington, DC 20515

Dear Representative Moore:

I am writing in response to your Questions for the Record following the House Ways & Means Committee hearing titled "Examining Chronic Drug Shortages in the United States."

Q: *What is the impact of McKesson not being a distributor on retail pharmacies that may have exclusive contacts with McKesson and want to carry Mifepristone? What is McKesson doing to ensure women have access to this critical, FDA-approved medication as quicky as possible? Can you give us a status update on how you are working with pharmacies to make this happen and when distribution will begin?*

A: McKesson plays a critical role in providing pharmaceuticals and medical supplies to hospitals, pharmacies, doctors' offices, clinics, and other healthcare providers so patients get the care they need. At this time, McKesson is being granted limited access to distribute mifepristone 200mg to certain certified CVS retail pharmacy locations serviced by McKesson, with an anticipated initial distribution date in late March. It is not uncommon for manufacturers of pharmaceuticals with special handling, a Risk Evaluation and Mitigation Strategy (REMS) program, or other unique requirements to have a restricted distribution channel. Other McKesson customers that wish to access mifepristone 200mg may reach out to the authorized distributor(s) selected by the manufacturers and will not be restricted from doing so by the terms of any McKesson contract.

Q: *What steps does McKesson take to ensure that its employees have access to Mifepristone?*

A: To the extent legally permissible, mifepristone is covered under McKesson's employee medical plans.

Sincerely,



Eugene Cavacini
Senior Vice President and Chief Operating Officer
McKesson Pharmaceutical Solutions & Services

McKesson Corporation
6555 State Hwy 161
Irving, TX, 75039

www.mckesson.com

HONORABLE MIKE CAREY
15TH DISTRICT OF OHIO

CONGRESS OF THE UNITED STATES
HOUSE OF REPRESENTATIVES
WASHINGTON, D.C. 20515

February 20, 2024

Dear Mr. Allan Coukell:

I have the distinct pleasure of representing Hikma Pharmaceuticals, USA, a top-10 U.S. generic medicines manufacturer which has facility in Columbus, Ohio. When I have met with them, they have shared concerns for the long-term sustainability of the U.S.-based generic manufacturing industry due to many systemic issues that you all raised in the hearing, which have led to drug shortages.

As a manufacturer and supplier of generic injectable medicines, what are your recommendations to protect the generic pharmaceutical manufacturing industry and ensure availability of affordable essential medicines for Americans? What policies should we consider that would bolster U.S.-based manufacturing of generic drugs?

In your opinion, what is the potential impact to our generic drug supply chain if we fail to invest in domestic manufacturing? What would be the single most important policy change Congress should consider to protect our U.S. medicine supply chain and support domestic generic pharmaceutical manufacturers?

Sincerely,

Mike Carey
Member of Congress

Ways and Means QFR Response

Question from Hon. Mike Carey (OH-15):

I have the distinct pleasure of representing Hikma Pharmaceuticals, USA, a top-10 U.S. generic medicines manufacturer which has facility in Columbus, Ohio. When I have met with them, they have shared concerns for the long-term sustainability of the U.S.-based generic manufacturing industry due to many systemic issues that you all raised in the hearing, which have led to drug shortages.

As a manufacturer and supplier of generic injectable medicines, what are your recommendations to protect the generic pharmaceutical manufacturing industry and ensure availability of affordable essential medicines for Americans? What policies should we consider that would bolster U.S.-based manufacturing of generic drugs?

In your opinion, what is the potential impact to our generic drug supply chain if we fail to invest in domestic manufacturing? What would be the single most important policy change Congress should consider to protect our U.S. medicine supply chain and support domestic generic pharmaceutical manufacturers?

Response:

Civica is a non-profit drug manufacturer based in Lehi, UT, and Petersburg, VA. Hikma is an important partner to Civica, as a manufacturer producing numerous sterile injectable drug products that are distributed under the Civica label.

While the United States benefits 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.

Our chief recommendation to improve the resilience of the drug supply, and thus the availability of essential medicines, is to change the incentives for drug purchasers. Currently, hospitals and

[1] For 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

other health care providers that purchase drugs – and the large, consolidated group purchasing organizations that do so on behalf of providers – are predominantly concerned with purchasing the lowest-cost generic version of a drug, without regard to its location of manufacture, quality maturity of the supplier, or likelihood of a quality failure that will cause a failure to supply.

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 especially when the market considers price instead of considering price alongside other important factors such as quality and supply resiliency.

In contrast, 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.

The Ways and Means Committee has a broad range of tools at its disposal, through its authority over provider reimbursement and quality, to support providers in purchasing generic essential medicines. For example, the Committee could require or incentive purchasers to have drug shortage prevention strategies that include:

- Evaluation of manufacturer quality history, to create market demand from manufacturers that are less likely to have a failure to supply;
- Maintenance of adequate buffer inventory to mitigate short-term supply disruptions, and
- Committed price-volume contracts that bring long-term stability to the market.

Taking quality into account when choosing suppliers is not synonymous with choosing domestic suppliers, but it will help quality domestic manufacturers maintain market share when competing against manufacturers in low-wage countries where FDA oversight is inconsistent and quality problems proliferate.

In addition, Congress may also wish to evaluate the impact of consolidated purchasing on the viability of the generic pharmaceutical industry, and the effect of federal payment policies that erode the already thin margins on low-cost pharmaceuticals.

The policies outlined above focus on using hospital payment and related levers to ensure that generic drug purchasing takes supply resiliency and quality into account, thus creating a stable market for quality manufacturers. However, Congress should also recognize that U.S. manufacturers are operating at a disadvantage when competing against countries whose governments have directly subsidized their own domestic pharmaceutical industries.

Many old, but essential generic injectable drugs sell for less than $3 per vial, and often less than $1. At these prices, it may not be commercially viable for companies to make the large investments required to build new U.S. manufacturing facilities. Therefore, for certain critical

product categories, such as cancer drugs or penicillin antibiotics, creating a viable domestic industry will require direct federal support.

While new manufacturing facilities typically cost hundreds of millions of dollars, the federal government, through the Administration for Strategic Preparedness and Response (ASPR), can make highly cost-effective one-time investments on a drug-by-drug basis to ensure that quality U.S. manufacturers have approval to make essential medicines and are ready to start producing when a drug shortage begins.

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 two years to develop an ANDA submission and obtain FDA approval to market the drug, the market is slow to respond to any shortage.

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 ASPR support, U.S. manufactures can develop targeted ANDA products and maintain a stockpile of active pharmaceutical ingredient specifically for the purpose of increasing U.S. manufacturing capacity and mitigating future drug shortages.

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Statement

of the

American Hospital Association

for the

Committee on Ways and Means

of the

U.S. House of Representatives

"Examining Chronic Drug Shortages in the United States"

February 6, 2024

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 House Committee on Ways and Means regarding the important topic of drug shortages in the United States.

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] This comes on top of the estimated $200 million annually that hospitals and health systems spend paying higher prices to acquire alternative therapies.[2] 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 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 more affordable health care by lowering costs; 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.

A 2019 report from the Food and Drug Administration's (FDA) Drug Shortages Task Force found there are three major root causes for drug shortages.[3]

1. **Lack of incentives to produce low margin drugs.** Manufacturers of older generic drugs, in particular, face intense price competition, uncertain revenue streams and high investment requirements, all of which limit their ability to invest in resilience.

2. **The market cannot identify and preferentially buy from those with better quality management practices.** All manufacturers must meet regulatory requirements for adherence to the FDA's Current Good Manufacturing Practices (CGMP), which set expectations for company processes to be allowed to do business in the U.S. marketplace. Some companies do more than simply conform to these requirements. They take additional steps intended to ensure a reliable supply of the drugs manufactured at their facilities. Currently, purchasers,

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[1] https://wieck-vizient-production.s3.us-west-1.amazonaws.com/page-Brum/attachment/c9dba646f40b9b5def8032480ea51e1e85194129
[2] https://www.fiercepharma.com/pharma/drug-shortages-cost-u-s-care-providers-at-least-200-million-annually-pose-patient-safety
[3] https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions

including hospitals and health systems, have only limited information to assess the state of quality management of any specific drug manufacturing facility and have little information linking the drug products they buy with the facilities where they were manufactured. The lack of information does not enable the market to reward drug manufacturers for mature quality management, back-up manufacturing capabilities or risk management plans, nor does it penalize manufacturers that fail to invest in modernization of their equipment and facilities to ensure a reliable supply.

3. **Logistical and regulatory challenges make it difficult for the market to recover after a disruption.** Over the past two decades, the drug supply chain has become longer, more complex and more fragmented as companies have located more production overseas and increased the use of contract manufacturers. Although typical markets would respond to a shortage by increasing production, the complexity of the supply chain, and logistical and regulatory challenges, can limit the ability of drug manufacturers to do so. When companies wish to increase production, they may have to obtain approvals from multiple different national regulatory bodies and/or find a new source of active pharmaceutical ingredients (APIs). If a new manufacturer wants to enter the U.S. market and start selling a drug in shortage, the manufacturer must first develop and file an application with the FDA and await its approval.

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.

Supply chain issues can adversely impact patient care by delaying treatment, worsening patients' health outcomes or requiring patients to switch to non-optimal treatment regimens. Congress should act to strengthen the ability of the pharmaceutical supply chain to respond when there is an emergency that creates a sudden rise in demand for medications or a significant disturbance in the supply chain that threatens the availability of critical medications. We recommend that Congress consider providing additional authorities to the FDA to mitigate and prevent drug shortages, such as by developing and disseminating manufacturing quality ratings that could enable hospitals and Group Purchasing Organizations (GPOs) to choose to do business with more reliable manufacturers, sending a market-based signal to support a reliable supply chain, and expanding the agency's authority to require manufacturers to notify the agency about unusual spikes in demand of essential medications. Congress could also consider expanding the authority of the FDA to require manufacturers doing business in the U.S. to have an emergency response plan that anticipates likely disruptions in the manufacture of critical drugs, describes what steps would be taken to rapidly restore production and to run drills practicing putting those steps in place. These could be embedded in the CGMP requirements.

Specifically, the AHA recommends that Congress enact legislation including:

1. **Diversifying manufacturing sites as well as sources of critical raw materials to ensure supply chain sustainability.** Currently, the U.S. relies heavily on both China and India for the API and key starting materials (KSMs) necessary to manufacture pharmaceutical products. Further, many manufacturers of these products utilize manufacturing facilities located in both China and India. The overwhelming reliance on a limited number of countries for these pharmaceutical products necessary to care for patients in the U.S. raises serious concerns and poses significant risks to patients and burden on health care workers should a disruption occur. Congress should encourage redundancy in the supply chain through policy initiatives focused on spurring diverse sites of production, including where possible, onshore or near shore manufacturing of critical API and KSMs.

2. **Increasing end-user inventories and incentivizing additional cushion.** The current just-in-time approach to supply chain logistics functions creates a hazard that becomes a reality during a significant supply chain disruption or emergent need to surge care delivery. Steps need to be taken to "feed" the supply chain with the goal of ensuring enough product is available, or capable of being made available, when demand increases. For example, supporting an increase in end-user inventory of critical medications as well as supplies held across the existing manufacturing and distribution infrastructure in the U.S. will help add necessary capacity to deal with interruptions in the availability of a critical drug. These actions may decrease the need for large national and state stockpiles, which can be difficult to manage and maintain, and present significant operating costs, product expiration and waste issues.

3. **Requiring the FDA to develop ratings** of the quality management processes of drug manufacturers which are predictive of supply chain and manufacturing vulnerabilities and make these quality ratings publicly available.

4. **Requiring drug manufacturers to disclose to the FDA the locations where their products are manufactured**, including contract manufacturer locations, as well as the locations from which they source KSMs, API and excipients used in their finished products, in order illuminate the extent of vulnerability for a product and to allow the development of targeted supply strengthening measures.

5. **Requiring drug manufacturers to notify the FDA of unusual spikes in demand** of essential drugs to allow the agency to take steps to mitigate or prevent any impacts on availability and prevent potential shortages.

6. **Requiring the FDA to identify those essential drugs**, including their KSM, API and excipients and component parts, that should have increased domestic

manufacturing capacity to improve the resilience of the U.S. drug and device supply chain and make recommendations to incentivize their production.

The AHA has been supportive of several bills that have sought to address supply chain issues which we believe will help address the issue of drug shortages. For example, this year, the AHA supported the **Mapping America's Pharmaceutical Supply (MAPS) Act (H.R. 6992)** in the House, which would require the Department of Health and Human Services to update its essential medicines list and create a database to help predict vulnerabilities in the U.S. pharmaceutical supply chain.[4]

We thank you for the opportunity to submit comments the House Committee on Ways and Means regarding drug shortages and look forward to continuing to work with you on this important issue.

[4] https://matsui.house.gov/sites/evo-subsites/matsui.house.gov/files/evo-media-document/matsui_038_xml_v4.pdf

American Academy of Dermatology Association

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U.S. House
Committee on Ways & Means

Examining Chronic Drug Shortages in the United States

February 6, 2024

Statement for the Record
American Academy of Dermatology Association

Chairman Smith and Ranking Member Neal, 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, *Examining Chronic Drug Shortages in the United States*.

Dermatologists diagnose and treat more than 3,000 diseases, including skin cancer, psoriasis, immunologic diseases, and many genetic disorders.[i] 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 patients to access affordable treatments. Generic oral and topical prescription drugs and drugs administered through injection or intravenously, such as antibiotics, saline, lidocaine, 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.[ii]

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

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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 which requires 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 forward 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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[i] The 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.
[ii] https://www.fda.gov/media/131130/download.

American College of Emergency Physicians®
ADVANCING EMERGENCY CARE

February 6, 2024

The Honorable Jason Smith
Chairman
Committee on Ways and Means
1139 Longworth House Office Building
Washington, D.C. 20515

The Honorable Richard Neal
Ranking Member
Committee on Ways and Means
1129 Longworth House Office Building
Washington, D.C. 20515

Dear Chairman Smith and Ranking Member Neal,

On behalf of the American College of Emergency Physicians (ACEP) and our nearly 40,000 members, thank you for holding today's critical hearing to examine the pervasive problem of chronic drug shortages. 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 lifesaving 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 survey 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).

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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, MD (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 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 comments to the Task Force. In October 2019, the Task Force issued a report entitled, "Drug Shortages: Root Causes and Potential Solutions." 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.[1]

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 medications, where the container itself is in shortage and the medication may be available in different

[1] 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

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.[2] 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.[3] 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.[4]

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 establishment making a drug to comply with manufacturing standards resulting in an FDA warning letter.[5] 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

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[3] Mazer-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

[4] The 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_shortages.pdf.

[5] United 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.

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 fifty 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 fillings 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."[6] 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.

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

[6] Drug Shortages: Root Causes and Potential Solutions

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.[7] 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 anti-kickback 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 manufactures, 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 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)

[7] Barlas 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/

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,



Aisha T. Terry, MD, MPH, FACEP
ACEP President

American College of Emergency Physicians®
ADVANCING EMERGENCY CARE

February 6, 2024

The Honorable Jason Smith
Chairman
Committee on Ways and Means
1139 Longworth House Office Building
Washington, D.C. 20515

The Honorable Richard Neal
Ranking Member
Committee on Ways and Means
1129 Longworth House Office Building
Washington, D.C. 20515

Dear Chairman Smith and Ranking Member Neal,

On behalf of the American College of Emergency Physicians (ACEP) and our nearly 40,000 members, thank you for holding today's critical hearing to examine the pervasive problem of chronic drug shortages. 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 lifesaving 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 survey 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).

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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, MD (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 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 comments to the Task Force. In October 2019, the Task Force issued a report entitled, "Drug Shortages: Root Causes and Potential Solutions." 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.[1]

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 medications, where the container itself is in shortage and the medication may be available in different

[1] 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

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.[2] 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.[3] 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.

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[6] Drug Shortages: Root Causes and Potential Solutions

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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,



Aisha T. Terry, MD, MPH, FACEP
ACEP President

February 6, 2024

The Honorable Chairman Jason Smith
House Ways and Means Committee
1139 Longworth House Office Building
Washington, DC 20515

The Honorable Ranking Member Richard Neal
House Ways and Means Committee
1129 Longworth House Office Building
Washington, DC 20515

Re: Hearing Examining Chronic Drug Shortages in the United States.

Dear Representatives Smith and Neal:

Thank you for holding this hearing on the causes and impacts of pharmaceutical drug shortages on patients in the United States. The American Society of Health-System Pharmacists (ASHP) is the largest association of pharmacy professionals in the United States, representing 60,000 pharmacists, student pharmacists, and pharmacy technicians in all patient care settings, including hospitals, ambulatory clinics, and health system community pharmacies.

We are a critical source of information regarding ongoing drug shortages. We list every drug shortage reported on our drug shortage database as soon as it is investigated and confirmed, usually within 24-72 hours.[1] We also provide practitioner-focused resources to help the healthcare community manage shortages. Examples include information on unapproved drugs and unlabeled uses (when well-researched and reported to be safe and effective); recommendations for therapeutic alternatives; drug to drug comparisons and comparisons within individual drug classes; and safety recommendations.

Status of the Pharmaceutical Drug Supply Chain: ASHP works closely with the Food and Drug Administration (FDA) to monitor pharmaceutical drug shortages. Our members have witnessed the impact pharmaceutical drug shortages have on patient care. We have found that pharmaceutical drug shortages are not being resolved and new shortages are increasing. Specifically, ongoing and active shortages are the highest since 2014. Shortages of local anesthetics and basic hospital drugs, albuterol solution, common oral and ophthalmic products, and ADHD treatments are affecting significant numbers of organizations and patients. Chemotherapy drugs, often without alternatives, are increasingly in short supply and have returned to the list of top-five drug classes.

ASHP makes the following attached recommendations that will are within the Committee's jurisdiction.

Diversity of Supply Chain: Ensuring diversity in the drug supply chain is critical to providing the resiliency necessary to weather increases in demand as well as disruptions in supply, whether foreign or domestic. Not only will this avoid disruptions due to quality and supply issues abroad, but also domestic disruption. Without diversity of production, a disruption either domestically or abroad can result in severe shortages. Domestic manufacturing is not immune from disruptions that lead to

[1] https://ashp.az1.qualtrics.com/jfe/form/SV_25KOx5N9FJYhuyp and https://www.ashp.org/drug-shortages/current-shortages.

shortages. Hurricane Maria devastated the island of Puerto Rico in 2017, resulting in shortages of small-volume parenteral solutions (SVPs) like saline or dextrose.[2] Last year, Pfizer's North Carolina plant was struck by a tornado, damaging 40,000 pallets of packaging supplies and finished products.[3] [4] Manufacturing diversity and redundancy, including geographic diversity, should be prioritized to ensure manufacturing resilience and to reduce shortages. Critical to a strong and diverse pharmaceutical supply chain is transparency into FDA inspections of domestic and foreign production facilities.

Domestic Production: While diversity in the supply chain is critical to its elasticity, the FDA should be directed to identify key starting materials, active pharmaceutical ingredients, and finished dosage forms of essential medicines, including vaccines, that should have domestic manufacturing capacity to improve the resilience of the U.S. drug supply, and incentivize their production without limiting access to foreign sources of these products. Financial incentives, such as grants or tax incentives, would help facilitate these efforts.

Quality of Pharmaceutical Drugs are Impacting the Supply Chain: Deficiencies in the quality of the manufacturing process as well as the final product is exacerbating pharmaceutical drug shortages. For example, earlier this year, FDA investigations of Intas Pharmaceuticals' generic manufacturing plant in Gujarat, India, raised serious concerns about the plant's data collection, test controls and procedures, quality controls, and compliance with written procedures that all ultimately raise questions about access to quality prescription drugs.[5] Reducing shortages of medications requires not merely increased production, but also bolstering the reliability of the manufacturing processes. Requiring the FDA to provide greater transparency, as well as the ratings of the manufacturer quality management processes that are predictive of supply chain and manufacturing vulnerabilities, will ensure continued supply of these life-saving pharmaceutical drugs. Transparency in drug manufacturing quality will allow health systems and pharmacies to make more informed decisions about the products they buy.

Pass-Through Payments: Medicare payment policy for inpatient and provider-administered generic drugs, particularly inclusion of inpatient drug costs in diagnosis-related groups (DRGs) encourages healthcare providers and their group purchasing organizations (GPOs) to aggressively negotiate the price of generic drugs and shift purchase volume to lower cost manufacturers. To encourage greater investment in manufacturing capacity and quality, federal policy should provide manufacturers of critical generic drugs with greater certainty of their ability to recover their investment and receive purchase volume for these products. Such policy should also give healthcare providers certainty that they can rely on the manufacturer to provide a particular level of supply for the term of the contract. ASHP recommends that the Centers for Medicare & Medicaid Services (CMS) provide an add-on

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[2] https://www.fda.gov/drugs/drug-safety-and-availability/fda-works-help-relieve-iv-fluid-shortages-wake-hurricane-maria
[3] https://cdn.pfizer.com/pfizercom/Rocky-Mount-Update-31JUL23.pdf
[4] https://www.ashp.org/-/media/assets/advocacy-issues/docs/GRD-Letter-to-EC-on-SVP-Shortages; https://www.reuters.com/business/healthcare-pharmaceuticals/pfizer-says-supply-some-drugs-may-be-disrupted-after-nc-tornado-2023-07-24/
[5] https://www.fiercepharma.com/manufacturing/burn-after-reading-fda-blasts-intas-cascade-failures-after-investigators-find-heaps and https://www.fda.gov/media/164602/download.

payment to providers for critical generic drugs determined by the U.S. Department of Health and Human Services (HHS) to be at risk of experiencing a shortage if those providers certify that they have entered a contract to acquire at least 50% of their historical purchase volume for those products via long-term contracts.

- To ensure manufacturers invest in supply chain stability and quality, the contract must include a requirement that the manufacturer will maintain a six-month buffer supply of finished product, and include meaningful penalties for failure to supply contracted products, including when manufacturing disruptions result from regulatory violations or supplier disruptions.
- To receive add-on payments, providers must ensure that they enter long-term supply contracts with manufacturers that participate in FDA's quality manufacturing maturity (QMM) program and voluntarily make their QMM metrics publicly available.[6]
- Providers and manufacturers could attest to meeting these requirements rather than providing proprietary contract information to HHS.
- Providers should be free to delegate long-term supply contracting to their GPO to meet these requirements.
- To minimize the administrative burden, add-on payments should be made based on the provider's total Medicare spend on the contracted drug product, rather than requiring per-beneficiary accounting for medication use.

Buffer Supplies: Encouraging healthcare providers and their distributors to maintain a buffer supply of critical medicines would reduce the impact of manufacturing disruptions on patient care. ASHP recommends that the federal government provide low- or no-cost financing to encourage private sector maintenance of a buffer inventory of critical drugs.[7]

- Providers and distributors should continue to have discretion to determine what products they stockpile.
- Providers should continue to be free to contract with GPOs, drug distributors, or manufacturers to manage storage and rotation of drugs stockpiled on their behalf.
- Private sector buffer supplies should be phased in slowly to minimize the risk of a demand surge that could result in shortages as providers and distributors build their stockpiles.

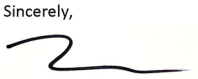
ASHP thanks you for holding this important hearing and considering our recommendations. We look forward to continuing to work with you to ensure Americans have access to the life-saving medications they need. If you have questions or if ASHP can assist your office in any way, please contact Frank Kolb at fkolb@ashp.org.

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[6] https://www.bloomberg.com/news/articles/2023-05-18/teva-plans-cuts-to-generic-drug-production-amid-shortages#xj4y7vzkg

[7] Recommendations from ASHP and other healthcare providers in 2021 called for incentivizing the creation of private-sector reserves of essential medicines, medical devices, and supplies not adequately provided by the Strategic National Stockpile. (https://www.ashp.org/News/2021/12/16/healthcare-groups-release-drug-supply-chain-recommendations)

Sincerely,



Tom Kraus
American Society of Health-System Pharmacists

ASSOCIATION OF STATE AND TERRITORIAL HEALTH OFFICIALS

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2July 7, 2023

The Honorable Cathy McMorris Rodgers
Chair
House Energy & Commerce Committee
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Mike Crapo
Ranking Member
Senate Committee on Finance
219 Dirksen Senate Office Building
Washington, D.C. 20510

Dear Chair Rodgers and Ranking Member Crapo:

On behalf of the Association of State and Territorial Health Officials (ASTHO), we are grateful for the opportunity to support policy development and solutions to address the increase in drug shortages impacting our country's public health and healthcare systems. Our comments are focused on current examples of how shortages are impacting patient care and recommendations to support state and territorial health agencies.

ASTHO is the national nonprofit organization representing the state and territorial public health agencies of the United States, U.S. territories, and Washington, D.C. ASTHO's members, the chief health officials of these jurisdictions, are dedicated to formulating and influencing sound public health policy and assuring excellence in state-based public health practice.

There has been substantial national attention on the impact of drug shortages across our country. The public health impact of drug shortages is significant and jeopardizes progress toward treating public health threats, such as syphilis and other childhood illnesses. For example, there are several treatment options available to those with tuberculosis. Rifapentine is part of a 12-week treatment regimen for latent tuberculosis when combined with weekly Isoniazid. This specific regimen is often preferred because it is shorter than the other treatment regimens and is easier for a patient with its once-weekly schedule, increasing the likelihood of adherence. However, there have been instances in which patients who were started on this regimen were required to switch to a different regimen as a result of the current shortage of Rifapentine, which not only decreases the likelihood of their adherence to the treatment but also potentially increases the likelihood of them developing resistance to their medication.

Similarly, there is a current shortage of penicillin G benzathine (Bicillin L-A), which is the only approved and acceptable treatment to treat syphilis in pregnant people. Untreated syphilis in pregnant women can cause miscarriage, stillbirth, or possibly contribute to a baby's death after their birth.[1] Currently, the United States is experiencing a surge of syphilis, as reported cases of syphilis have increased by 74% since 2017 and congenital syphilis cases have increased by 203% in the past five years.[2] State health agencies have been reporting shortages of Bicillin L-A for several months. In at least one state, local health departments have been advised to use Bicillin L-A to treat only those diagnosed with primary and

[1] https://www.cdc.gov/nchhstp/pregnancy/effects/syphilis.html#:~:text=Syphilis%20in%20pregnant%20women%20can,the%20infection%20as%20a%20newborn.

[2] https://www.cdc.gov/std/statistics/2021/default.htm#:~:text=Reported%20cases%20of%20syphilis%20(all,in%20the%20past%20five%20years.

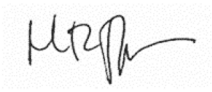
secondary syphilis, along with those who are pregnant. There is also a shortage of critical chemotherapy medications such as Carboplatin[3], Methotrexate[4], and Cisplatin[5] that has forced hospitals in some states to implement contingency and/or conservation strategies that directly impact patient care. Overall, we cannot overstate our concerns over potential outbreaks considering the lack of access to these critical medications. Simply put, this crisis is jeopardizing the health and well-being of countless Americans and impacting our ability to interrupt the spread of public health threats.

Recommendations

1. Establish a clearinghouse of existing drugs, medical countermeasures, and other critical products such as infant formula[6] to increase visibility and support state and territorial health agencies' understanding of potential shortages and their impact throughout our healthcare system and other related factors that may be impacting our medical supply chain.
2. Convene a taskforce comprised of representatives from federal public health agencies, drug manufacturers, and state, territorial, local, and tribal public health agencies to better understand the current issues related to drug shortages and develop a plan of action to be submitted to Congress.
3. Review existing manufacturing infrastructure to determine alternatives that will reduce the likelihood of a shortage and/or respond to an outbreak.
4. Explore medication exchange processes that exist between states for opportunities to streamline such exchanges and reimbursement of medications during shortages or periods of constrained supply.
5. Improve the current system for reporting drug shortages to delineate specific shortage areas, as well as report on localized areas in which there are supply-related issues.

Thank you for the opportunity to contribute to this important work. We look forward to continuing the conversation in the future. Please contact Jeffrey Ekoma, ASTHO's senior director of government affairs, at jekoma@astho.org for additional information.

Sincerely,



Michael Fraser, PhD, MS, CAE, FCPP
Chief Executive Officer
Association of State and Territorial Health Officials

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[3] https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Carboplatin%20Injection&st=c

[4] https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Methotrexate%20Injection&st=c

[5] https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Cisplatin%20Injection&st=c

[6] https://www.hhs.gov/formula/index.html

CHADD Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD)

February 20, 2024

The Honorable Jason Smith
Chairman, Ways and Means Committee
1011 Longworth House Office Bldg.
Washington, D.C., 20510

The Honorable Richard Neal
Ranking Member, Ways and Means Committee
372 Cannon House Office Building
Washington, DC 20510

RE: Examining Chronic Drug Shortages in the United States Hearing House Committee on Ways and Means, February 6, 2024

CHADD appreciates the opportunity to submit a statement for the record on the above-mentioned hearing of the House Committee on Ways and Means (the Committee).

CHADD is recognized as the national clearinghouse for objective information about Attention-Deficit/Hyperactivity Disorder (ADHD) and operates the National Resource Center on ADHD (including a call center), an evidence-based program funded by the Centers for Disease Control and Prevention (CDC). We are the largest advocacy group for individuals with ADHD.

CHADD's General Comments:

CHADD thanks the Committee, specifically Rep. Kevin Hern and Rep. Don Beyer, for recognizing *the current significant shortage of ADHD prescription stimulant medications in the U.S.* during your February 6, 2024, drug shortages hearing. We urge the Committee to develop policy measures that directly address the ADHD stimulant medication shortage. Such measures are crucial to the, at least, 17 million individuals living with ADHD in the United States**. Many of these people living with ADHD are on Medicaid, as their income is 33% lower than the income of people without ADHD, and their lack of access to ADHD medication is a *serious public health concern*.**

Prescription stimulant medications, the most effective and most commonly prescribed medications for the treatment of ADHD, *can be life sustaining in the short term and lifesaving in the long term.* As discussed below, research shows that, compared to the general population, people with untreated ADHD have a shorter lifespan and are much more susceptible to suffering severe accidental injuries, driving accidents, substance use disorder, suicide, sexually transmitted diseases, obesity, diabetes II, and coronary heart disease. ADHD significantly contributes to the Youth Mental Health Crisis in the U.S. Further, the markedly high costs associated with untreated ADHD—ranging from $143 to $266 billion annually—make ADHD far too costly a disorder to leave untreated.

The U.S. Food and Drug Administration (FDA) and the Drug Enforcement Administration (DEA) have not been able to effectively respond to the shortage. Policy measures from the Committee are desperately needed.



CHADD Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD)

Specifically, CHADD asks that the Committee consider the following:

1. Develop policy measures that would enable whatever government entity is appropriate (The Surplus Agency) to maintain a surplus of ADHD stimulant medications. These policy measures would be modeled—as appropriate for Schedule II drugs—upon the example of Civica RX as described in the testimony of Mr. Allan Coukell, BSc at the Senate Finance Committee's December 5, 2023 drug shortage hearing and this Committee's February 6th drug shortage hearing.[1]

2. We ask the Committee to consider these elements of the Civica RX model in particular:

- Long-term purchase and supply contracts to add stability to the market, contracting directly with suppliers and purchasers, rather than through middlemen, if possible.
- Maintaining an approximately six-month buffer inventory of every drug.
- U.S. sourcing whenever possible, with the EU and Canada as a second choice. Do not source finished drugs or API from China or India unless there is no other source.
- Intensive quality oversight of suppliers.
- A single cost-plus price, available to every purchaser to ensure that ADHD stimulant medications are made equally available to independent pharmacies and big chain pharmacies and that these medications are equally available in all parts of the U.S., including rural and underserved areas. In this case, purchasers would not be hospitals as in the Civica RX model.

3. Because, in general, each patient finds that only one ADHD stimulant medication works for that patient, the surplus should contain a six-month supply of each type of ADHD stimulant medication. "The Surplus Agency" can confer with the FDA, CHADD's Professional Advisory Board, and the American Professional Society of ADHD and Related Disorders regarding the list of ADHD stimulant medications that should be maintained in surplus.

4. "The Surplus Agency" can give grants to researchers to determine on a fixed basis if the surpluses are adequate or should be increased. See for example,[2] the National Survey of Children's Health and Trends in Stimulant Prescription Fills Among Commercially Insured Children and Adults — United States, 2016–2021.

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[1] https://www.finance.senate.gov/imo/media/doc/1205_coukell_testimony.pdf

[2] National Survey of Children's Health (NSCH) and CHADD, Understanding ADHD, *General Prevalence*, http://chadd.org/Understanding-ADHD/About-ADHD/Data-and-Statistics/General-Prevalence.aspx (Last updated 2024); Danielson ML, Bohm MK, Newsome K, et al. MMWR Morb Mortal Wkly Rep 2023;72:327–332. http://dx.doi.org/10.15585/mmwr.mm7213a1



CHADD Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD)

Background on the ADHD Drug Shortage:

Since October 2022, CHADD has received a significantly higher than normal number of calls about the nationwide shortage of ADHD stimulant medications. This drug shortage has reached crisis level. We have heard, for example, reports of pharmacies being charged, or charging, much higher prices for ADHD prescription stimulant medication, no longer accepting insurance, and not having the medication. Individuals report running from one pharmacy to another in search of their medication. All components[3] of the ADHD stimulant medication supply chain may well be playing a role (*e.g.*, manufacturers, distributors, PBMs), as well as measures to address this country's opioid epidemic. For example, under the nationwide opioid settlements, distributors are limiting the amount of all controlled substances pharmacies can stock.[4]

The current ADHD prescription stimulant medication shortage is not the first such shortage, but it is the worst. Individuals prescribed ADHD medications and their families frequently tell CHADD about their difficulties in obtaining ADHD medications. The status of ADHD stimulants as Schedule II controlled substances results in serious supply disruptions and recurring drug shortages that date back almost a decade. In a 2016 survey of more than 1,000 CHADD members, more than half of respondents indicated that they or a family member diagnosed with ADHD have problems accessing their prescribed ADHD medications.[5]

What is ADHD? ADHD is a neurodevelopmental disorder, characterized by developmentally inappropriate inattention, and in many cases, impulsivity and hyperactivity as well[6] and has a strong biological basis,[7] including structural and chemical abnormalities in the brain.

These symptoms result in significant functional impairments in daily life, reflected in impaired functioning in major life activities (home, school, social, occupational, etc.) and lead to high economic and societal costs:

- Research has shown **economic costs of ADHD in the United States** that range from **$143 to $266 billion (B), annually**.[8]

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[3] Mulcahy, Andrew W. and Vishnupriya Kareddy, Prescription Drug Supply Chains: An Overview of Stakeholders and Relationships. Santa Monica, CA: RAND Corporation, 2021. https://www.rand.org/pubs/research_reports/RRA328-1.html.

[4] AmerisourceBergen Injunctive Relief, *into effect July 1, 2022*, https://www.amerisourcebergen.com/pharmaceutical-distribution/fighting-the-opioid-epidemic/injunctive-relief/faq ; Distributor Settlement Agreement, dated July 21, 2021, https://nationalopioidsettlement.com/wp-content/uploads/2023/02/Final-Distributor-Settlement-Agreement-3.25.22-Final-Exhibit-C-as-of-5.27.22-Exhibit-G-and-I-as-of-02.22.23.pdf

[5] CHADD, Health Insurance Survey 2016 (unpublished Nov. 2016).

[6] Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD), Understanding ADHD, *About ADHD-Overview*, https://chadd.org/about-adhd/overview/ (Last updated 2023).

[7] CHADD, Understanding ADHD, *About ADHD, The Science of ADHD*, https://chadd.org/about-adhd/the-science-of-adhd/ (Last updated 2023).

[8] Jalpa A. Doshi., et al., *Economic Impact of Childhood and Adult Attention-Deficit/Hyperactivity Disorder in the United States*, 51:10 Journal of the American Academy of Child and Adolescent Psychiatry 990 (2012).



Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD)

- Youth with ADHD have substantially lower standardized achievement scores and school grades, as well as higher rates of grade retention and school dropout than their peers.[9]

- For individuals with ADHD, compared to those without, "employment reduction is between 10 and 14 percentage points, the earnings reduction is approximately 33%, and the increase in social assistance is 15 points."[10] **Thus, many people with ADHD are on Medicaid.**

- Schools spend $4,689 more per year educating a student with ADHD than a student without ADHD, including costs incurred through grade retention, and disciplinary incidents.[11]

- The total economic burden to families of raising a child with ADHD over the course of child development has been found to be, on average, more than five times greater than raising a child without ADHD.[12]

- A meta-analysis finding that "childhood ADHD was significantly associated with adolescent and adulthood arrests, convictions, and incarcerations" also indicated that early treatment of ADHD could change these outcomes.[13]

Prevalence of ADHD: ADHD is one of the most common mental health conditions in youth in the U.S. and **generally persists into adulthood with associated symptoms and impairments**.[14] At least 5.3 million (8.7%) children and adolescents are now currently diagnosed with ADHD in the

[9] Barkley, Russell A. (Ed), Attention-deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment (4th ed), Part I, Chapter 6, Educational Impairments in Children with ADHD, (p. 169,) New York, NY, US: Guilford Press, Kindle Edition.

[10] Fletcher, Jason M., *The effects of childhood ADHD on adult labor market outcomes*, Health Econ. Feb;23(2):159-81 (2014), abstract available at https://pubmed.ncbi.nlm.nih.gov/23427026/

[11] Robb, J. A., et al. (2011). *The estimated annual cost of ADHD to the US education system*. School Mental Health, 3,169–177. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4123753/

[12] Zhao, Xin, et al., *Family Burden of Raising a Child with ADHD*, Journal of Abnormal Child Psychology, 47:1327–1338 (2019), abstract available at https://pubmed.ncbi.nlm.nih.gov/30796648/

[13] Mohr-Jensen, C. et al., *A meta-analysis and systematic review of the risks associated with childhood attention-deficit hyperactivity disorder on long-term outcome of arrests, convictions, and incarcerations. Clinical Psychology Review*, 48, 32-42, (2016), abstract available at https://pubmed.ncbi.nlm.nih.gov/27390061/

[14] Doshi, Jalpa A., et al., *Economic Impact of Childhood and Adult Attention-Deficit/Hyperactivity Disorder in the United States*, 51:10 Journal of the American Academy of Child and Adolescent Psychiatry 990 (2012); See also Pliszka, Steven, et al. *Practice Parameters for the Assessment and Treatment of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder*, 46:7 Journal of the American Academy of Child and Adolescent Psychiatry 894, 895 (2007), available at https://www.aacap.org//App_Themes/AACAP/docs/practice_parameters/jaacap_adhd_2007.pdf



Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD)

U.S.,[15] and up to 5% of adults have an ADHD diagnosis or experience ADHD symptoms but have not yet been diagnosed.[16]

Treatment of ADHD: The longest and largest study of ADHD treatment found **prescription central nervous system stimulant medication to be the primary treatment option** to safely and effectively reduce the core symptoms of ADHD (as opposed to the symptoms of co-occurring disorders).[17]

Public Health Problem:[18] *A growing body of research* indicates people with ADHD are at higher risk of poor health outcomes compared to the general population and are subject to a shortened life expectancy—**if they are untreated.** The findings clearly show that ADHD must now be viewed as a *public health problem* producing a substantial impact on the health, quality of life, and economic viability of the U.S. population.

Specifically, research studies[19] have documented a greater occurrence of:

- *Nonspecific lung, cardiovascular, and other chronic diseases* in adults with ADHD.
- *Greater substance use/abuse*: 20-30% of teens and adults with ADHD may qualify for a substance use disorder diagnosis.
- *Obesity*: Teens and adults with ADHD are 1.5-3x more likely to qualify as obese.
- *Eating disorders*: 15-20% of females with ADHD qualify for a diagnosis.
- *Accidental injuries* (wounds/lacerations, broken bones, burns, poisonings, closed head trauma, etc.): Children, adolescents, and adults with ADHD have a 1.5-3x greater likelihood of accidental and repeated injury, pedestrian-automobile accidents, cyclist-auto accidents, and vehicular driving accidents.

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[15] CHADD, Understanding ADHD, *General Prevalence*, http://chadd.org/Understanding-ADHD/About-ADHD/Data-and-Statistics/General-Prevalence.aspx (Last updated 2024)

[16] Danielson ML, Bohm MK, Newsome K, et al. Trends in Stimulant Prescription Fills Among Commercially Insured Children and Adults — United States, 2016–2021. MMWR Morb Mortal Wkly Rep 2023;72:327–332. http://dx.doi.org/10.15585/mmwr.mm7213a1

[17] *See*, The MTA Cooperative Group, *A 14-Month Randomized Clinical Trial of Treatment Strategies for Attention-Deficit/Hyperactivity Disorder*, 56:12 Journal of the American Medical Association (1999), available at http://archpsyc.jamanetwork.com/article.aspx?articleid=205525 ; Also see, CHADD, Understanding ADHD, About ADHD, Treatment of ADHD, https://chadd.org/about-adhd/treatment-of-adhd/

[18] *The Adverse Health Outcomes, Economic Burden, and Public Health Implications of Unmanaged Attention Deficit Hyperactivity Disorder (ADHD): A Call to Action to Improve the Quality of Life and Life Expectancy of People with ADHD*, Proceedings of the ADHD Public Health Summit Washington, D.C. October 7, 2019.

[19] Barkley, R. A. (2015). Health problems and related impairments in children and adults with ADHD. In R. A. Barkley (ed.) *Attention deficit hyperactivity disorder: A handbook for diagnosis and treatment (4th Ed)* (pp. 267-313). New York, NY: Guilford Press.



- *Exposure to traumatic events and victimization*: Rates of physical abuse are estimated to be 3x greater for children with ADHD.

- *Risky sexual behavior*: Earlier age at first sexual intercourse, greater number of sex partners, 4x risk for sexually transmitted disease, and 8-10x risk for teenage pregnancy.

- *Suicide attempts and completions* (3-5x greater risk due to impulsivity): Research has found that **ADHD should be viewed as a major health condition that confers** increased risk for early death due to suicide.[20]

- *Type II diabetes*: As a correlate of their greater rates of obesity, poorer diets, and limited exercise, teens and adults with ADHD are 2.8-3.3x more likely to develop Type 2 Diabetes.[21]

- *Coronary heart disease*: The factors cited just above, and the greater penchant for substance use and abuse, create a significantly greater risk for future coronary heart disease as early as age 27 and double the risk for dementia in later life.[22]

The human costs of untreated ADHD and why untreated or undertreated ADHD is a significant contributor to the Youth Mental Health crisis in the U.S.:

- Far before the pandemic, children's mental health and mental health care were declining in the U.S.[23] Suicide became the second most common cause of death among children (after accidents),[24] and suicide rates among Black children ages 5 to 11 greatly increased.[25] In general, lower socio-economic status was found to be associated with increased mental health problems in children and adolescents.[26]

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[20] *Barbaresi, William J.,* et al., Mortality, ADHD, and Psychosocial Adversity in Adults With Childhood ADHD: A Prospective Study, *Pediatrics 131:4 (2013), full article available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3821174/*

[21] Chen, J. J. et al. (2013). Association of attention-deficit/hyperactivity disorder with diabetes: a population-based study. Pediatric Research, 73, 492-496. Also Chen, M. H et al. (2018). Risk of Type 2 diabetes in adolescents and young adults with attention- deficit/hyperactivity disorder: A nationwide longitudinal study. Journal of Clinical Psychiatry, 79(3), 17m11607.

[22] Goodwin, R. D. et al. (2009). Do mental health problems in childhood predict chronic physical conditions among males in early adulthood? Evidence from a community based prospective study. *Psychological Medicine, 39(2), 301-311.*

[23] Whitney, D.G., et al., *US national and state-level prevalence of mental health disorders and disparities of mental health care use in children*. JAMA Pediatrics, 173(4), 389-391. (2019), *available at*: https://jamanetwork.com/journals/jamapediatrics/fullarticle/2724377

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CHADD Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD)

- **In 2007, children with ADHD** were found to have **higher health and mental health service use** than children with **any other mental health or neurodevelopmental disorder.**[27]

- During the pandemic, symptoms of anxiety, depression, other mental health disorders[28] and emergency department visits for suspected suicide attempts by adolescents[29] all increased. By early 2021, emergency department visits in the U.S. for suspected suicide attempts by adolescent girls were 51% higher and by adolescent boys, 4% higher, than for the same time period in 2019.[30]

- ADHD is one of the major, and most common, mental health conditions affecting youth,[31] and plays a part in other mental health concerns, including anxiety, depression, and many other psychiatric disorders, and—significantly—non-suicidal self-injury, suicidal ideation and deaths. (See above under Public Health Concern.)

- **At least two-thirds of individuals with ADHD have coexisting conditions, including many other psychiatric conditions**,[32] and the difficulties of dealing with them are compounded by the underlying ADHD.

- Research indicates that youths with ADHD develop depressive disorders at up to 5x the rate, and anxiety disorders at up to 3x the rate, of youths without ADHD.[33]

- Girls with ADHD have higher rates of non-suicidal self-injury and suicide than all youth without ADHD and boys with ADHD.[34]

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CHADD Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD)

In conclusion, CHADD appreciates the opportunity to submit a statement for the record for the House Committee on Ways and Means February 6, 2024, hearing on drug shortages. CHADD is available and prepared to discuss any questions regarding the aforementioned concerns.

On behalf of CHADD, thank you for accepting our statement, and we look forward to working with you further.

Sincerely,

Laurie Kulikosky

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Jeffrey Katz, PhD
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Duke | MARGOLIS INSTITUTE for Health Policy

Ways and Means Committee

United States House of Representatives

February 5, 2024

Dear Chairman Smith, Ranking Member Neal, and members of the Committee,

The Duke-Margolis Institute for Health Policy ("Duke-Margolis" or "the Institute") appreciates the opportunity to provide comments and recommendations regarding the pressing issue of chronic drug shortages.

The Duke-Margolis Institute's mission is to improve health, health equity, and the value of health care through practical, innovative, and evidence-based solutions. Duke-Margolis has conducted years of research and stakeholder engagement aimed at promoting drug supply chain reliability and preventing drug shortages, most recently including the work of the Duke-Margolis ReVAMP Drug Supply Chain Consortium that was founded in 2023. Through the Consortium, we're working to generate effective policy solutions that promote a reliable drug supply chain to improve patient outcomes by reducing the frequency and severity of drug shortages.

The recommendations herein do not necessarily represent the views of Consortium Members and are not intended to limit the ability of Consortium members to provide their own comments on behalf of their independent organizations, but are informed by the Institute's work with Consortium Members.

Since the Duke-Margolis ReVAMP Consortium's founding, we have published 3 major work products that outline promising recommendations to improve drug supply chain reliability. We recommend that Congress take action on these 3 areas:



1. **Advance Federal Coordination**. Congress should provide requisite authorities and funding to the HHS Supply Chain Resilience and Shortage Coordinator to lead a cross-cutting effort to reduce drug shortages, including funding for the establishment of a public-private partnership tasked with developing supply chain reliability measurement and tracking mechanisms.
2. **Improve Quality Management and Supply Chain Reliability Practices.** Congress should provide dedicated funding for FDA's Quality Management Maturity Program, and Congress should direct the establishment of a product-level Drug Supply Chain Reliability pilot program. Development of both of these initiatives could be led by the public-private partnership mentioned above.
3. **Enable Demand-Side Reforms for Reliability.** Congress should authorize and provide funding for CMS to establish a reliable drug supply payment adjustment to cover the cost to hospitals, outpatient clinics, physician offices, and other settings of shifting to more reliable purchasing practices, including:
    i. Purchasing through committed contracts
    ii. Purchasing from manufacturers that demonstrate reliability.

In this document, we summarize key recommendations in each of these three areas. We focus first and foremost on demand-side reforms for reliability, as those relevant policy actions are most squarely within the Ways and Means Committee's purview.

Impact and Root Causes of Chronic Drug Shortages

Drug shortages are a pressing and chronic issue. As of last week, over 100 drugs were on the U.S. Food and Drug Administration's (FDA) drug shortage list. About a third of these are essential medicines, and about 75% have been in shortage for over a year. Over 60% of drugs in shortage are sterile injectable drugs, a category of medicines commonly used to treat life-threatening conditions such as cancer and sepsis in hospitals and clinics across the country every day. Drug shortages are associated with higher mortality rates, medication errors, delays in life-saving cancer treatment and other critical medical procedures, and significant financial costs to the health care system.

The majority of drug shortages are caused by manufacturing quality issues. Many prescription drugs, especially more complex drugs such as sterile injectables, require specialized manufacturing facilities to ensure sterility, purity, and other critical product attributes. Too frequently, manufacturing quality issues are detected – for example, when a manufacturer runs final product testing on a batch of drug product, they may find a sterility, particulate, or other manufacturing quality issue. This may necessitate shutting down the production line, scrapping batches that have already been produced, and other remediation activities and delays. All of this may lead to the drug not being available in adequate quantities for patients.

Ultimately, this poor performance in manufacturing reflects problems in health care purchasing and payment. Payers and providers lack insights into manufacturers' supply chains and quality management practices and generally have not invested enough on their own into gaining further insights. Drug purchasers choose suppliers based primarily on price, not reliability. Contracting practices that are currently prevalent often enable purchasers to switch suppliers whenever a lower short-term price is available from another supplier—an understandable path to short-term cost savings, but one that contributes to manufacturer uncertainty about what volume they should produce. Reimbursement from the Centers for Medicare and Medicaid Services (CMS) in the hospital and outpatient settings is generally the same regardless of which generic supplier a healthcare institution chooses, creating further incentive for choosing the lowest-price option.

Manufacturers of these older generic medicines therefore compete by offering the lowest possible price, and resulting low margins make it difficult for the manufacturers to invest in equipment upgrades, risk management plans, and other steps that would ensure better quality management and reliability.

Chronic drug shortages occur most frequently in older, inexpensive, generic drugs. The FDA Drug Shortages Task Force report found that drugs in shortage have a median price of less than $9/dose, have been on the market for a median of 35 years, and usually have generic versions on the market. In addition, a report from IQVIA in 2023 found that over half of drugs in shortage are priced at less than $1 per extended unit. While generic medicines represent about 90% of prescriptions filled in the U.S., they represent less than 20% of U.S. prescription drug spending. Ensuring affordability of medicines for patients is an incredibly important priority. However, that priority is most important when considering new branded drugs that still have patent protection and tend to be more expensive. ***For older generic medicines, the primary barrier to patient access is availability, not affordability***.

Policy Solutions to Chronic Drug Shortages

Enable Demand-Side Reforms for Reliability

Since the root causes of chronic shortages are economic incentive issues, effective solutions should enable a shift to a new market equilibrium that places much more value on reliability in drug purchasing.

Duke-Margolis staff recently authored an article in Health Affairs entitled "Demand-Side Reforms to Prevent Drug Shortages: Medicare's Role In A Successful National Strategy." The article lays out policy options to prevent drug shortages, which we summarize here in the following paragraphs.

We propose a "reliable drug supply payment adjustment" that would adjust Medicare payments to hospitals based on whether they engage in reliable drug purchasing practices when buying certain essential generic medicines. We lay out two major criteria for what purchases could qualify for the payment adjustment.

The first is committed contracting. Committed contracting involves a commitment by the purchaser to buy a certain volume and by the manufacturer to supply that volume. In truly committed contracting models, meaningful financial penalties exist for both sides if their commitments are not met. Common provisions of committed contracting models include strong failure-to-supply language, fixed volumes with take-or-pay agreements, longer-term commitments, limited ability for price challenges, and centralized buffer inventories. This type of contract exists now, but the model is not very widely implemented. Increasing their use can help stabilize the market.

The second important criterion is purchasing from reliable suppliers. Developing evaluation tools such as FDA's Quality Management Maturity Program can provide clear and standardized information regarding the manufacturers that are investing in reliable production practices. There is more work to be done in developing and implementing these supply chain measurement and evaluation tools, and, as discussed further below, we recently outlined some steps that can be taken to advance such tools in a policy brief on this topic.

For a targeted list of essential generic medicines, we propose payments to hospitals for purchases that meet the "process measures" above. These payments would help to cover the cost of shifting to a new market equilibrium. Payments to support this shift toward reliability would likely be relatively affordable and cost-effective since the base prices of generic medicines are quite low on average.

These payments also may not need to be permanent. Incentive payments may be appropriate at first to cover the cost of shifting to more reliable purchasing, but as the market adjusts, CMS could transition to requiring certain practices that prove to be effective in preventing shortages. There is precedent for this approach to improving the way hospitals and health systems do business – for example, CMS issued incentive payments to hospitals for adopting Electronic Health Records in the early 2010s, and then gradually transitioned to reducing reimbursement rates for those who had *not* adopted EHRs as they became the industry standard and embedded in bundled payment rates.

"Outcomes measures", such as the hospital "Drug Shortage Scorecard" proposal from Brookings, could retroactively reward hospitals if they bought from manufacturers who actually delivered a reliable supply of a shortage drug. This would encourage providers, and the GPOs and wholesalers that act on their behalf, to expand the robustness of their supplier vetting and put committed contracts in place

with more reliable suppliers. Questions on this scorecard approach remain, including how often shortages can be fairly and accurately tied to missteps by a specific manufacturer(s), expectations for higher payments to address payment uncertainty, feasibility of program administration, and a need for coordination between CMS and FDA. However, if these questions could be addressed, outcomes-based payment programs would provide strong incentives for drug purchasers to use reliable suppliers. To support this, CMS and FDA could pilot the creation of a sample scorecard under a memorandum of understanding.

Improve Quality Management and Supply Chain Reliability Practices

As we've described, changes to payment and contracting for essential generic medicines will be most effective if payments can be carefully targeted and tied to accurate measures of supply chain reliability.

FDA's Quality Management Maturity Program is designed to evaluate manufacturing facilities based on their sustained commitment to quality management practices that can prevent drug shortages over time. This can be a critical tool in helping purchasers to identify more reliable suppliers. Congress should support the rapid development and implementation of QMM by allocating dedicated funding to it. While QMM has great potential, some refinements to the program are needed as well. In December, Duke-Margolis issued a policy brief on this topic, recommending that QMM be focused initially on essential, vulnerable drugs and the facilities that produce those drugs.

That issue brief also includes a recommendation for Congress to direct the development and piloting of a product-level Drug Supply Chain Reliability (DSCR) Program, building on FDA's QMM Program. The QMM Program assesses quality management practices at the manufacturing facility level. The insights generated by the program will be valuable for purchasing and contracting decisions. However, other important factors that contribute to supply chain reliability beyond the facility level and beyond the quality management domain, such as a manufacturer's backup raw material suppliers, manufacturing flexibilities and redundancies, inventory buffers, and risk management plans, are also necessary to consider. A DSCR Program that includes QMM evaluations as a primary input, but also encompasses other product-level aspects of supply chain reliability, will provide actionable information to purchasers looking to ensure their suppliers will deliver the drugs patients need, in adequate quantities, when they're needed.

Advance Federal Coordination

Drug supply chains are complex, and, as described above, effective solutions will require coordination across multiple federal agencies – CMS and FDA, but also ASPR, DoD, and others beyond HHS. Duke-Margolis last year published a white paper on this topic, including outlining a framework that could be used to guide the priorities of the recently announced HHS Supply Chain Resilience and Shortage Coordinator position. Congress should provide this Coordinator with the requisite authorities and funding to lead a cross-cutting effort to improve drug supply chain reliability, including producing measurable reductions in the frequency and severity of shortages of critical drugs. This cross-cutting effort should include the establishment of a public-private partnership that works to develop improved measures of supply chain reliability to help accomplish the goals laid out above. A public-private partnership model would ensure engagement from private sector stakeholders including manufacturers, health care providers, group purchasing organizations, wholesalers, and others in the development and implementation of necessary reforms to improve drug supply chain reliability.

Conclusion

Many of the most important and effective policy solutions that can help to address the economic root causes of drug shortages lie within the purview of this committee, and of the Senate Finance Committee, which has also held recent hearings on this topic. The Duke-Margolis Institute appreciates the bipartisan, bicameral efforts underway to address this critical challenge and the opportunity to contribute to the solution by providing this comment.

We thank the Committee for its efforts, and look forward to continued collaboration to prevent chronic drug shortages.

Sincerely,

Stephen Colvill

Thomas Roades

Gerrit Hamre

Cameron Joyce

Mark McClellan



Charles N. Kahn III
President and CEO

STATEMENT
of the
Federation of American Hospitals
to the
U.S. House of Representatives
Committee on Ways and Means

Re: "Examining Chronic Drug Shortages in the United States"
February 6, 2024

The Federation of American Hospitals (FAH) submits the following Statement for the Record in advance of the House Committee on Ways and Means hearing entitled "Examining Chronic Drug Shortages in the United States." Managing drug shortages is a continuing struggle for hospitals, impacting patient care, hospital financial health, staffing and information technology requirements. We appreciate the Committee's leadership in exploring what factors are causing chronic drug shortages in America.

The FAH is the national representative of more than 1,000 leading tax-paying 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.

Persistent drug shortages are having an ongoing, negative impact on our patients. They have far-reaching implications, including the implementation of time-consuming and costly measures to ensure our hospitals continue to provide world-class care. Our hospitals report that drugs in short supply are commonly prescribed, essential products, such as opioid injectables, saline, sodium bicarbonate, sterile water, epinephrine, and dextrose.

The health care supply chain is complex, with many active participants involved in ensuring adequate access to drugs used to provide hospital care. 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.

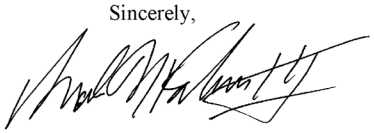
750 9th Street, NW, Suite 600, Washington, DC 20001 • 202-624-1500 • FAX 202-737-6462 • www.fah.org

We urge the Committee to consider policy proposals to require drug manufacturers to report potential drug and Active Pharmaceutical Ingredient (API) shortages to the Food and Drug Administration (FDA) in a timely manner. Timely reporting of potential shortages allows the FDA to proactively address and mitigate the impact on patients, health care providers and hospitals, and the broader health care system. By having access to early warnings, the FDA can work collaboratively with manufacturers to identify alternative sources, encourage domestic production, give an early warning to health care providers, and implement strategic measures to prevent or minimize the impact of shortages. This requirement helps maintain a consistent supply of vital medications while fostering transparency and accountability within the pharmaceutical industry, ultimately safeguarding the well-being of patients who depend on these essential drugs.

Finally, we encourage the Committee to pursue policies that create incentives for domestic manufacturing of drugs with a focus on increasing the domestic production of generic drugs, hospital injectables, and hospital products. This approach reduces dependency on foreign sources and bolsters the responsiveness of the supply chain to meet the demands of hospitals and health care facilities. Encouraging the production of generic drugs domestically is essential for enhancing the resilience of our nation's pharmaceutical supply chain, ensuring a stable and reliable source of medications for health care providers and, most importantly, patients.

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 me or a member of my staff at (202) 624-1534.

Sincerely,



HDA
Healthcare Distribution Alliance
HEALTH DELIVERED

Healthcare Distribution Alliance

Statement for the Record
House Committee on Ways and Means
U.S. House of Representatives

February 20, 2024

"Examining Chronic Drug Shortages in the United States"

1275 Pennsylvania Avenue NW, Suite 600, Washington, DC 20004 • Main (202) 963-1200 • Web www.hda.org

Statement for the Record – Healthcare Distribution Alliance

On behalf of the Healthcare Distribution Alliance (HDA), we thank you for the opportunity to provide an overview of the pharmaceutical distribution industry and share our perspective on drug shortages. We applaud the Committee's efforts to examine the issue of drug shortages and the impact shortages have on patients and the pharmaceutical supply chain. We agree that drug shortages deserve attention, and we support changes that will preserve the strength and efficiency of the pharmaceutical supply chain, along with patient access, while tackling this challenging issue.

Overview of Pharmaceutical Distributors

HDA's 37 distributor members form the backbone of the U.S. pharmaceutical supply chain, handling approximately 95 percent of medicines dispensed or administered in the United States.[1] We understand the risk that drug shortages pose, and distributors work to address them daily. Distributors mitigate and manage drug shortages as a core part of their business operations. Distributors ensure supplier diversity and maintain regular communication with supply chain partners. These partners include the manufacturers of brand, specialty, and generic medicines. Partners also include more than 330,000 downstream customers distributors serve every day, including hospitals, clinics, physician offices, and pharmacies in every state in the country.

Overview of Drug Shortages

The issue of drug shortages is highly nuanced and dynamic. Distributors' unique role in the supply chain provides a perspective on the upstream availability of products and the downstream needs of the provider community. Distributors can look to historical drug shortage trends to gauge potential shortages in the future.

The drivers of drug shortages vary significantly, and as a result, there is no single or simple solution to prevent drug shortages. Essentially, drug shortages can be divided into two categories: supply-driven shortages and demand-driven shortages. Supply-driven shortages occur because of upstream disruptions to manufacturing capacity or due to a natural disaster or geopolitical unrest.[2] Demand-driven shortages occur when available supply is outstripped by unforeseen situations, such as medical surges resulting from a natural disaster or potentially a disease outbreak.[3]

Unfortunately, our nation faces challenging drug shortages driven by supply and demand issues affecting the availability of certain medicines. Federal agencies, Congressional committees, and the Administration have made solving drug shortages a national priority. Solutions being considered to address drug shortages include increasing domestic manufacturing capacity, extending the shelf-life of drugs, increasing stockpiling or buffer inventory, and adjusting reimbursement for certain generic drugs.

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[2] Healthcare Distribution Alliance. Understanding Supply-Driven Shortages. Published 2023. https://www.hda.org/getmedia/dada514b-7d2d-4d15-8c91-ed6f05c48443/HDA-Understanding-Supply-Driven-Drug-Shortages-Factsheet.pdf.

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How Distributors Mitigate Drug Shortages

HDA and our members understand the critical impact of drug shortages on patients and providers. Distributors work to mitigate shortages by building redundancy into their sourcing programs and everyday business practices. They do this by purchasing medicines from numerous suppliers in multiple regions of the world.[4] Distributors also work to forecast demand and anticipate demand surges.[5] Specifically, distributors use demand forecasting to inform anticipatory purchasing decisions, such as preparing for seasonal demand spikes for cold and flu season.[6]

How Distributors Manage Drug Shortages

When drug shortages occur, distributors manage them to ensure consistent and reliable access to available prescription medicines. Distributors use tools such as fair-share allocation, which ensures product availability to as many customers as possible.[7] Fair-share allocation is beneficial to facilities that do not have the financial resources or physical capability to hold large inventories of drugs.[8]

Generic Drug Shortages

The passage of Hatch-Waxman created today's generic drug industry. This law was intended to lower the price of medicines by increasing generic competition. Since the passage of this law in 1984, thousands of generic medicines have entered the marketplace, resulting in trillions of dollars of savings[9] for payers and consumers. While generic drug prices have come down, in many cases, they have come down so far that generic manufacturers cannot remain in the market or are forced to operate on unsustainable margins.

How Distributors Support Generic Stability and Reliability

The generics industry has adapted to the realities of today's payer-driven marketplace, including prices from government-funded programs such as Medicare and Medicaid. In almost all cases, Medicare and Medicaid demand that the lowest-priced, clinically effective product be made available to beneficiaries.

Distributors recognize the economic reality of the generics marketplace, and as a result, they focus on creating stability and reliability for both upstream manufacturers and downstream customers. When partnering with manufacturers, distributors focus on the ability of the manufacturer to produce a reliable supply at a sustainable price. To promote stability with the manufacturer, distributors often partner with manufacturers on a long-term basis.[10]

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Economic Dynamics That Affect Provider Reimbursement

Each stakeholder in the pharmaceutical supply chain has faced pressure to lower drug prices for the last 40 years. This financial pressure has resulted in stakeholders often operating in a constrained marketplace. Distributors must source products not only from reliable and dependable manufacturers, but at prices that the downstream payer-driven market demands.

Healthcare providers, including but not limited to pharmacists, often face financial pressures from payers through low reimbursement rates, particularly for generic medicines. As a result, providers often look for the lowest-priced drugs when they order from their distributors.

HDA Solutions to Prevent Drug Shortages

While some financial pressures confronting generic manufacturers are direct byproducts of the free market system, HDA and its members want to share a few recommendations that could help combat drug shortages.

Federal Coordination – Given the unique position distributors have in the supply chain, we are willing to work collaboratively with our downstream trading partners to share information with government officials when we experience demand surges that have the potential to strain available supply. Partnerships with the federal government and trading partners may increase transparency and visibility throughout the supply chain to better assess vulnerabilities. Increased transparency efforts must include confidentiality agreements, so information is not pre-maturely shared, thus creating potential disruptive purchasing behaviors.

Strategic Investment - The federal government should invest in domestic manufacturing capabilities to address drug shortages. These federal investments should be strategically focused to reshape production capacity for active pharmaceutical ingredients, key source materials, and finished dose formulations for medicines vulnerable to drug shortages.

Stabilizing the Generic Supply Chain - We suggest implementing the following two policies to address market failures in the generic marketplace.

1. We recommend reviewing the outcomes of Hatch-Waxman, which aims to lower drug prices and increase the number of generic medicines in the market. A National Academy of Medicine study should be conducted to review the impact of Hatch-Waxman and Generic Drug User Fee Amendments (GDUFA) policies to determine if they are currently sustainable in today's healthcare marketplace. In addition, determine if the FDA has the necessary resources to conduct foreign inspections.

2. We also recommend that CMS and the FDA coordinate to review the number of suppliers for a given product over five years to determine if the deflation experienced is sustainable to avoid market failure. This review should also determine whether the number of ANDA approvals for each respective national drug code (NDC) losing patent exclusivity precipitates product "dumping" and forces generic companies to exit the market.

Reimbursement Policy – We also recommend adjusting reimbursement policies to increase pharmacy and provider reimbursement for generic medicines. Economic approaches to address drug shortages must acknowledge the financial strain and complex reimbursement providers face.

Conclusion

HDA and its members recognize the challenges drug shortages pose to our nation's healthcare systems and patients. We are committed to working with manufacturers and providers to mitigate and manage them when they occur. We applaud the Committee for its efforts to act on drug shortages.

HDA and its members stand ready to provide our continuing perspective and insight on behalf of the pharmaceutical distribution industry and partner with you on real solutions to this complicated challenge.



February 6, 2024

The Honorable Jason Smith
Chair
House Ways and Means Committee
Washington, D.C. 20515

The Honorable Richard Neal
Ranking Member
House Ways and Means Committee
Washington, D.C. 20515

Dear Chair Smith and Ranking Member Neal:

The Healthcare Leadership Council (HLC) thanks you for holding a hearing on, "Examining Chronic Drug Shortages in the United States."

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 patients need it is critical to the best patient outcomes 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 drug supply chain.

The U.S. is facing a nearly ten-year peak in drug shortages. In spring 2023, medications in shortage surpassed 300 for the first time since 2014.[1] There are shortages of particular concern across clinical care, including oncology treatments, local anesthetics and basic hospital drugs, asthma medications, ophthalmic medication, attention deficit hyperactivity disorder treatments, and others.

Generic drugs comprise most 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 are GSIs.[2] The current market only incentivizes lowest price when it comes to purchasing decisions,

[1] Drug Shortages Statistics, American Society of Health System Pharmacists (ASHP), (accessed December 4, 2023), https://www.ashp.org/drug-shortages/shortage-resources/drug-shortages-statistics.
[2] Drug 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

driving much of the current shortage. To ensure the lowest price point, generic manufacturers sacrifice additional protocols or mechanics that ensure they can reliably meet regulatory quality standards. The lack of resources dedicated to supply chain resilience results in these manufacturers pausing production for long periods of time or exiting the market.[3]

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.[4] 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 decisions. 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 has on patients is yet to be measured. The impact may be high. 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 two-year survival rate from 88 percent to 75 percent.[5]

While direct patient treatment is the most critical consequence of drug shortages, research and development 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 – with a 2015 survey of southeastern United States health systems reporting most respondents were required to purchase drugs at a 300-500% markup from alternative supplies for hard-to-find medications.[6]
As Congress explores mechanisms to increase drug supply resiliency, we recommend the following policy solutions:

Shortages, Brookings' Hamilton Project, (June 2023) www.brookings.edu/wp-content/uploads/2023/06/20230621_ES_THP_GSI_Report_Final.pdf.
[3] Demand-Side Reforms to Prevent Drug Shortages: Medicare's Role in a Successful National Strategy. (January 26, 2024), https://www.healthaffairs.org/content/forefront/demand-side-reforms-prevent-drug-shortages-medicare-s-role-successful-national-strategy
[4] New 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.
[5] The 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.
[6] Impact of Drug Shortages on Patients Safety and Pharmacy Operation Costs, (April, 2023) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6248141/

Reauthorize the Pandemic and All Hazards Preparedness Act in the same bipartisan fashion it has been supported since the original authorization 17 years ago

HLC has been a leader in disaster readiness policy since 2017 – working with Duke-Margolis Institute for Health Policy to develop key recommendations that would enable the federal government to better respond in the event of a disaster. While many of the recommendations have been implemented through legislative or administrative action, the expiration of the Pandemic and All Hazards Preparedness Act (PAHPA) threatens that progress. Without the emergency flexibilities and reserves established by the legislation, the United States is at greater risk of being inadequately prepared, leading to an overwhelmed healthcare infrastructure. We remain particularly concerned about the state of the national stockpile, that even with PAHPA in place was quickly depleted during the COVID-19 pandemic.[7]

Invest in a Robust Government Stockpile and a Targeted Buffer Inventory

We recommend substantially and consistently funding the Strategic National Stockpile. It is 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.

HLC 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.[8] Unlike an emergency stockpile, the buffer inventory would be held by a supplier or wholesaler and disbursed as needed 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.

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. These 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.[9] Congress should expand these efforts by allowing the FDA to fast-track abbreviated new drug applications and expedite manufacturing inspections and approvals for drugs facing a critical shortage.

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[7] The Strategic National Stockpile was not Positioned to Respond Effectively to the COVID-19 Pandemic, (October, 2023), https://oig.hhs.gov/oas/reports/region4/42002028.pdf

[8] 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.

[9] Ibid.

- **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), providers, 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 via 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 tracking 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 Sam Carley at (202) 449-3445 or scarley@hlc.org.

Sincerely,

Maria Ghazal
President and CEO

HSCA
HEALTHCARE SUPPLY CHAIN ASSOCIATION
Innovators In Evidence-Based Sourcing

February 20, 2024

The Honorable Jason Smith
Chairman
Committee on Ways & Means
United States House of Representatives
Washington, DC 20515

Re: Statement for the Record on the House Ways & Means Committee's *"Examining Chronic Drug Shortages in the United States"* Hearing on February 6, 2024

Dear Chairman Smith:

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 February 6, 2024, hearing examining chronic drug shortages in the United States. 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 help secure access to critical medical products, providing savings for patients, providers, Medicare, Medicaid, and taxpayers. Both independent and industry funded studies confirm the effectiveness and tremendous value of GPOs, finding that GPOs deliver annual cost savings of 12-18%.[1] [2] GPOs allow rural 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 reliability and stability of supply. We recognize that market conditions change, and when they do, GPOs work with suppliers to adjust contracts. GPOs work

[1] Burns, 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
[2] Dobson, 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.

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diligently to ensure member hospitals and providers can access the products they need to care for their patients most effectively.

American hospitals, particularly those in rural areas, are facing ongoing financial challenges that threaten their ability to stay open. GPOs allow small and rural healthcare providers who often lack the negotiating power to access competitive pricing for essential supplies to utilize the same efficiencies and discounts as large healthcare 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 analytics, which are especially important in rural and underserved areas. Individual practices and community hospitals often do not have the resources, scale, and expertise to perform this 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 so that patients and providers have consistent access to the drugs, products, and devices they need.

GPOs Take Steps to Prevent and Mitigate Drug Shortages.

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 reliability 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 are leaders in working to prevent and mitigate drug shortages. Every HSCA member GPO has innovative programs that work 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

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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 to the Committee:

Invest 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.

Create 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 (P.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.

Increase 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 Congress require manufacturers to include on their package inserts and boxes the finished product manufacturing location, including for contract manufacturers, and API source(s) on all products.

Increase 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.

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.

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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
Healthcare Supply Chain Association (HSCA)

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United States Pharmacopeia (USP) Statement for the Record

Submitted to the House Committee on Ways and Means
Hearing on Examining Chronic Drug Shortages in the United States

February 6, 2024

The United States Pharmacopeia (USP) is pleased to submit the following statement for the record on the hearing "Examining Chronic Drug Shortages in the United States."

USP is an independent, scientific, global non-profit organization founded in 1820 when eleven 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.

USP commends the Committee for holding this hearing on a critically important issue to our nation's patients and public health, as well as national and economic security. 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. **Our policy recommendations, explained in more detail below, are:**
1) Promote sustainable prices for generic medicines by valuing supply chain resiliency
2) Advance broader geographic diversification of the manufacturing base including incentives to advance more U.S.-based medicine production
3) Use existing early warning capabilities and invest to fill gaps in the supply chain map
4) Utilize a vulnerable medicines list to guide policy interventions and investments
5) Coordinate supply chain resilience and reliability efforts

Collectively, these efforts 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.

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[1] USP's governing bodies, in addition to the Council of the Convention, include its Board of Trustees and Council of Experts.

Understanding Factors Driving Medicine Supply Chain Vulnerabilities

Over the past year, there have been more three hundred 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

[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.

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 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

[3] FDA. 2019. Drug Shortages: Root Causes and Potential Solutions. Available at: https://www.fda.gov/media/131130/download.
[4] Supply chain vulnerabilities exist for antimicrobial medicines: USP Medicine Supply Map analysis | Quality Matters | U.S. Pharmacopeia Blog.

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 another 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.

[5] The 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.

Quality concerns

USP underscores that supply chain resilience and medicine quality are inextricably linked. Quality problems in manufacturing exacerbate the risk of causing a supply chain disruption or failure. 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 cause of most drug shortages is unsustainably low prices. Lower margins undermine initiatives to ensure supply chain resiliency by limiting 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.

[6] *Ibid.*

- 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.[7]
- 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.[8]
- The development of tools and standards to help reduce the technical barriers to wider adoption of AMTs and support medicine quality.

3. Use existing early warning capabilities and invest to fill gaps in the supply chain map

Both government and non-governmental stakeholders should use 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

[7] *See* Building geographic diversity in the medicines supply chain.
[8] *See* Recognizing Challenges and Opportunities to Support Adoption of Advanced Manufacturing Technologies for Medical Products.

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 four 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.