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SAFEGUARDING PHARMACEUTICAL SUPPLY CHAINS IN A GLOBAL ECONOMY

WEDNESDAY, OCTOBER 30, 2019

House of Representatives,

Subcommittee on Health,

Committee on Energy and Commerce,

Washington, D.C.

The subcommittee met, pursuant to call, at 10:02 a.m., in Room 2123, Rayburn House Office Building, Hon. Anna G. Eshoo [chairwoman of the subcommittee] presiding.

Present: Representatives Eshoo, Engel, Butterfield, Matsui, Castor, Sarbanes, Schrader, Kennedy, Cardenas, Welch, Ruiz, Kuster, Kelly, Barragan, Blunt Rochester, Pallone (ex officio), Burgess, Shimkus, Guthrie, Griffith, Bilirakis, Bucshon, Brooks, Mullin, Carter, and Walden (ex officio).

Also Present: Representatives Soto and Flores.

This is a preliminary, unedited transcript. The statements within may be inaccurate, incomplete, or misattributed to the speaker. A link to the final, official transcript will be posted on the Committee's website as soon as it is available.

Staff Present: Jeff Carroll, Staff Director; Waverly Gordon, Deputy Chief Counsel; Tiffany Guarascio, Deputy Staff Director; Megan Howard, FDA Detailee; Josh Krantz, Policy Analyst; Aisling McDonough, Policy Coordinator; Joe Orlando, Staff Assistant; Alivia Roberts, Press Assistant; Tim Robinson, Chief Counsel; Kimberlee Trzeciak, Chief Health Advisor; C.J. Young, Press Secretary; Jennifer Barblan, Minority Chief Counsel, Oversight and Investigations; Margaret Tucker Fogarty, Minority Legislative Clerk/Press Assistant; Peter Kielty, Minority General Counsel; James Paluskiewicz, Minority Chief Counsel, Health; and Kristin Seum, Minority Counsel, Health.

Ms. Eshoo. Good morning, everyone.

The Subcommittee on Health will now come to order.

The chair now recognizes herself for 5 minutes for an opening statement.

There is a hidden health crisis in this country that will affect us all: the crippling inadequacy of the American drug supply. And, today, 90 percent of the medications that Americans take are generics. That is because they are cheap, and they are supposed to be just as safe and effective as expensive brand-name drugs. But I believe the generic industry is broken, and it is putting millions of Americans' health at risk.

Our generic drug supply is broken in three devastating ways: shortages of lifesaving medications, subpar manufacturing that contaminates our drugs, and an over-reliance on foreign production of critical drugs and their ingredients.

The first crisis is the shortage of lifesaving medications. Right now, hospitals are rationing critical drugs. This month, children and their families woke up to the news that they may not be able to get the pediatric cancer drug vincristine -- little children who, with this drug, would be cured of their cancer and now can't get the drug they need. This should not be happening in the United States.

The second crisis is subpar manufacturing contaminating our drugs and contributing to shortages. Over the last year, we have seen recalls of common blood pressure medications because they contain carcinogens. One of the drugs affected, losartan, is the ninth most commonly used drug in our country. Our generic drug supply is so fragile that the FDA often must make the hard choice between enforcing quality at a plant and avoiding a shortage.

The third crisis is an over-reliance on foreign production for critical medications,

which is a national security risk. China globally dominates the manufacture of active pharmaceutical ingredients, often referred to as "API," and China has gained a chokehold over the global supply of penicillin. In fact, according to a witness on our second panel, Rosemary Gibson, there are no plants in the United States that manufacture penicillin.

If tensions with China escalate, Beijing could use U.S. dependence on critical drugs as an economic weapon and exploit the health and safety of both our Armed Forces and the American people, and this is a threat to our Nation's security.

China flaunts the FDA's rules. An analysis of FDA inspection reports published on Tuesday this week in STAT News found Chinese plants were cited for data-integrity issues nearly twice as often as American plants. These data issues include falsifying drug tests or deleting findings that could indicate contaminated or poor-quality drugs.

Taken together, these overlapping crises of shortages, subpar manufacturing, and foreign reliance threaten the overwhelming majority of drugs taken by Americans every day.

This is a crisis, and today we will define it in depth. And, most importantly, we have to focus on solutions. Much of what we will hear today will sound shocking, not only because of the scary state we find our drug supply in but also how little attention it has received. And it has been years in the making.

I am issuing a call to action to the FDA, to industry, and to all Members of Congress, but most especially our committee, to take these problems seriously and work together on a bipartisan basis to address them. If we fail to act, America will continue to be vulnerable to potential foreign adversaries and at the mercy of subpar plants or cutbacks on quality, and we cannot allow this to happen.

The chair now recognizes Dr. Burgess, ranking member of the Subcommittee on Health, for 5 minutes for his opening statement.

[The prepared statement of Ms. Eshoo follows:]

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Mr. Burgess. And I thank the chair for recognition.

This committee, the Committee on Energy and Commerce, has a long history of being engaged in the safety of the pharmaceutical supply chain, and certainly our continued oversight work today is critically important.

Our investment in research and development yields significant scientific breakthroughs in the form of new treatments and new cures for patients that were, in fact, probably not even thought of years ago. But there is an increased need for an efficient and secure pharmaceutical supply chain to ensure safe access to active pharmaceutical ingredients coming from across the globe.

Nearly 80 percent of active pharmaceutical ingredients come from other countries. The Food and Drug Administration examines these critical ingredients once they are imported or offered for import to the United States, subjecting them to the Food and Drug Administration's requirements.

This committee should remember the United States faced a deadly contamination of the blood thinner heparin in 2008. I think, in fact, as part of that hearing, the question was even raised, how would we continue to exist without heparin? As a practicing physician, I will tell you, that would be very, very difficult.

Heparin contains an active pharmaceutical ingredient that was coming from China, is still coming from China, but that ingredient was adulterated, resulting in hundreds of adverse effects and the deaths of 81 American patients.

I got~~have~~ to tell you, as a physician, you think of someone in a dialysis center who pushed the flush solution into an AV shunt to clear it for the dialysis, and that patient immediately expired? That is obviously terrible for the patient and their family, but that

doctor or that nurse is going to carry that around with them the rest of their lives.

When we studied at the time, more than 1 million multidose vials were sold each month in the United States. Now, the Food and Drug Administration did conduct an investigation but was unable to pinpoint the exact source of the adulteration, but it does appear to have been a Chinese active pharmaceutical ingredient production site.

Ultimately, the manufacturer of the heparin, including the adulterated active pharmaceutical ingredient, known as hypersulfated chondroitin sulfate in common parlance -- eventually, they did recall all their heparin. This amounted to roughly half of the heparin supply in the United States.

As a result of this contamination, the Food and Drug Administration asked manufacturers of products containing heparin to test the active pharmaceutical ingredients with not one but two tests that were now recommended by the FDA.

That molecule, that contaminant molecule, was cleverly designed so that it hid behind the normal peak of the heparin molecule when it was examined by the scientific equipment, and it required a more sensitive test to be able to elucidate the two peaks on that graph.

Despite efforts by the Food and Drug Administration, numerous letters sent by members of this committee, and hearings on this mass heparin contamination, we have still not identified the culprit or the contamination source. This committee remained engaged on the issue for years and, in fact, I dare say, is still engaged on this contamination, but we have never learned the true cause of the contamination.

To this Member, that serves as an example of how seriously we must take the safety of the pharmaceutical supply chain. The international supply chain for

pharmaceuticals is complex. Merely investigating contamination after patients start dying fails to adequately protect Americans. An understanding of this global system is instrumental to ensure a safe pathway for the important active pharmaceutical ingredients used in drugs taken every single day. This continues to be an issue as pharmaceutical manufacturing grows increasingly global and manufacturing shifts away from the United States.

As a physician, I do know the importance of being able to prescribe the exact drug or treatment that a patient needs. A safe and efficient international supply chain is essential to avoid drug shortages and, therefore, ensuring that physicians can focus on what their patient needs rather than what is available.

In June of this year, I wrote a letter, along with Chairman Pallone, Republican Leader Walden, Ms. DeGette, and Mr. Guthrie, to the FDA about a series of recalls involving drugs manufactured overseas that contain trace amounts of known carcinogens. While it is important to ensure safety by recalling these drugs, it shows that the threat of contamination is starkly real.

The Food and Drug Administration Safety and Innovation Act, which was signed into law in 2013, codified the Food and Drug Administration's authority to inspect drugs and active pharmaceutical ingredients manufactured outside the United States. Since then, the FDA has issued guidance and final rules on agency procedure concerning adulterated drugs, domestic and foreign registration, and inspection and destruction of imported drugs refused admission to the United States. This was an important step in the direction of ensuring a safe pharmaceutical supply chain, and I certainly look forward to hearing more about it today.

Thank you. I will yield back.

[The prepared statement of Mr. Burgess follows:]

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Ms. Eshoo. The chair thanks the ranking member.

I now have the pleasure of recognizing the chairman of the full committee, Mr. Pallone, for his 5 minutes for an opening statement.

The Chairman. Thank you, Chairwoman Eshoo.

American consumers rely heavily on prescription drug products that help them live longer and healthier lives. Over the last several months, this subcommittee has taken action to lower drug costs to ensure that all Americans can access the prescription drugs that they need. And making prescription drugs more affordable is a top priority of this committee. After all, prescription drugs are essentially useless if people cannot afford them.

Today, we are focusing on another important component of prescription drugs, and that is maintaining the safety and quality of medications in our marketplace.

The Food and Drug Administration plays a central role in ensuring the safety of drugs in our market. The rigorous drug review process at FDA is recognized worldwide as the gold standard. While regulatory processes can always be improved, American patients should take comfort in the knowledge that drug products approved by the FDA are the most rigorously reviewed in the world.

And FDA's authority is not limited to those drugs manufactured here in the U.S. It can inspect and review information related to both finished dose drug products and the active pharmaceutical ingredients, or API, that come from other countries.

Over the years, this committee has acted to improve FDA's authority to the regulate what is a complex and increasingly global supply chain. We have provided FDA with the ability to inspect facilities on a risk-based schedule. We gave FDA the ability to

enter into agreements with other regulatory authorities to share inspection information for foreign facilities. And we required entities in the drug supply chain to maintain and track information related to drug products.

All of these authorities are particularly important given recent trends in pharmaceutical manufacturing. Many manufacturers are getting their pharmaceutical ingredients from manufacturers overseas, particularly from China and India. And some of the ingredients from abroad have caused seriously quality concerns with certain drug products.

So we need to make sure that FDA has the authority it needs to address these concerns and to remain vigilant over the marketplace. We also need to ensure that manufacturers are still incentivized to produce their pharmaceutical ingredients and products domestically.

Some manufacturers are implementing innovative manufacturing methods, like continuous manufacturing, to make their processes more efficient and to keep their facilities here in the U.S. Encouraging the use of continuous manufacturing methods has long been a priority of mine, not only because these methods are the next frontier of manufacturing but also because they are quality production methods that help U.S. manufacturers compete in the global market.

So, earlier this week, I reintroduced legislation with Representative Guthrie to expand support for continuous manufacturing. This bipartisan legislation will foster the development of emerging technology by expanding opportunities for FDA to partner with universities across the country that are leading these efforts, including my own Rutgers University in my congressional district. And it is the next step in my work on the

continuous manufacturing grants program that was included in the 21st Century Cures Act.

So I look forward to hearing from the witnesses today, particularly Dr. Woodcock, about the safety and sourcing of active pharmaceutical ingredients. It is critical that we ensure American patients have access to the highest-quality medications in the world.

And I particularly want to thank Ms. Eshoo, because she has been, you know, advocating that we look into this and have this hearing for some time now, and so it is really important that we do this. Thank you, Chairwoman.

I yield back.

[The prepared statement of the chairman follows:]

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Ms. Eshoo. The chair thanks the chairman.

And now it is a pleasure to recognize the ranking member of the full committee, who broke our hearts with his announcement -- and I am going to say this every time I introduce him --

Mr. Walden. No.

Ms. Eshoo. -- Mr. Walden from Oregon, for his 5 minutes for an opening statement.

Mr. Walden. Well, thank you, Madam Chair.

And I have another big announcement to make here and now. I do believe it is our chairman's birthday today, Mr. Pallone.

Ms. Eshoo. Happy birthday.

Mr. Walden. So could we do, like, the Boehner birthday song? This is your birthday song, it doesn't last too long, hey! That is it.

The Chairman. Thank you.

Mr. Walden. Yeah, and with that age thing happening, this hearing is really important for you going forward, I think, so we want to get these drugs available, safe.

Ms. Eshoo. We have to get these drugs --

Mr. Walden. Yeah, I am just about unleashed up here now. This is pretty good. I think that is it.

I appreciate, Madam Chair, your holding this hearing, and, Mr. Chairman, thank you as well. This really is serious, important work, and we have great witnesses here to help us understand what is going on.

Making sure our government agencies have the tools necessary to ensure safety

and quality of the U.S. drug supply is a top priority for this committee.

Recent recalls issued for a class of drugs known as angiotensin II receptor blockers, or ARBs, which are generally used to treat high blood pressure, and media attention on the questionable conditions and practices at foreign manufacturing facilities have led to public concern about the country's sourcing of finished drug products and active pharmaceutical ingredients overseas.

Historically, medicines intended for use in the United States have been produced in the United States. However, over the last several years, more drug manufacturing has moved offshore. Much of the shift can be attributed to low wages and less regulation in other countries, resulting in lower production costs for drug manufacturers. With the shift overseas, it has become more difficult for us to verify these products are made in compliance with what I would say are the world's best standards, those in the United States.

And, as you know, to our witnesses, this committee has had a long interest in FDA oversight of the manufacturing of finished drug products and active pharmaceutical ingredients intended for the U.S. drug supply.

In 2012, with the passage of the Food and Drug Administration Safety and Innovation Act, Congress provided FDA with new resources needed to inspect both domestic and foreign generic drug facilities.

Data from the most recently issued GAO report in 2016 found that the FDA had increased its foreign drug inspections and it had enhanced its ability to prioritize drug establishments for inspection. For example, the GAO found that the FDA foreign inspections increased from 333 in 2007 to 842 in 2015.

However, it has been reported that FDA surveillance inspections of foreign facilities have declined in the past 2 years, including in China, where inspections fell by almost 11 percent.

And I know while inspections are not the only means of ensuring the drug supply is properly protected, it is an important piece of the puzzle, and we must ensure the FDA has the appropriate oversight measures in place.

Because of our continued concern over the quality and safety of the U.S. drug supply, we have requested, in a bipartisan manner, answers from the FDA about practices currently in place to adequately oversee foreign drug manufacturing. We have also requested an updated report from GAO on the FDA's drug inspection program, because if there are gaps in the agency's ability to properly oversee these facilities, action must be taken to resolve those shortcomings and protect the public's health.

The United States' reliance on overseas manufacturing not only raises quality concerns but it also poses national security risks as well. Foreign-manufactured medical products critical to the strategic national stockpile are subject to the same quality and safety concerns, but dependence on foreign countries for drugs used as medical countermeasures could also leave Americans vulnerable to chemical and biological threats, among others.

Further reliance on foreign suppliers, particularly in those countries with which we have unstable relationships, poses an increased risk to Americans. If a country monopolizes the production of a drug and wishes to retaliate against the United States, they could substantially increase drug prices or dramatically reduce supply in an attempt to cause shortages, limiting access to critical medications. And that is in the absence of

a crisis. In a time of crisis, such possible actions could cost American lives.

My concerns are amplified by the fact that some of the legislation that is headed to the floor on drug pricing may further complicate this matter and drive innovation in manufacturing overseas, leaving the American people at the mercy of foreign manufacturers, particularly China, who have shown a strong interest in creating their own biotech manufacturing base for lifesaving and life-sustaining drugs.

So I look forward to the expert witnesses we have today. I really appreciate this hearing. I know this is an issue you care deeply about, Madam Chair, and have fought for improvements on for a long time.

And so we look forward to your testimony.

With that, I yield back.

[The prepared statement of Mr. Walden follows:]

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Ms. Eshoo. The chair thanks the gentleman, and he yields back.

I just want to remind members that, pursuant to committee rules, all members' written opening statements shall be made part of the record. So get those excellent statements in.

[The prepared statements follow:]

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Ms. Eshoo. I now would like to introduce the first panel of our witnesses for today's hearing.

It is an honor to welcome Dr. Janet Woodcock. She is the Director, we all know, of the FDA Center for Drug Evaluation and Research.

And I want to thank you for the work that you have done, the work that you have done with my staff. This is in many ways a heavy lift, but what you have done has helped to enlighten us and prepare us for this all-important hearing today.

Welcome to Mr. Michael Wessel. He is a commissioner at the U.S.-China Economic Security Review Commission.

And we are very grateful to you for being here today as well.

Just a word about the lighting system. I think you both know; certainly Dr. Woodcock does. Green, you know what that is. Yellow means the red light is coming, and then we have full stop.

So, Dr. Woodcock, welcome. Thank you for dedicating your adult life to the work at the FDA and, most importantly, at the Center for Drug Evaluation and Research. You are recognized for 5 minutes for your opening statement.

STATEMENTS OF JANET WOODCOCK, M.D., DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION; AND MICHAEL WESSEL, COMMISSIONER, U.S.-CHINA ECONOMIC SECURITY REVIEW COMMISSION

STATEMENT OF JANET WOODCOCK, M.D.

Dr. Woodcock. Thank you, Madam Chair and members of the committee.

Lack of a reliable supply of critical medicines creates a significant risk for national security, not just for our military but for all our citizens.

An active pharmaceutical ingredient, or API, is the actual drug that is then made into a tablet, injection, and so forth. APIs are typically made at a site that specializes in their production, and then they are sent to other facilities to be made into what we call finished pharmaceuticals. I will focus on APIs.

The U.S. has a minority of facilities. We have about 28 percent of all facilities that manufacture APIs for the U.S. market. Twenty-six percent of all such API sites are in the EU and 13 percent in China and 18 percent in India.

Given that many APIs are for minor conditions that are treated, say, with OTC drugs, we also looked at the WHO Essential Medicines List. Twenty-one percent of those APIs can be made in the U.S. Fifteen percent are made in China and 64 percent elsewhere.

Looking at medical countermeasure drugs, only 11 percent of API sites for biological threat agents are in the U.S., 29 percent of sites for chemical threats, and 46

percent for radiation threats.

You can see that many kinds of disruptions around the globe could threaten U.S. patients' access to critical drugs.

These numbers also don't reflect the relative volume of product from any given region, only the existence of facilities that FDA has approved to make the specific APIs. FDA currently does not get up-to-date information on volume or production and capacity of any site around the world. These data are dynamic, and they can change rapidly. Further, other critical factors, such as availability of raw materials, can also have major impact on supply, and the U.S. itself is not a major source of these materials.

The U.S. pharmaceutical sector, as has already been said, like many other manufacturing sectors, has moved out of the country, starting in the late 1990s. And this trend has been accelerating based on economic factors.

So what can be done about this? I think that is possibly the most important question.

Well, one thing, FDA has been advocating for modernization of drug manufacturing since the early 2000s. Advanced pharmaceutical manufacturing covers a range of technologies that are widely used in other industries, such as continuous production, use of automation, and digitization. These techniques result in smaller facilities, less environmental impact, and the need for a smaller but highly skilled workforce -- all factors that make production in the U.S. more feasible.

For example, Genzyme Sanofi recently announced they had completed test runs in a new bioprocessing facility in Framingham, Massachusetts. According to them, this facility will make all kinds of biological products in a continuous, end-to-end process, will

use 94 percent less solvents and produce 80 percent less CO2 while consuming 80 percent less energy, not generate any paper -- reams of paper are usually generated -- but being 80 times more productive.

Similarly, FDA recently approved a new cystic fibrosis drug made by Vertex Corporation that uses continuous processing for the finished dosage form, and that is also in Massachusetts. These examples show that drug manufacturing in the U.S. is quite feasible using advanced technologies.

FDA is also working with ASPR, BARDA, and DARPA on how we might regulate mobile, miniaturized manufacturing modules that could be used in crisis or military situations. These are dubbed by BARDA "Pharmacy on Demand." These projects foreshadow, in my opinion, a new generation of pharmaceutical manufacturing techniques that is now emerging and that we can put against this problem.

FDA is working hard to assure a robust and reliable drug supply for the U.S. We feel it is important both to reestablish the pharmaceutical manufacturing sector in the U.S. but also help bring about a high-quality, resilient drug supply for all the world's citizens.

Thank you.

[The prepared statement of Dr. Woodcock follows:]

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Ms. Eshoo. Thank you, Dr. Woodcock.

I now would like to recognize our second witness, Mr. Wessel.

You are recognized for 5 minutes for your opening statement, sir.

STATEMENT OF MICHAEL WESSEL

Mr. Wessel. Chairwoman Eshoo, Ranking Member Burgess, members of the subcommittee, thank you for the invitation to appear here today.

This hearing addresses a critical issue for our economic and national security interests and directly affects every one of our citizens. To paraphrase Samuel L. Jackson, what's in your medicine cabinet? Our citizens have a right to know.

My name is Michael Wessel, and I am a member of the U.S.-China Economic and Security Review Commission, but my remarks today represent my views and not those of the Commission or any individual commissioner.

In July, the Commission held a hearing exploring the growing U.S. reliance on China's biotech and pharmaceutical products. Five years ago, the Commission held a hearing on China's healthcare sector, drug safety, and the U.S.-China trade in medical products.

In the 5 years between hearings, I can't say my confidence in the safety of Chinese drug and active pharmaceutical ingredients has gotten better. Our reliance on Chinese supplies has increased while their regulatory system has failed to keep pace with the growth of the sector. And we are losing our ability to meet our needs at a faster pace.

Chairwoman Eshoo, your op-ed in The Washington Post with Congressman Schiff

was spot-on. As you indicated, the problem demands action and bipartisan solutions. The U.S.-China Commission was unanimous in its call for action, and we look forward to working with you and your colleagues to produce workable solutions to protect our country's interests.

The issue, as I said, is of critical importance. Pharmaceuticals are often life-sustaining or lifesaving. For many, taking medication is not an option; it is a necessity.

Consumers generally don't have an option on what drug to procure based on the source of its ingredients. And all too often, they have no idea where those sources are.

China has an active plan to become an increasingly dominant source of medicines to the world. Pharmaceuticals and medical devices are a key sector in their "Made in China 2025" and 13th 5-year industrial plans. Billions of dollars of support are coupled with government policies, investment strategies, and intellectual property acquisition approaches, both licit and illicit. China wants to win, and it has a plan to do so.

Already, they supply significant portions of the APIs, as much as 80 percent by some estimates. Our concerns are not limited to just direct impacts from China, as drug firms across the globe often utilize Chinese APIs.

China understands the importance of the sector as an economic and innovation engine but also because of its national security implications. Our increasing dependence on China poses many risks, not only due to potentially unsafe medications but because of China's ability to potentially weaponize its supply chains should it so choose.

Let's not forget that several years ago China blocked exports of rare-earth minerals to Japan over a territorial dispute. What would happen if China threatened

supplies of certain critical drugs and APIs?

As a DOD witness told our commission, quote, "The national security risks of increased Chinese dominance of the global API market cannot be overstated." We are losing our ability to supply not only the medicines our warfighters may have to rely on but the ability to address other critical health crises here.

The bioeconomy is increasingly important. As global competition and manufacturing has increased, some areas of our country have been able to weather the changes with a rise in employment in the healthcare sector. We can't afford to trade away this sector.

In terms of global medical supply chains, increasingly, all roads lead to China. Those roads are rocky, sometimes treacherous, and all too often unsafe. With thousands of suppliers in the still-developing regulatory infrastructure, we can't trust the safety and security of Chinese supplies. Our experience, from heparin to valsartan to other drugs, indicates that there are clear and present dangers.

Our inspectors -- and we have far too few -- do not have unfettered access to inspect Chinese facilities. Problems with visas, delayed and often limited access to facilities, and the need for additional resources have all hampered our ability to protect our interests.

So, in short, we are overly reliant on China, we cannot trust the supply chains, and our national and economic security demand that we act. We must reduce our vulnerabilities.

In my prepared testimony, I identified several recommendations made by the China Commission that will appear in our upcoming report. It is not a partisan issue; it is one where we can apply commonsense solutions to address a national concern.

Thank you.

[The prepared statement of Mr. Wessel follows:]

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Ms. Eshoo. Thank you very much, Mr. Wessel.

I just wanted to -- first of all, I ask for unanimous consent to place into the record the Washington Post op-ed dated September 10, 2019.

Hearing no objections, so ordered.

[The information follows:]

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Ms. Eshoo. We did invite Christopher Priest, the Acting Deputy Assistant Director of the Defense Health Agency. He is out of the country. And I hope in subsequent hearings that we will have the benefit of his testimony as well.

But we thank both of you for your excellent testimony. There is much to get to. And I will start by recognizing myself for 5 minutes of questions.

Dr. Woodcock, does the FDA know what percentage of American drugs have their active ingredient sourced from China?

Dr. Woodcock. We do not know the volume. We know the sites that we have approved and that they can -- are capable of providing drug API. However, we don't know which suppliers might be used. Many applications have multiple suppliers of API that they can use. And so we don't know on a real-time basis.

Ms. Eshoo. So there isn't any requirement from FDA relative to the drugs that you approve, what the source is?

Dr. Woodcock. Yes, we do know all the sources, but --

Ms. Eshoo. You do know the sources, but --

Dr. Woodcock. -- we do not know what percentage of --

Ms. Eshoo. I see.

Dr. Woodcock. Yes.

Ms. Eshoo. Now, Rosemary Gibson, who is going to testify on the next panel, has raised concerns about U.S. reliance on China for API in antibiotics. Does the FDA know how much of the ingredients for antibiotics are sourced from China?

Dr. Woodcock. We know where the facilities are that can produce antimicrobials around the world, but, again, we don't know the percentage of that that currently is

being sourced from China.

We get annual reports every year, and so we can retrospectively see what happened. But we don't have -- this is a dynamic situation, and so we don't know in real-time.

Ms. Eshoo. What is the capacity of the United States to take this back, relative to API?

I know that cost is always a factor, and so we end up, what I call, bottom-fishing. But the testimony so far is that I think we all agree that this poses a threat. I mean, drugs are not any old commodity in our country. This is the health and security of our people and our national security.

So how do we regain the capacity? Do we have a capacity for API in the United States?

Dr. Woodcock. There is capacity. There is the potential to do it. But there isn't an economic incentive.

Ms. Eshoo. That is what it is, is the economic incentive. Uh-huh.

Dr. Woodcock. Our assessment is that the companies in the U.S. could not compete, using current technology, against other countries who have lower labor costs, less environmental regulation, and so on.

Ms. Eshoo. But, in your estimation, if we moved to advanced pharmaceutical manufacturing, that we can indeed recapture the API market?

Dr. Woodcock. The APIs are going to be a little bit harder than making the finished dosage forms with advanced manufacturing, because every API, every synthesis, if you think about it, making each molecule has different steps. However --

Ms. Eshoo. But we did that at one time. China hasn't always dominated the global market on this.

Dr. Woodcock. We and Europe, back many -- maybe decades ago, did have API manufacturing here, but they moved. If you recall, Congress gave incentives for Puerto Rico, and a lot of pharmaceutical plants moved to Puerto Rico. And then, as the economic situation evolved, they moved to India, China, and other countries.

Ms. Eshoo. But as I understand it, India is at least 80 percent dependent on China's API.

Dr. Woodcock. We showed, in the testimony I gave, where approved API facilities are. They are not dominant, China is not dominant, as far as the number of facilities it has. Now, whether it is dominant on volume, we can't currently --

Ms. Eshoo. But you can't just go by the number of facilities. You have to go by what each facility produces. That is the key number.

Dr. Woodcock. And that changes over time.

Ms. Eshoo. Uh-huh.

In my opening statement, I referred to our generic drug supply being so fragile that the FDA has to make hard choices between enforcing quality at a plant and avoiding a shortage. Can you speak to this, please?

Dr. Woodcock. Sometimes this is true, both for innovator drugs and generic drugs. If we have quality problems at a plant, we have to make a medical decision, okay, is the patient foregoing that, or can we put in remediation additional steps that would render the product safe enough to use in that --

Ms. Eshoo. But it is a squeeze for you. It is a --

Dr. Woodcock. Yeah. Well, it --

Ms. Eshoo. -- squeeze for you to do that.

Dr. Woodcock. -- puts us in a difficult position.

Ms. Eshoo. Yeah. Uh-huh. It is. These are hard choices.

Commissioner Wessel, your mandate is to report on national security implications of U.S. trade with China. Can you just spend a moment describing the national security implications of our dependence on China for these active pharmaceutical ingredients?

Mr. Wessel. Well, yes. Thank you. And, again, your piece with Congressman Schiff helped identify much of that.

We are increasingly dependent on China by volume, both directly and indirectly. They have the opportunity, of course, to weaponize those supplies should they so choose. They did that with Japan. We have seen them in these current trade tensions with the U.S. favor certain sectors over others.

They have also a plan to dominate the sector globally, not just directly the APIs and pharmaceuticals but biotech. They want to be 70 percent indigenously self-sufficient. That means that they are going to exclude and preclude others from producing these products.

They are pricing us out of the market. That happened, as you will hear later, on penicillin and on other products. Price is the critical issue, but when China gives tens of billions of dollars of subsidies to their manufacturers, those who operate based on market principles simply can't compete.

Ms. Eshoo. Thank you. They have a plan --

Mr. Wessel. Yes.

Ms. Eshoo. -- and we don't.

Thank you very much.

I now would like to yield to the ranking member for his 5 minutes of questions. Dr. Burgess, you are recognized.

Mr. Burgess. Thank you.

And thanks to our witnesses.

Dr. Woodcock, always good to see you. You are a frequent flyer at our committee, and we appreciate that.

Mr. Wessel, you have posed an interesting question about China weaponizing their supply chain. I was here in 2008 when we studied the heparin problem, and I referenced hypersulfated chondroitin sulfate. That was not just a contaminant that got into the heparin. That was a molecule that had been developed and patented under Chinese authority.

Who knows why someone thought it was a good idea to put it in their heparin supply? I am presuming it was like an unscrupulous shopkeeper who puts a thumb on the scale, because this would increase the test for the bioavailability of blood thinner, which is one of the things that made it so difficult to detect when it was realized there was a problem.

But, look, I am from Texas. I never attribute anything to coincidence if I can explain it in conspiracy. So when you talk about weaponizing the supply chain -- and I remember all of that discussion around heparin -- it is almost like that was a test of someone testing our system, can we detect and react, and how quickly do we come to that conclusion, and how do we react. So that is what I think of when you talk about

China weaponizing the supply chain.

Mr. Wessel. Well, thank you. And 12 years later, we haven't taken all the steps that we need to. Their test, if, in fact, that is what it was, they came up with the ability to plan forward and dominate the industry and make us further vulnerable. So the question is now, are we going to take all the information we have and put together a plan, an action plan, to try and mediate and mitigate the risks we face?

Mr. Burgess. Right. And, of course, we are not even talking about the melamine in the dog food, which poisoned all of our pets.

So, Dr. Woodcock, let me ask you, does the FDA have a role to play in the redevelopment of bringing that -- onshoring that industry?

I remember, a few years ago -- well, it has been a number of years ago -- we were worried about bird flu, the first bird flu, not the second one. And there was a contaminant, Serratia, in the vaccine, and suddenly there wasn't enough flu vaccine to go around. And our defense appropriations bill in that year, 2005, included dollars to reshore or re-o~~rur~~-onshore-development of the flu vaccine.

Does the FDA have a role to play in those scenarios?

Dr. Woodcock. In the sense of, as you know, we have been working on pushing advanced manufacturing. Part of the problem with influenza vaccine is the method of manufacture, which is very limiting. So we have been supporting advanced manufacturing.

And probably these new, sort of, idea of mobile, miniaturized units, we are going to require somewhat of a new regulatory scheme.

But all this leads to more regional manufacturing around the world rather than

what we have now, which is world travelers. They are made in this country, and then they are sent over here, and then they go over here. We have these long supply chains. This is not a good situation, really, for anyone.

Mr. Burgess. Do you have a role in looking at, what is it -- are there other agencies? You mentioned the environmental concerns. Are there ways to streamline this? Does the FDA have a role to play in streamlining interagency work to streamline and reshore some of this manufacturing?

Dr. Woodcock. We certainly -- you know, our partners in this have primarily been the agencies, the Defense Department and HHS, ASPR and BARDA, that are actually working on developing these new technologies. We do work with EPA and others but not in -- we don't get into their regulations and requirements.

Mr. Burgess. Yeah.

I am going to run out of time, but let me just ask you quickly, when we had the issue with the heparin and there was some discussion then and, of course, with swine -- some illness that is occurring in pigs in China right now, do we have a contingency plan?

I know at one time we said we don't want to use heparin that is recovered from bovine sources because of mad cow disease. But do we have a plan to look at that?

Dr. Woodcock. Yes, we do. And we have been in discussion -- we had a Science Board -- I took this question to the FDA Science Board a number of years ago. They endorsed the fact that we should move forward. We are in discussion -- have discussed with potential manufacturers of bovine heparin. And we have done studies with CBER about inactivation of the potential agent of BSE through the manufacturing process to --

Mr. Burgess. And let me just ask you -- I am going to run out of time. But on the vincristine question, in 2012, you helped us when Doxil, doxorubicin, was in short supply in this country and we got -- so I guess an emergency reimportation question.

Dr. Woodcock. Uh-huh.

Mr. Burgess. Is that possible for the short term with vincristine to help our patients who are suffering?

Dr. Woodcock. My understanding about vincristine is Pfizer has told us -- and we have a number posted on our website, as do they -- they have supply, and people can call and get vincristine right now. Our shortage people are staying on top of that situation day by day.

Mr. Burgess. All right. Is that plainly visible on your website? The --

Dr. Woodcock. Yes.

Mr. Burgess. -- FDA website, or is it Pfizer?

Dr. Woodcock. A phone number, uh-huh, posted on our shortage website.

Mr. Burgess. All right. Thank you.

Ms. Eshoo. And, Dr. Woodcock, that was as of when that Pfizer posted this and you did?

Dr. Woodcock. Two days ago, I think.

Ms. Eshoo. I see. All right. Because I mentioned it in my opening statement that -- and I didn't want members to think that it was an error. When I wrote that, these were not available.

Dr. Woodcock. Yeah. This is a very dynamic situation.

Ms. Eshoo. It is. It is. Very important one. I mean, it is a critically important

one. The idea that there are small children that need this drug in order to live, and it wasn't available. But thank God we have some supply now. But it just points to this peak-and-valley situation that we have.

Mr. Pallone isn't here, so I am going to go to our friend Mr. Butterfield.

You have 5 minutes for your questions.

Mr. Butterfield. Thank you very much, Ms. Eshoo.

And thank you to the two witnesses for your testimony today.

You know, as I have sat here listening to the testimony, this is a big deal. This is very, very important. And I am glad you are having this hearing, because I am learning so much about this. We must ensure that FDA is equipped to oversee this very complex and global drug supply.

Some years ago, I heard the statistic that 80 percent of our drug supply comes from overseas. I didn't know if that was an exaggeration, but it appears not to be an exaggeration. It appears to be the case. And the testimony today seems to reflect different data points on the reliance, which I would like to better understand.

And so, Dr. Woodcock, you note in your testimony that, as of August of this year, only 28 percent of the manufacturing facilities making APIs that supply the United States were located here in the U.S., and the remaining 72 percent of API manufacturers were located overseas. Thirteen percent of the overseas API manufacturers were located in China.

I was sitting here trying to do the math a few moments ago, and it has been many years since I have really done a deep dive into mathematics, but if it is 13 percent of the foreign market, wouldn't that be a greater percent of the total? I guess that is my first

question.

We hear that 13 percent of the APIs are manufactured outside of the U.S. -- in China. But if you take that 13 percent and compare it to the total, I would say somewhere around 20 percent -- I have done the math. I think it is about 22 percent of the market would be in China, if you look at the overall supply chain.

Dr. Woodcock. If I could have the first slide up?

Mr. Butterfield. Yes.

Dr. Woodcock. Could I have the slides up? And I will show you.

Having trouble advancing it. I don't know where the projector is. There we go.

All right. So there you see. That 13 is a percentage of the whole.

Mr. Butterfield. Oh, it is of the whole, not just --

Dr. Woodcock. Yes.

Mr. Butterfield. Okay.

Dr. Woodcock. So that is why the pie chart -- that is the whole API, all the facilities. But this, as we said, is by facilities; it is not by volume.

Mr. Butterfield. All right.

Dr. Woodcock. China has --

Mr. Butterfield. Let me ask you this. Do these numbers reflect both brand and generic API facilities?

Dr. Woodcock. They do.

Mr. Butterfield. Okay.

You note in your testimony that the data available to FDA related to API manufacturers has several limitations. Some have suggested that FDA should also have

access to information related to volume. You told Ms. Eshoo that a few moments ago.

Does the FDA have access to information today about the volume of API or finished dose products produced in each facility? And I think the answer is no. You get it retroactively.

Dr. Woodcock. Correct.

Mr. Butterfield. You get it retroactively. And how would this information be helpful to you in your work?

Dr. Woodcock. Well, I believe we have -- in the President's budget, we have a request for certain different authorities, because, first of all, we could use this in shortages. Because, as you all have been saying, it is very difficult to understand our vulnerabilities unless we understand where the drugs are actually being made, how much.

For example, vincristine had two suppliers for a while, but one supplier had 98 percent of the market. Okay? So when that supplier goes out, then we are in deep trouble, right?

So it would help with shortages. It would also help with the kind of vulnerabilities that Commissioner Wessel was talking about, and others, and the members, which is to understand where, actually, we have sourcing that is concentrated in one region, particularly for drugs that are critical.

Frankly, China has a lot of API manufacturers for over-the-counter drugs, such as toothpaste, wart removers, and so forth. We probably wouldn't be in a national security issue if we didn't have those. So what we really need to do, as the chairwoman was saying, is look at penicillin or look at other critical drugs. And we would have that

information then.

Mr. Butterfield. Thank you, Madam Chair. I don't have time for my third question. I will yield back. Thank you.

Ms. Eshoo. The chair thanks the gentleman.

And I now would like to recognize Mr. Shimkus for his 5 minutes of questioning.

Mr. Shimkus. Thank you, Madam Chairman.

I have been writing, trying to scribble down notes, and I think I am failing, but let me go first to this question, Commissioner Wessel. So we know that the Chinese rip us off, and we know that they steal our intellectual property.

So, similar to the fights we have had recently on steel, the President responded with tariffs and fights because, in my part of the woods and a lot of steel-making regions, obviously coal regions, there is dumping. And they just undercut our prices, drove the manufacturing business -- so I think that is a valid concern.

This is a tough dilemma, because we are driving -- we want low-cost drugs. We are having all these fights on how we get low-cost drugs. So we, in essence, by that push for low-cost drugs, have encouraged foreign manufacturers of at least part of the processes, the APIs, to go where they can produce it at lower cost.

We were in this -- Dr. Woodcock, we were in this debate a couple years ago on the inspection regime. And so I was just curious, in listening to the statements, how -- and I know the answer is going to be we need more inspectors. We need more money to have inspectors, inspection in foreign facilities.

And then I countered years ago, saying, well, I was a risk-based-system guy, not just hit, hit, hit. And I thought maybe our facilities were overinspected versus what we

were doing overseas.

You are shaking your head "yes." You believe that is true?

Dr. Woodcock. We have, since that time, and with the help of Congress and FDASIA, we now do more inspections overseas than domestic, but that was definitely not the case back in the early 2000s.

Mr. Shimkus. And that is good clarification.

I guess my question is, with all these areas, we give FDA the -- we give them the stamp of approval, right, that then they can enter in our market. We need to follow that up with an inspection regime. Are we creating more facilities that get the stamp of approval versus our ability to inspect those?

In other words, I mean, sometimes we look at it the other way. We look at, we need more inspectors. But maybe we should slow up the approval process so that we have the right amount for the amount of inspectors we need.

Dr. Woodcock. I don't think we have the ability to say, well, we are going to stop pharmaceutical innovation or the generic drug program because we have run out of inspectors.

Mr. Shimkus. No, I am not saying that. I am saying, do we have the authority to say, we are going to make a choice between -- we only have this many inspectors, they can only do this amount of facilities, and that is the approval process that we are going to have overseas?

Dr. Woodcock. Right. Well, under the generic drug user fee program, as you know, the generic drug industry pays fees based on the number of inspections that are done. So we do get income. Most recently, in the last several years, we have had

trouble with hiring people, and that is why our inspections have gone down.

We peaked in foreign inspections around 2015, 2016, with 1,041 foreign inspections, both pre-approval and surveillance inspections. So I am not sure that --

Mr. Shimkus. Okay. Let me move on real quick, because I am running out of time, and I want to -- you talked about advanced manufacturing practices and how, you know, we are leading the way.

My concern would be, again, Commissioner Wessel, is that we need to be smart about where we allow these. If you talk to manufacturers who go to China, they allow the facility to be built. While it is being built, there is a Chinese national right next to the U.S. manufacturer who then observes, recreates, retrains, and builds a facility right next-door, the same one, ripping off our technology.

So if we are ahead in advanced manufacturing practices, I would hope -- and it is safer, more efficacious, at lower cost -- then I would hope our manufacturers would be very, very careful about trusting a regime that right now, in the international trade arena, that we cannot trust.

And, with that, my time has expired. Thank you, Madam Chair.

Ms. Eshoo. The gentleman yields back.

I just want to make a comment about the drugs that we are talking about. We are talking mainly about generic drugs. And I think it is important to keep in mind that manufacturing does take place offshore, obviously, but we are not talking about development; we are talking about manufacturing and the challenges that that represents --

Mr. Shimkus. But if the gentlelady would yield, I mean, you do have a risk of

shortages even in the generic space in this debate.

Ms. Eshoo. Agreed.

Mr. Shimkus. So, then, shortages require increased cost. So even though they are generic, they may not be inexpensive.

Ms. Eshoo. But there is a linkage, and it is generics, and it is manufacturing versus development. And we are talking about old generics, like penicillin.

I now would like to recognize the gentlewoman from California, Ms. Matsui, for her 5 minutes of questioning.

Ms. Matsui. Thank you, Madam Chair.

And I would like to thank the witnesses for appearing here today.

As our pharmaceutical supply chain becomes increasingly global, it is critical that we continue to assure the quality of medicines manufactured abroad in order to protect the safety of Americans at home.

While our focus today is on the manufacturing of our drug products, I would like to quickly raise an issue that impacts access. The Ryan Haight Online Pharmacy Act of 2008 provided vital consumer protections against the distribution of dangerous substances via the internet, yet it preserved the value of telemedicine where appropriate.

Community addiction and mental health treatment centers were largely excluded from the legislation due to a registration issue with DEA. My bipartisan bill, the Improving Access to Remote Behavioral Health Treatment Act of 2019, would ensure that these facilities could register with DEA to remotely prescribe controlled substances, using telemedicine in a secure and effective environment.

And I want to thank my colleagues on the subcommittee, Representatives Brooks

and Kuster, for leading this effort with me. And I encourage the consideration of patient access policies as we continue our work to strengthen the drug supply chain.

Now, most healthcare organizations experience drug shortages. They result in nearly $230 million in additional costs annually for hospitals because of higher costs of substituting drugs. Shortages can be caused by a variety of issues, from low-quality manufacturing processes to supply-chain disruptions, to manufacturers simply leaving the market.

The importance of preventing drug shortages has long been a priority of this committee. And in the manufacturing context, we know that low-quality processes, those that result in failures or disruption in production, can lead to shortages.

Dr. Woodcock, do you believe that drug manufacturers are minimizing investments in manufacturing quality? And if so, how do these quality problems contribute to drug shortages?

Dr. Woodcock. Yes. As we go over in our report we issued yesterday on drug shortages, about 62 percent of the shortages can directly be traced to manufacturing problems, which usually have to do with lack of keeping up in investment and so forth.

And we feel that there is a market failure here, there is an economic problem, where cost minimization and driving to the lowest price then disincentivizes investment by manufacturers, which then gets them out of the market or gets them eventually into manufacturing difficulties.

Ms. Matsui. Right.

Now, could you speak a bit more about FDA's recent announcement that the agency is considering allowing manufacturers to voluntarily disclose quality ratings?

How would such a disclosure help incentivize a greater focus on quality generally?

Dr. Woodcock. What we found in our analysis is that the market, the people who purchase drugs, are pretty much blind to any quality above the fact that FDA has approved it, all right, which is a standard that ensures those drug products are okay --

Ms. Matsui. Right.

Dr. Woodcock. -- but it doesn't ensure that reliability over time. And, more and more, hospital systems and every -- are calling for that reliability.

Ms. Matsui. Sure.

Dr. Woodcock. They want to know they can get the drug over time. And so we feel, if we could rate quality maturity, which is something that ensures reliability, and assign some type of system, that that would then hopefully incentivize some rewarding value --

Ms. Matsui. Right.

Dr. Woodcock. -- out in the healthcare system purchasing chain.

Ms. Matsui. Sure.

RPTR PANGBURN

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[11:02 a.m.]

Ms. Matsui. Now, you mention in your testimony that FDA has determined that there are three drugs in the World Health Organization's essential medicines list whose API manufacturers are based only in China including a drug to treat tuberculosis and other infections. Well, that is a small portion of the overall 370 U.S. marketed medicines on the list. I am still concerned about the sole reliance on China for these key ingredients globally. How can Congress and the FDA work together to encourage more manufacturing domestically? That is a big question, I know, but broadly.

Dr. Woodcock. Right. Well, I think the steps that have been taken already to work on advanced manufacturing, and, as you know, there are some organizations now stepping forward that are interested primarily because of the shortage problems in supplying drugs to the United States more as a nonprofit type of entity or under certain different arrangements. They will require, though, assurance, the manufacturing, that there is a stable market for their product at a reasonable price. For example, the Vincristine, which is a lifesaving drug for children with leukemia and other cancers. I understand for that sterile vial it costs about $8 which is less than, you know, a couple venti lattes or something like that. And so we are sowing what we reap, so to speak, if we are only willing to pay that much, then people are going to drop out of the market.

Ms. Matsui. Absolutely, yes.

Dr. Woodcock. And so I think -- but what these manufacturers tell me, these new type of manufacturers are going to use advanced manufacturing. That is what they

tell me, that that is how they think they can do sustainable supply for short supply drugs in the United States.

Ms. Matsui. Okay. Good. Thank you. I have gone over my time.

I yield back.

Ms. Eshoo. With every members' questioning and your answers, we keep learning more.

It is a pleasure to recognize Mr. Guthrie for his 5 minutes of questions.

Mr. Guthrie. Thank you. We couldn't have planned -- Ms. Matsui and I work well together, but we couldn't have planned that question leading to my question. You said that continuous manufacturing is going to be the answer to some of these problem issues. Chairman Pallone and I introduced a bill this week to create a grant program into an FDA and university to look at continuous -- to grant programs for advances in advanced manufacturing, continuous manufacturing. How specifically is that going to help?

Dr. Woodcock. Well, as we talked about in many hearings before, there hasn't been an academic base supported in pharmaceutical manufacturing in the United States for a long time. This has been a neglected area. I mean, it is such an important commodity when you think about semiconductors or you think about other things. There is all this study of it and so forth. This has gone on behind sort of a firewall, is make the drug over here and get it to us, right? And so I think we need a strong academic base because, as I said, even these miniaturized mobile units, that is a whole new concept, and it is going to take a lot of study and research to really bring this, but it has so much promise for small volume drugs like for rare diseases or for outbreaks and so

forth, but if we don't have the academic base, and they don't produce the workforce that we need, right, to actually bring about this change, then we are not going to get there.

Mr. Guthrie. Okay. Thank you for that. And, also, Dr. Woodcock, we have learned today that FDA currently has several limitations for API data. In your testimony, you mentioned that manufacturers are not required to report to FDA whether they are actually producing an API at a facility and the quality of that at the facility. Does FDA have the administrative authority to require this API data?

Dr. Woodcock. We can get this in annual reports, but as I said, that is too late, okay? That is what happened before, and so, no, we don't have the authority to ask for the sort of real-time data on a continuous basis.

Mr. Guthrie. Do you think manufacturers should be required in some cases to report this information in order to help CDER fully monitor APIs?

Dr. Woodcock. Yes. We have several proposals along with the President's budget, one of which is that certain manufacturers are making really critical components have risk-management plans, okay, that they really have contingency plans for what is going to happen if there is a shortfall of their suppliers, for example. But second of all, we think for certain drugs that might be very useful for us to get that real-time information so we can respond earlier, and we know what is going on for critical drugs.

Mr. Guthrie. But to get the real-time information, it is going to take legislatively -- there is not authority there currently to do what you think we need to do?

Dr. Woodcock. Not to my knowledge.

Mr. Guthrie. So Congress is going to have to act?

Dr. Woodcock. That is correct.

Mr. Guthrie. So, when Congress acts, how would you ensure the propriety information is kept properly?

Dr. Woodcock. Well, we get giant amounts of proprietary information now, so we would probably use advanced technology, cloud-based, blockchain, and so forth to have that electronically submitted to us, but we are pretty good about keeping data safe.

Mr. Guthrie. Okay. Thanks. And then, also, my colleague, Eliot Engel, have been very interested in the drug shortages as everybody on the committee, but Eliot Engel and I sent letter to FDA in September on this issue. I was very pleased to see the drug shortage report that came out yesterday. It is clear work is needed to stop these shortages and assure Americans have the drugs they need. What are the main root causes of drug shortages and to what extent are shortages due to the API manufacturing primarily being based in foreign countries? And, Mr. Wessel, you can answer if you would like to as well.

Dr. Woodcock. Sure. Our root cause analysis said, you know, really it is -- first of all, you know, there is an economic problem here.

Mr. Guthrie. It seems to always be the lower priced drugs.

Dr. Woodcock. It is a market problem that drives to the bottom, and there is no incentive to make these drugs when you could make -- if you are a generic manufacturer, you could make newer generics, okay, that have much higher prices, right, and so people drop off and so maybe the last person standing is someplace, you know, someplace far away, and then they have a problem with their -- you know, there is also no incentive to upgrade your facilities and so forth because there is no transparency to the purchasers

about the robustness of that manufacturing site.

Mr. Guthrie. And in the pricing mechanism -- oh, Mr. Commissioner, has something.

Mr. Wessel. Let me just add and I agree with all of that. Part of this is also about the ecosystem as we move forward. So we are talking about continuous manufacturing, advanced manufacturing. China is already on that. We have seen with the Thousand Talents Program, which is their program of bringing educated researchers and executives from the U.S. to China where they pay a bounty of $160,000 on average to those individuals, so some of the experts we are relying on to help rebuild our industry are migrating to China so some of the continuous manufacturing they will be doing as well. We have to ring fence our intellectual property, provide greater support for it, and also look at this as a national security asset and treat it differently.

Mr. Guthrie. All right. Thank you. My time has expired.

I yield back.

Ms. Eshoo. The chair thanks the gentleman. Excellent questions.

It is a pleasure to recognize the gentlewoman from Florida, Ms. Castor, for her 5 minutes of questions.

Ms. Castor. Well, thank you, Chair Eshoo, for calling this hearing and welcome to our witnesses.

Dr. Woodcock, I would like to investigate in greater detail FDA's ability to directly monitor and ensure the safety of products that are manufactured outside the United States specifically China. This committee has heard various in hearings, this one and in prior hearings, problems with access to Chinese facilities. In past hearings, the FDA has

noted the difficulty in gaining access even to necessary travel documents to be able to travel to China to perform inspections. Some have even noted that when FDA is able to obtain the necessary travel documents, some facilities receive warning of an FDA impending inspection. Witnesses on our next panel have claimed that, even where the manufacturers has not received a direct warning about an impending FDA inspection, facilities may refuse to comply with FDA inspectors.

In your testimony, you said there are 13 percent of active pharmaceutical ingredients manufacturing sites in China. So that is probably a manageable number. Has FDA had ready access to these facilities in order to verify the safety of the products and ingredients manufactured there?

Dr. Woodcock. Well, we currently are not having trouble getting visas and getting people into the country. We also have people in the country office who do inspections. We have inspection personnel in China. If we are refused, what we do is put out an import alert and not let that product be imported into the United States or a finished drug product made from that facility be imported into the United States. And that has happened somewhat recently a number of times, but there is a very effective and very fast sanction that we can put into place to prevent American patients from being exposed to those medicines.

Ms. Castor. So would you say over the past couple of years you have been refused inspections a number of times? Do you know how many times?

Dr. Woodcock. I don't have -- we can get back to you on the exact figures.

Ms. Castor. So, when that happens, you do issue a report because you can't guarantee the safety of the product?

Dr. Woodcock. Right. That is correct.

Ms. Castor. What about the FDA office in China? There are certain staffing concerns. We have heard that it is difficult for the FDA to hire and retain staff in China and that the staff numbers have decreased by as much as 25 percent in the last 2 years with some offices closing. Why has it been so difficult for the agency to hire and retain professional staff in China and what, if anything, can Congress or FDA do to address these issues?

Dr. Woodcock. Well, it is a complicated process to get people to go and move with their family and stay in a different country for quite a number of years, but we have had -- overall, we have had hiring problems overall, and we are shorthanded at the agency, including our field organization ORA who these inspectors come from.

Ms. Castor. How many authorized positions in China for the FDA? Do you know?

Dr. Woodcock. I think there are 30 -- somebody can give me that graph, something like that.

Ms. Castor. And what is the current staffing level?

Dr. Woodcock. Well, the numbers I had that we were fairly up to speed, but then I was told by the ORA senior leadership yesterday that those numbers have dropped, so it sounds like it is a dynamic situation, and I would have to get back to you on the exact numbers who are there today.

Ms. Castor. Okay. But FDA has other tools that it can employ post-market to analyze the products coming out of these facilities, so those are in addition to inspections. Can you discuss the additional regulatory tools and authorities FDA has in the

post-market space to monitor the safety and quality of those products, and are they helpful in mitigating some of the challenges with inspections?

Dr. Woodcock. Well, in general, we monitor safety of all drug products. We get 2 million reports a year from doctors, pharmacists, patients, manufacturers, and so forth about problems, including quality problems, that are noted. We follow-up and analyze all those. We also have our Sentinel network that actually monitors adverse events around the country, and we have several hundred million lives of people in that network, and then we do a testing program. We do sample. Sometimes we do random. Sometimes we do directed samples, and we test them according to USP standards, and, generally, they all -- they pass. So the drugs in the United States that we test pass the USP standards for marketed drugs. So we have -- and we can, Congress gave us the authority, to ask in lieu of or in advance of inspection to ask from data from the plants so we can remotely look at the information either before we go or in lieu of getting there, so we have multiple ways.

In addition, for APIs, we require the finish dosage for manufacturer to do testing and also to audit their supply chain to make sure that that API manufacturer is, you know, doing the right thing, and it is in their best interest to do that. And we inspect the finished dosage for a manufacturer, we make sure that they are doing those activities to monitor their raw ingredients or their APIs. So there are multiple redundant things in the system.

Ms. Castor. Thank you very much.

Yield back.

Ms. Eshoo. I thank the gentlewoman.

But, Dr. Woodcock, in the FDA, Center for Drug Evaluation and Research is not in charge of inspections, correct?

Dr. Woodcock. Correct. Correct.

Ms. Eshoo. I think it is important for us to note, but we can always get the person that is responsible for that in future hearings.

The gentleman from Virginia, Mr. Griffith, is now recognized for his 5 minutes of questioning.

Mr. Griffith. Thank you very much, Madam Chairman.

Dr. Woodcock, as always, it is good to see you here. You are one of my favorite witnesses because I can always count -- even if I don't like the answer -- I can always count on you telling me what you know, or sometimes you have to say we don't have that information, and that may be in that situation now. Zantac, is any of that manufactured or was any of that manufactured in the United States?

Dr. Woodcock. I don't think so. There are some manufactured in Europe, but ranitidine, which is Zantac, it is a different problem. It isn't an inherent contaminant.

Mr. Griffith. So we have made that determination because some of the early articles that came out in September thought it was a contaminant and then there were other articles that said it is the drug itself is unstable. So have you all made a decision on that?

Dr. Woodcock. Our chemists think, all right, that the ranitidine in the presence of nitrite, which might be in the excipients; it might be during the manufacturing process --

Mr. Griffith. Hang on. Not only me, but people back home -- might be in

the -- tell me what that word was?

Dr. Woodcock. Excipient.

Mr. Griffith. Excipient, what does that mean?

Dr. Woodcock. The stuff, the powder that is put into the pill along with the active ingredient to make a tablet, uh-huh.

Mr. Griffith. So -- but you think it was not that there was lax manufacturing anywhere; you think it was that component. How quick are you going to be able to tell whether it is the powder or the base drug?

Dr. Woodcock. What we have found is very low levels of NDMA in various ranitidine preparations we have looked at.

Mr. Griffith. And for the folks back home, NDMA is the contaminant item which is a carcinogen that causes cancer?

Dr. Woodcock. Yeah. Well, it is a genotoxic agent, yes. And we have found various levels of that in different preparations of ranitidine, almost all of them. And our chemists believed that it is formed by a molecule ranitidine reacting with something either during the manufacturing synthesis or during the finished dosage form or during storage, all right? And there has also been an allegation that in the body, it is transformed into higher doses of NDMA. We have not been able to verify that yet. We are still doing testing to look at that.

Mr. Griffith. Okay. So my followup question is, is that if -- I don't think we are manufacturing here either, but I figured you would know better than I, if we were manufacturing it in the United States instead of having to follow the Europeans and the Canadians and other countries, would we have been in the lead because we would have

picked up on this problem sooner, or do you think it just didn't matter?

Dr. Woodcock. This is a product that was approved in 1984 and is used worldwide very widely, all right, and nobody found it. It was developed in Europe, all right? I don't think this had anything to do with where it was manufactured or what have you, and the fact that Canadians and the Europeans have -- Europeans announced that they are doing an assessment. We have been in the lead in my mind in many ways. We developed the test assays for this contaminant in the product and we posted them, and these are being used internationally, and we have tested a huge number of samples, maybe 1,500 samples, to try and figure out what is going on here.

Mr. Griffith. All right. So, again, for folks back home for those of us who use the Zantac or the generic -- and I use both -- it has a histamine blocker, which most of the other antacid type medicines do not have, which for people with allergies, the histamine blocker made Zantac the go-to product, is there another product with histamine blockers in it?

Dr. Woodcock. Well, we have famotidine and the others we have tested, they do not have nitrosamine.

Mr. Griffith. So they don't have the cancer-causing drug, but they do have a histamine blocker.

Dr. Woodcock. Yes, yeah.

Mr. Griffith. All right. I appreciate that.

Dr. Woodcock. We have posted that on our website, so it should be available.

Mr. Griffith. I will be looking it up later. That being said, you know, one of the concerns that happens is, because there is a concern in the public -- and I think rightfully

so -- that foreign manufacturers, particularly China, maybe even India, is happening with so many of our drugs, the minute you hear there is a problem, the first instinct is, well, it got contaminated because of lax standards overseas. Don't you think that is fair for the public to think that?

Dr. Woodcock. I think it is fair for the public to think. It is simply is not probably the case with ranitidine.

Mr. Griffith. I understand, yes, ma'am. I appreciate it.

And I yield back.

Ms. Eshoo. We are going to work hard so you don't have any heartburn, but you got to switch.

Mr. Griffith. Too late.

Ms. Eshoo. But many countries have removed it from the market, and there are other older remedies that you could use. I appreciate what FDA has done, but know that a lot of countries remove this from their shelves before we did.

Now, I would like to recognize the gentleman from Oregon, Mr. Schrader, for his 5 minutes of questions. No. Am I right? Yes.

Mr. Schrader. Thank you very much, Madam Chair. Appreciate it.

Ms. Eshoo. Thank you.

Mr. Schrader. Dr. Woodcock, thank you for coming before the committee again. Appreciate it very much. You gave some statistics regarding the origin of some of the APIs. How confident are you in those numbers? Seems to be a lot of discussion out there about it.

Dr. Woodcock. We are quite confident. It is simply that it doesn't talk about

the volume. It just says: Okay, U.S. can produce 28 percent. We have an API manufacturer in our country that can produce, right. But it doesn't say how much of those the U.S. is producing.

Mr. Schrader. I think that is a key factor as you are alluding to the volume of actual production that gets into the hands of the consumer and stuff. It is something that I think we would all like to know. There have been some interesting books. We are going to hear from an author later today that talk about some of the historic issues that we have had in terms of monitoring some of the generics, some of the APIs from China and India, in particular. What has FDA done since that time period to increase the inspections and make sure, to the best of your ability, that Americans are protected with the right ingredients uncontaminated?

Dr. Woodcock. Well, after Congress passed FDASIA, it really gave us a lot more authorities. We had begun increasing for an inspections in 2005 because the industry had kind of moved before that, and we had to react and get more inspectors overseas, but under FDASIA, we were allowed -- before we were supposed to, according to statute, inspect domestic facilities every 2 years, and there was no requirement to inspect foreign facilities. These were older statutes, right. So that was changed. We were given a risk-based approach, which we have implemented, and, as I said, by 2015/2016, we had reversed that ratio and we had more foreign inspections every year, which we continue to have, than we have domestic inspections.

Mr. Schrader. Do you feel that your abilities or your manpower is commensurate with the need at this point in time?

Dr. Woodcock. I couldn't say. If we were fully staffed, it might be, but right

now, we are not fully staffed and so we are not, I would say, getting our reaches into what it needs to be.

Mr. Schrader. All right. I appreciate that. Mr. Wessel, I appreciate your being here today and your perspective is pretty unique. China is encouraging a lot of manufacturing, particularly in this area, generics, APIs. India now following suit. Are we doing enough in this country to encourage American manufacturing of some of these critical ingredients that Dr. Woodcock references threats to our national security?

Mr. Wessel. I certainly don't think we are. It certainly goes across a number of different industries, but just for this one, I don't think we are up to the task. We are not responding to the priority that China and other countries place on the sector.

Mr. Schrader. Very good. While I would tend to agree, obviously, based on the concerns and what we have been hearing and hopefully out of this hearing will come some opportunities, some thoughts about how we might incentivize some domestic manufacturers for some of the critical ingredients, some of the critical generics that we struggle to get to every American in a cost-effective manner.

And I will yield back the balance of my time.

Ms. Eshoo. The chair thanks the gentleman.

Pleasure to recognize the gentleman from Florida, Mr. Bilirakis, for his 5 minutes.

Mr. Bilirakis. Thank you, Madam Chair, appreciate it. And thank you so much for really holding this hearing and having so much interest in it, and I really appreciate it.

And, also, I want to thank you on another note with regard to the genocide resolution yesterday. I know you were an integral part of getting that on the floor, and I know it affects your family as well mine as well, so I appreciate it so much, and I was

happy to be the Republican lead on that.

So, Dr. Woodcock, in 2013, FDA created a pilot program in India that eliminated advanced notice and instead used short notice or unannounced visits. For additional secrecy leading up to visits, FDA inspectors travel were arranged through U.S. embassies instead of through the FDA offices or manufacturers, as I understand. According to reports, the program exposed widespread malfeasance that had otherwise been hidden due to advanced warning. Among the findings, inspectors found bird infestations, missing samples, and fake labs. Under this program, FDA issued a 60-percent increase in official action indicated findings. However, in 2015, it was shut down without explanation.

Are you aware of the pilot program that I am referencing, first of all?

Dr. Woodcock. I am aware. This was within ORA as was said. That is not within the center for drugs, it is the Office of Regulatory Affairs, which runs the inspectorate, and my understanding is the India office itself on its own initiative ran this program for several years.

Mr. Bilirakis. Okay. Thank you.

Mr. Wessel, you mentioned in your testimony that patients ought to have a right to know where their medication comes from. In what ways could labeling country of origin for active ingredients improve patient safety?

Mr. Wessel. I believe sun shine is a great disinfectant. The fact that, as we saw with lead paint on toys many years ago, melamine in dog food, that simply consumer awareness and having the information can help put pressure on the system to make some changes. So this would allow consumers to be able to pressure manufacturers,

distributors, and government to make sure that there is more attention to where the products are coming from.

Mr. Bilirakis. Well, thank you very much.

And, again, I really thank you, Madam Chair, for holding the hearing, but also, again, we want inexpensive drug prices for our constituents, but they have got to be safe. They have got to be safe, and I really appreciate it. Thank you.

Mr. Burgess. Will the gentleman yield?

Mr. Bilirakis. Yes, I will. Please.

Mr. Burgess. Thank you.

Dr. Woodcock, I just wanted to ask you briefly. You talked with Morgan Griffith about the Zantac. There is an anti-anxiety drug that was also recently named. I think it was Ativan or the generic of Ativan, can you give us any update on that?

Dr. Woodcock. No, I am not actually aware of it, so I will get back to you on that.

Mr. Burgess. All right. Thank you.

Ms. Eshoo. The gentleman yields back.

I want to thank him for his questions.

It is a pleasure to recognize the gentlewoman from Delaware, Ms. Blunt Rochester, for her 5 minutes of questioning.

Ms. Blunt Rochester. Thank you, Madam Chairwoman, for holding this important hearing on the heels of last week's critical committee action to protect patient access to prescription drugs. In addition to making drugs more affordable, we should ensure that access is not further impeded by vulnerabilities in the U.S. pharmaceutical supply chain. I have some questions that I would love to ask, but I just wanted to follow

up on something that you said, Dr. Woodcock. The work that you do is so critical and you mentioned the fact that you are not fully staffed, and I was curious, is that a recruitment issue? Is that a retention issue? Is that a funding issue? What causes the lack of full staffing?

Dr. Woodcock. Well, it appears to be a process issue, so government personnel issues are, you know, very difficult, but we have put in place some corrective plans, and we hope particularly for the field organization, they have received a direct hiring authority, and, hopefully, they will rapidly rebuild their staffing.

Ms. Blunt Rochester. Thank you for sharing that. I served as State personnel director in the State of Delaware, and so when I hear workforce issues, it kind of piques and especially for, again, something as critical as the work that you are doing. I am curious about the kind of data FDA collects related to the location of manufacturing facilities today and whether or not we can do anything to improve the quality of FDA's data. Particularly, I am interested in whether FDA receives enough information about the supply chain to get a full picture of where active pharmaceutical ingredients and finished products are currently manufactured.

Dr. Woodcock, you noted in your testimony that CDER maintains a site catalog of all drug manufacturing facilities making drugs for the U.S. market. You said this information comes from approved applications or facility registrations. Importantly, you also noted that manufacturers which produce APIs are not responsible for noting the volume of APIs they produce. I want to better understand how FDA interacts with API manufacturers currently and whether those interactions vary depending on the type of product. My understanding is that, under the generic drug user fee amendments,

otherwise known as GDUFA, API manufacturers are required to register with the FDA and to pay a GDUFA fee. Is that accurate?

Dr. Woodcock. Yes.

Ms. Blunt Rochester. Are API manufacturers also required to register and pay a fee under other user fee programs, or is GDUFA the only program with this requirement?

Dr. Woodcock. I think the -- I would have to get back to you. We have so many user fees. There are a couple exceptions, though, on registration that I think are loopholes that we are concerned about. One is if an API manufacturer is going to send to a finished dosage form manufacturer who is not in the U.S. either, then they could import into the United States without us necessarily knowing about it.

Ms. Blunt Rochester. Okay.

Dr. Woodcock. And it is very technical, so we would have to work with you on that.

Ms. Blunt Rochester. Okay. We will follow up with you.

Dr. Woodcock. Second, for OTC, both domestic and foreign for OTC drugs, the finished dosage form manufacturer -- they can ship before they register and the same is true for compounding bulks, APIs. They can ship without registering necessarily with the FDA, so these are, we feel, loopholes. So, if there is interest in tightening the scheme, that these are things that should be looked into.

Ms. Blunt Rochester. Excellent. Thank you. We will follow up with you on that. And as a result of the differences between these programs, do you feel that the FDA has more information or a better understanding of the facilities which are producing API which is used to make generic drugs, and should we consider other requirements in

other product areas that would provide FDA with more information about the facilities that manufacture API?

Dr. Woodcock. Well, the thing that probably isn't clear is that for most of these that are applications, so if you do a new drug application, biosimilar application, they have to file with their separate entity what is called a master file with FDA that has all the technical information in it, and we have to review that, and we inspect the facility. And so, if they don't pass the inspection or pass the review, their scientific information, then we won't approve the finished dosage form. So that is how that -- we have quite a bit of control in the new drug space, and that is how we do it.

Ms. Blunt Rochester. Excellent. We will follow up with you on the two areas, but thank you.

And I yield back.

Ms. Eshoo. The gentlewoman yields back. Now it is a pleasure to recognize the ranking member of the full committee, Mr. Walden, for his 5 minutes of questions.

Mr. Walden. Thank you very much, Madam Chair.

So, Dr. Woodcock, again, thank you for being here. I had to go up to the other hearing and back and forth. With respect to the contaminated lots of ARBs that were found to contain traces of carcinogens, FDA stated that those byproducts could not have been detected in routine inspections. Is that correct?

Dr. Woodcock. That is correct. We had to develop special tests for them. They are in that nanogram or microgram range so they are very low levels.

Mr. Walden. And so you now feel like you have the right capabilities to do the test for impurities during routine inspections?

Dr. Woodcock. Yes -- no, not inspections. We are requiring the manufacturers to test for these, all right, and there is multiple nitrosamines, so we have discovered five or six different nitrosamines in different ARBs. So the tests that we have put forth will detect all of those, and we are asking the API manufacturers and the FDF manufacturers to test. And so during inspection, the inspectors can look and make sure they are performing those tests correctly.

Mr. Walden. You know, when this whole issue of drug supply and purity and all that really came to light for me both in the classified briefings we have had on some of these matters, but also after I led the bipartisan delegation down to Puerto Rico and the Virgin Islands, and, you know, things we just think fundamentally will always be there suddenly weren't. And that whole supply chain becomes real real fast in our today modern in real-time delivery systems, and we have got to address this somehow, and so it is a big concern.

In his written testimony, Commissioner Wessel referenced a statement made by the Commission's July hearing about FDA's ability to address safety violations in China. At that hearing, a witness testified that, from 2013 to 2018, out of 864 inspections in China that FDA recommended as official action indicated, FDA officials downgraded 78 of those. By contrast, in the same time period of 11,642 inspections that FDA investigators conducted in the U.S. and recommended as OAI, only one inspection was downgraded in that time. Why might a recommendation for official action indicated be downgraded? What does that mean?

Dr. Woodcock. After -- an inspector's findings, which are -- they put in their 483 form that they leave with the company -- are their observations. They go back and work

with their compliance officer and try to work up a case based on that and then they send it to center for drugs and says: We think this case should be like this, okay?

Then we look at it also at the same time the manufacturer has responded to the 483. They have a brief amount of time to respond to that form. They put in a list of corrective actions or clarifications or whatever. Then all this information is sent to the Center for Drugs and we make a decision. Right now, for domestic, the downgrade rate is 60 percent, and the upgrade rate that we do is 4 percent. In foreign, the downgrade rate is 27 percent, and the upgrade rate is 3 percent, okay. So there is a difference between -- we look at the legality of the sites, all right, that are being made and the charges. We look at other tools that we have. We can do regulatory meetings. We can ask -- we can do a whole lot of other activities to bring the firm into compliance, and so we make an overall decision, and we feel that some differences between us and the ORA are reasonable. We are kind of like the central group that tries to bring consistency across the entire -- as far as -- we call them the sentencing standards might be or whatever you want to call it, right, yeah.

Mr. Walden. So let me ask you one other question. I mentioned in my opening statement the media reports have cited a decline in the number of surveillance inspections of foreign drug factories conducted by FDA over the last 2 years. Has there been a decline in the number of surveillance inspections of foreign drug factories performed by the agency over the last 2 years and if so why?

Dr. Woodcock. There certainly has. We went from a 1,041 down to 740. We also had a decline in our domestic inspections, although they continue to be lower -- fewer, and the reason is we have staffing issues.

Mr. Walden. Have we appropriated the right amount of money to solve your staffing issues, or is it a hiring issue?

Dr. Woodcock. I believe we have the funding, but we are having trouble bringing people on board.

Mr. Walden. Okay. Thank you, Madam Chair, my time's expired.

Ms. Eshoo. Dr. Woodcock, the inspections abroad, are they surprise inspections, or do they inform the outfit that they are arriving tomorrow so that they can clean out the mice, the manipulated data? I could go on and on, but I think that that is an important thing for us to know.

Dr. Woodcock. We have discussed this with the field. Most of the inspections are preannounced, and there are several reasons for that.

Ms. Eshoo. Why would you do that? Why give them a heads up? It seems to me that you give them 24 hours or 48 hours to clean up the mess, and then it is -- I don't get it.

Dr. Woodcock. Currently, for an inspection, it costs the agency about $76,000. We have tried doing unannounced inspections, and the firm may not be in production, in which case it is not useful to inspect them. They may be shut down due to some national holiday that we didn't understand.

Ms. Eshoo. But you would know that when you set the date for an inspection? I mean, you show up that date or -- I mean --

Dr. Woodcock. We don't know whether they will be in production or not. We have tried and our for-cause inspections where we have a whistleblower or we have a problem, those are not announced, and so we do do unannounced inspections. But

most of the ordinary surveillance inspections are announced in foreign countries. In some countries where we have --

Ms. Eshoo. Do you think it was a prudent policy what you are describing?

Dr. Woodcock. Well, I think it is a tradeoff because we, as you hear, we are having trouble getting -- doing enough inspections because we are short staffed, and if we send a lot of people to plants that aren't open or aren't producing and so forth, then we waste peoples' time and we even have less coverage.

Ms. Eshoo. Well, I think with each question and each answer, I add to my list of things that we need to work on, so thank you.

I now would like to recognize Dr. Ruiz from California for his 5 minutes of questioning.

Mr. Ruiz. Thank you. As an emergency department physician, I know all too well the challenges that healthcare providers and health systems face when the drugs they need and rely on to treat patients are not available, especially in the emergency department when you need to treat emergencies. I hear a lot of concerns here today about the reliance on foreign sourcing for our API and finished drug products and what that means for a safety and quality standpoint. We have charged FDA with ensuring the safety and efficacy of our drug products before these products come to market, but we must be vigilant in ensuring that manufacturers continue to meet this standard post-arrival. Prior to the enactment of the Food and Drug Administration's Safety and Innovation Act, FDA was mandated to inspect domestic drug facilities every 2 years but had no similar mandate for foreign facilities. As a result, manufacturers located here at home were routinely inspected whereas, foreign competitors could sometimes go years

before being inspected. FDASIA addressed this by modifying FDA's authority to allow them to set their inspection schedule based on risk.

Dr. Woodcock, can you further discuss the risk-based inspection schedule that FDA uses today to guide inspections, and what criteria does the agency use and how has that worked in practice?

Dr. Woodcock. Certainly. Well, we think it has worked pretty well because, in 2014/2015, the number of foreign inspections got higher than the number of domestic inspections and has remained that way since. We do a risk-based approach like what if it has never been inspected, okay, that is a very strong factor. The inherent risk of the drug, perennial drugs, sterile drugs, they are harder to make, they are harder to keep sterile. That is a higher risk. We put that in. We look at the volume of the facility. We look at the inspectional history of the facility. If it has had problems, we should get back there quicker. Right now, we are inspecting foreign sites more frequently than U.S. sites.

Mr. Ruiz. Okay. Some stakeholders have been critical of this risk-based inspection model and question whether it has provided the agency enough flexibility to target facilities abroad such as in China. That may be cutting corners in quality manufacturing practices or data maintenance. Do you believe that the current risk-based inspection model has been helpful in allowing agency to target the facilities of most concern, and do you believe any changes are needed to this current model?

Dr. Woodcock. We would like to refine the model, but we don't believe country of origin should be a high-risk factor. For example, if you are making fluoride for toothpaste in China, that probably -- you are probably a higher risk if you are making a

sterile drug --

Mr. Ruiz. Is data maintenance and transparency, access to information and how cumbersome it could be a part of your risk assessment? Because some countries are not as transparent as others.

Dr. Woodcock. Right. Well, we make, as we said earlier, because FDASIA gave us if manufacturers give us a hard time in facilities, we can now declare the drugs adulterated if we can't get in and get the inspection done.

Mr. Ruiz. I would definitely consider transparency and how easy it is to get information that you need as part of the risk, right? I agree wholeheartedly that FDA should target its personnel/financial resources to the facilities in countries of most concern. That I definitely agree, but I also want to ensure that we do not return back to a situation where some facilities are inspected every 2 years, and others may go 4 years or longer without an inspection. So how is FDA working to ensure that this is not the case?

Dr. Woodcock. Well, the time since last inspection is part of the model.

Mr. Ruiz. Okay. So why have there been no inspections on some facilities for 4 years then? Are you allowing some inspections to go on for that long? Is that part of the model?

Dr. Woodcock. No.

Mr. Ruiz. So is it an implementation background? Do you need more personnel to conduct these facilities because they are not happening.

Dr. Woodcock. I believe they are happening. We have -- right now we know 100 facilities we haven't inspected. A few of them are in China. These probably are

the loophole ones that I talked about earlier where they can ship before they register if they make OTC drugs, for example.

Mr. Ruiz. Well, loophole or non-loophole, if they are not happening within the loophole, then we need to address the loophole.

Dr. Woodcock. Well, I agree with that.

Mr. Ruiz. So I think that is my point, and so how are we going to ensure that these facilities don't go 4 years without inspections?

Dr. Woodcock. We, as part of our risk model, we look at how -- facilities that haven't been inspected, and we have kind of a limit on that. You have to be inspected within a certain frequency.

Mr. Ruiz. Thank you for what you are doing. Thank you.

I yield back.

Ms. Eshoo. The gentleman yields back.

Pleasure to recognize Mr. Bucshon from Indiana for his 5 minutes.

Mr. Bucshon. Thank you very much, Madam Chairwoman. I was a doctor before I was in Congress, much like Dr. Ruiz. I was a cardiovascular surgeon. This is really important. One of the things I wanted to say right at the beginning is, I do appreciate the initial measured response to some of the contamination that was found in some of these products because, you know, you find something that immediately if you take the pill, you fall over dead, that is, obviously, you stop taking the medication. But there are millions of people who take really critical medications that should not be stopping them immediately without the advice of their physician. I want to make that clear that I think that measured response that came out of the FDA was really important,

and I just wanted to mention that because, you know, you say something causes cancer, you know, people immediately stop taking their ARB or, honestly, their Zantac could result in pretty substantial health risks. So talk to doctor. That is my point.

Dr. Woodcock, in your testimony, you mentioned that adoption of advanced manufacturing technologies may pose a challenge to the current regulatory framework. Can you expand on this a little bit and what that means? What you mean by that?

Dr. Woodcock. We have a lot of regulations that were written a long time ago back when drug manufacturing resembled a very large compounding pharmacy, for example, so some entities in the government and otherwise are thinking of little mobile manufacturing units and so forth that wouldn't even have a fixed site, okay. They travel around and so forth. That is just one example. And they could be turned on and make different things at different times and so forth, so we are going to have to change or adapt somehow our regulations to meet these new innovative methods. It is not like they are going -- as long as they make safe and effective products reliably, we need to have a way to make this happen.

Mr. Bucshon. Yeah. I think that is very important. The advice from the FDA to the Congress would be probably really important about what these barriers are, right, rather than the other way around where we try to -- what I will call nonexperts in the area might try to look at changing regulations that actually may not help you.

Dr. Woodcock. We would be happy to work with --

Mr. Bucshon. So that is an area I think in advanced manufacturing that not only this committee but others should probably look at, not only related to the drug supply chain but other products that we produce in our country, and it might help us produce

more in the U.S. versus overseas, right, can cut down the cost of production.

In addition, you know, what other barriers, other than regulatory barriers, are there other barriers to advanced manufacturing here at home? We talked about maybe the labor cost and other things, but I mean, are there other barriers you think that are causing this problem?

Dr. Woodcock. Well, the primary barrier -- first of all, we don't have, as we already said, academic base of ideas coming forth. We don't have a workforce that is used to this. We have a workforce that is used to traditional manufacturing. There is an upfront investment that has to be made and some companies have put their stake in the ground and said, we are going do this, but, of course, the generic industry isn't exactly, you know, have a lot of -- they have commodity products and so that upfront investment, I think, is one of the biggest barriers to having this --

Mr. Bucshon. So capital costs are a problem.

Dr. Woodcock. Yes, and some costs too in brick and mortar facilities around the world that would change.

Mr. Bucshon. I want to touch on one more thing and that is drug shortages. This is off of the beaten path a little bit from the contamination and where we are producing things, but my wife's an anesthesiologist, she still practices every day, and every day there is shortages of sometimes propofol, which is a critical drug and also paralytic agents, which are important. Do we know how many drug shortages can be attributed to quality issues surrounding the API ingredients as compared to quality issues related to the finished dosing form in the facilities? Are there issues there?

Dr. Woodcock. We don't know. I can get numbers. We haven't performed

that analysis, but I can tell you, for sterile drug production, a lot of it is in the finished dosage form because that has to be made sterile, and, of course, that is problematic especially if you can only sell it for a couple bucks.

Mr. Bucshon. A number of years ago, former Congressman Carney and I who is now the governor of Delaware put in some language into the FDA reauthorization to address drug shortages to try to help the FDA streamline some of these processes, and also the last thing I will say with your indulgence is, single sourcing is a big problem, right. And so I think the FDA, where they see single sourcing as a potential critical issue with a critical drug, that we need to do better maybe in trying to figure out ways to, maybe, at least have another option, so I appreciate that.

I yield back.

Ms. Eshoo. The gentleman yields back.

A pleasure to recognize the gentlewoman from Illinois, Ms. Kelly, for her 5 minutes of questioning.

Ms. Kelly. Thank you, Madam Chair, and I wanted to tell my colleague who just spoke that my spouse is an anesthesiologist also. Thank you for all your testimony today.

And thank you, Madam Chair and ranking member for hosting this committee.

Dr. Woodcock, you noted in your testimony that our domestic U.S. manufacturing facilities won't be able to offset the cost advantages of manufacturing in China by simply increasing the productivity of traditional manufacturing techniques, such as batch manufacturing. Importantly, you also noted that advances in manufacturing technology, such as continuous manufacturing could help manufacturers gain their

competitiveness with China.

Would you discuss further why simply increasing the productivity of traditional manufacturing isn't enough?

Dr. Woodcock. The traditional way these are made is called batch, and what they have is they call it unit operations, so I suppose if you are baking a cake, okay, so first you mix up the ingredients dry and then you try to get them uniformly mixed. So, if you think of a vat the size of this room and then you are trying do that, and then you have to store it and take samples and test for uniformity, okay. Then you might add some liquid ingredients or whatever and you do something, and then you have to store it and test and make sure the reaction occurred the way you thought, and then you might move it to another vat, okay. Continuous is more like an assembly line where the reactions occur along, you know, tubing, looks like the mad scientist, right, and there are sensors that are automated and computers watching to make sure everything is going the way it is supposed to be. So you could see that the kind of workers and the kind of setup you have is very different between these two, and they are just inherent limitations on sort of mass mixing and mass reactions that don't happen so much in a continuous flow setup with advanced oversight with computerized oversight.

Ms. Kelly. One of my colleagues asked about manufacturing in the United States, and I am also interested in the future of domestic manufacturing and especially learning more about the advances in drug manufacturing processes and whether such advances could help to bring pharmaceutical manufacturing back to the U.S.

Dr. Woodcock. Yes. Well, I definitely believe that would be the case, and I think this new generation, which hasn't been talked about very much, which is miniature

setups that are mobile and kind of plug-and-play and so forth, are going to be eventually the new generation, but we are far from there, and I think we need to put our brains against that. We need to invest, and we need to invest in academic research in that area and so forth, and I know that, in the military fields, they really need this kind of capacity, and we may need it for emergencies as well. So I think there are multiple opportunities and scenarios where we really need to push on advances in manufacturing.

Ms. Kelly. Can you tell us about the current state of advanced manufacturing in the U.S.? Do these new methods produce higher quality products or many manufacturers using this technology?

Dr. Woodcock. The adoption has been slow. We have approved I think five different applications, not all in the United States, but certainly a couple -- a number of them in the United States using advanced manufacturing. We approved a 3D printing drug that is printed, and I think that is something that we could see in the future much more, and we are working -- our emerging technology team is working with many manufacturers who said: We are going here. We are going to go in this direction.

So I think the future is starting to unfold particularly in biomanufacturing, bioprocessing for biological products.

Ms. Kelly. Where are we compared to other developed countries, and either one of you, what can we do more to help you?

Dr. Woodcock. Right. Well, leave the -- what we have received under Cures to give academic grants and support the academic base in the United States has been very helpful. We also got an appropriation, and we set up a center of excellence at FDA, and we are able to put in a little pilot lab, so our people can learn about these advanced

techniques and so forth, a pilot plant. So this type of investment, I think, continuing investment is very important.

Mr. Wessel. Let me just add quickly and I had the ability to serve on President Obama's advanced manufacturing partnership. He had both amp 1.0 and 2.0, and that went to many of these issues. This administration just had a summit on the bio economy. The FBI, the DOD, many others are looking at it. We have great advanced manufacturing. The question is whether we can take things off the lab bench into the production arena, whether we can ensure that the IP that we have developed remains here. The largest component of Chinese investment in the United States last year was in biotechnology through venture capital, et cetera. So, when you look at whole of government, we have to look at the entire food chain, if you will, for developing these capabilities.

RPTR MOLNAR

EDTR SECKMAN

[12:00 p.m.]

Ms. Kelly. Thank you very much.

I yield back.

Ms. Eshoo. I thank the gentleman. I have to tell you, if anyone was looking at me while Congresswoman Kelly was asking her questions and getting the answers, it is just really a slow burn up here to hear of the advances of China and how poised they are to grab what we have and run with it. So we have our work cut out for us here. We have to turn this around. We have to turn this around.

Pleasure to recognize the gentlewoman from Indiana, Mrs. Brooks, a wonderful partner on many things, and highly knowledgeable about BARDA. We have worked together on that and the reauthorization of it, and I know it has come up in the testimony. So I look forward to your questioning, and you are recognized.

Mrs. Brooks. Thank you, Madam Chairwoman, and thank you so much for holding this incredibly important national security hearing and with the focus on our supply chain. The chairwoman of this committee and I are co-chairs of the Biodefense Caucus, and we were very pleased that the work that was done last Congress, as well as this Congress, we were able to finally get PAHPA reauthorized and signed into law. Specifically in the reauthorization, we directed the ASPR to consider manufacturing capacity, and we have been talking about that quite a bit, and the outside sources, medical supplies, replenishing the products in the Strategic National Stockpile. And I might, Madam Chairwoman, as you continue to put a focus on this, may we bring the

leader of ASPR, Dr. Kadlec, and BARDA, Dr. Bright, in to talk about this because I think we need to continue to keep a focus on these vulnerabilities and issues and what are we doing to focus on the manufacturing as well.

I think I want to focus on the medical countermeasures and the Strategic National Stockpile. And I appreciated that you put -- there was a category in your written remarks, Dr. Woodcock. You mentioned what I will just call Cipro and doxycycline, critical drugs used to treat anthrax and plague, which are medical countermeasures. What is our American capacity to produce these two drugs in the case of a disaster, if you know?

Dr. Woodcock. I do not know.

Mrs. Brooks. If you could get back with us.

Dr. Woodcock. I could definitely get back to you on that, yeah. We didn't pursue our analysis for individual drugs.

Mrs. Brooks. That is fine, but obviously, things that are part of our Strategic National Stockpile is something that we are critically interested in learning what our capacity relative to American production is.

Dr. Woodcock. We have a chart here that says we have one U.S. API site for Cipro, and two for doxy in the United States, but how much volume and capacity they have, I do not know.

Mrs. Brooks. Right. And I think those would be important things for us to have, maybe even in a secured discussion. And relative to all of our medical countermeasures, and anything that is in the Strategic National Stockpile, I think it is important for us, as Members of Congress, to understand, in a classified setting, what our

capabilities are.

And I am also interested, because you have talked many times, and I am also interested, Commissioner Wessel, about incentivizing U.S. manufacturers, and incentivizing U.S. producers to add, whether it is essential medicines or medicines as part of our medical countermeasures. The products that are part of medical countermeasures are not something that Americans just run out and purchase. The government is the only real customer to have in the case of emergency, but even essential medicines, does the FDA monitor, on essential medicines, who is API manufacturing? Is it less than two countries of origin? Can you talk about that, essential medicines, not even medicines that are for, you know, either attacks natural or manmade?

Dr. Woodcock. No, we do not. And we would probably need that volume information in order to do that accurately, because simply knowing someone could produce an API, they have U.S. approval to produce an API, doesn't mean they have the ability or capacity to do it, especially if they have to do a surge production.

Mrs. Brooks. And so what should we be doing to incentivize government and industry working together to incentivize, to bolster the resources and capacity?

Dr. Woodcock. Well, we have been working with ASPR, DARPA, and BARDA, because in my opinion -- and I know this maybe goes against the flow, but instead of having finished dosage form that you store, the ideal scenario would be, you would have regionalized instant-production capacity, using advanced techniques, so you could rapidly produce whatever countermeasure you needed in a very fast manner. And I believe the military is also looking at the need for that as well. So that is where advanced

manufacturing, for everyone, and then for countermeasures kind of comes together.

We, the FDA, are not, you know, in the sort of incentive business, so we help everybody as much as we can, but we are not on the economic side, which are most of the barriers.

Mrs. Brooks. Commissioner, any incentive ideas --

Mr. Wessel. One of the -- our Commission, which is six Democrats and six Republicans, was unanimous in the view, the recommendations, which are in my testimony. One of those is looking at our procurement systems like DOD, VA, et cetera, to be able to prefer domestically produced items, to look at critical shortages, critical commodities and make sure, just as we do with Buy America as it relates to other products, that we apply certain procurement preferences to make sure we have the capacity.

Mrs. Brooks. Thank you both for your long and very important work. I yield back.

Ms. Eshoo. I thank the gentlewoman.

Pleasure to recognize the gentleman from New York, Mr. Engel, for his 5 minutes of questions.

Mr. Engel. Thank you, Madam Chairwoman.

Manufacturing issues at facilities that produce APIs can lead to drug shortages, which can have health consequences for patients with serious ailments. Recently, the childhood cancer community has experienced a shortage of an important pediatric drug.

So, Madam Chairwoman, I would like to ask unanimous consent to submit into the record, a letter led by Representatives Brian Higgins and Pete King, both of New York, co-chairs of the House Cancer Caucus, highlighting this important issue.

Ms. Eshoo. So ordered.

[The information follows:]

******** COMMITTEE INSERT ********

Mr. Engel. Thank you.

Dr. Woodcock, I have long been concerned with ensuring that FDA has all the authorities the agency needs to be efficient and effective in regulating the complex drug supply chain. I am very focused on ensuring the safety of products for our U.S. patients, but I am equally interested in ensuring that our U.S. manufacturers are able to continue to be leaders in drug development in a rapidly growing global economy. In my time on this committee, I have supported the passage of many bills to enhance the authorities and resources of the FDA, including FDASIA, DQSA, the 21st Century Cures, and more recently FDARA. As part of these bills, we have included provisions that would help to incentivize innovation and to ensure that manufacturers continue to bring their products to the FDA for approval first before any other country.

It is imperative that American patients continue to have access to safe, high-quality, and innovative medicines. So I want to better understand the risks of having API and finished products manufactured abroad rather than in the United States. I know there are real and important negative effects on American workers and on the U.S. economy to having this manufacturing go overseas, but are there real safety risks that arise exclusively from the fact that a product is manufactured abroad? In other words, are products that are manufactured abroad inherently worse than products manufactured in the United States?

Dr. Woodcock. Well, if you look at our inspection outcomes by country, all right, the EU has the highest rate of minimally -- of acceptable or better.

Mr. Engel. Did you say the EU?

Dr. Woodcock. Yes.

Mr. Engel. Yes, okay.

Dr. Woodcock. -- that is outside the United States. Rest of world is 94 percent, and the U.S. is 93 percent, which is not significantly different. Now, if you get to China, that is 90 percent, but that means 90 percent of facilities we inspect in China meet the acceptable standards. And India is 83 percent currently. So we believe that products that reach the United States are of adequate quality. They are fit for purpose. That is the whole point of our whole system. But, of course, we acknowledge that, in various countries, there are more barriers to our oversight than there has been in the United States. It has changed since you all passed FDASIA, which has been extremely helpful to us in many ways and really has enabled us to increase our inspection presence tremendously overseas. That has resulted, though, in a flood of OAI, unacceptable results, all these reports of problems. As we looked, we found a lot of problems. We think, though, over time, as we keep that inspectional intensity up, we will make sure that those facilities are at the level that the rest of the world is at. So that is kind of the state.

We don't believe there is inherent risk in making a drug in another country, other than the economic and those -- and the risk of natural disasters or shenanigans or whatever, but we believe that we need to make sure that the quality standards are uniform around the world. And it would be very nice for the U.S. to have an industrial base because redundancy is important. It is really important to have backup for all these. When we get to a single supplier in a remote area, you know, we are going to get into trouble.

Mr. Engel. Well, thank you. And I have another question, but I want to just

note that, while you were talking, Commissioner Wessel was nodding his head in agreement. I hope I am not telling secrets or anything, but thank you.

Recent press reports, as well as some of the testimony submitted for today's hearing, seem to imply that the safety and quality issues that we are seeing from drugs manufactured overseas are exclusive to generic drugs. Would you agree that safety and quality issues associated with foreign API and finished drug products are unique to only one segment of the industry?

Dr. Woodcock. Could you repeat that? I am very sorry.

Mr. Engel. Yeah. Press reports and some of the testimony that we have heard seem to imply that the safety and quality issues we are seeing from drugs manufactured overseas are exclusive to generic drugs. Is that true?

Dr. Woodcock. No. I don't believe so. I believe we also see safety and quality issues in drugs manufactured in the United States. And we take action against those as well promptly.

Mr. Engel. Okay. Thank you.

Thank you, Madam Chair.

Ms. Eshoo. I thank the gentleman. Recognize Mr. Mullin from Oklahoma for his 5 minutes of questioning.

Mr. Mullin. Thank you, Madam Chair.

Mr. Wessel, you had brought up a couple things in your testimony, and I kind of want to recircle back to those. How did China become the world's largest supplier of APIs?

Mr. Wessel. China has for a number of reasons. One, they have had a plan to

do so. They have been developing their chemical sector for a substantial period of time, and that goes all across from fertilizers through APIs, et cetera. So that is number one. Number two, beginning, I believe it was with their 11th, 12 -- 11th 5-year plan -- we are now on to the 13th 5-year plan, as well as Made in China 2025, they have prioritized the development of the bio-economy, from APIs through biotech, through medical equipment, et cetera, for development.

As part of Made in China 2025, they want to be indigenously self-sufficient for 70 percent of its need -- their needs. So that means you have to develop your own industrial capacity to support it.

Mr. Mullin. What China is doing, do you feel like they could weaponize our drug system?

Mr. Wessel. I think they very well could, and they have, as I have said, they have shown their willingness to do it with rare earths a number of years ago with Japan. I would say they have weaponized certain responses to the current tariff tensions, trade tensions between our two countries, to try and maximize their political response. They could very well do it in this sector if they so choose.

Mr. Mullin. Can you describe some of the ways that corruption impacts China's products?

Mr. Wessel. As I said in my testimony, and I think has been, the Chinese people have been more victim to this than we have in terms of --

Mr. Mullin. Which is one reason why they don't really have confidence in their own drug system.

Mr. Wessel. Well, that is certainly true, that certain test data, certain production

capabilities, they have cut corners, they have bribed officials relating to testing regiments, et cetera. And when found, they have been met with swift and decisive action by the government leaders. But because there are more than 4,000 facilities in China, all across the country, the opportunity for corruption is great.

Mr. Mullin. What do you say when they were found by government officials? I thought some of the reports we have seen, some of the government officials were part of this corruption process.

Mr. Wessel. Correct.

Mr. Mullin. So would you agree it is more accurate to say that the ones fell out of favor with the Federal Government was --

Mr. Wessel. It is -- the --

Mr. Mullin. Not our Federal Government, their government.

Mr. Wessel. The corruption fight probably is focused on two things. One, trying to root out opposing forces in the party, number one, but number two, there really is an effort at times to make sure that corruption, as in these areas, is addressed.

Mr. Mullin. I appreciate your testimony. I just make a point here. Listen, I am not a big pharmaceutical fan when it comes to what has happened with the opioid epidemic. They have brought a lot of scrutiny on themselves for what they have done. But I do think they play a very important role, and we play a role in this too. If we overregulate and we push out, where we make it not conducive for these pharmaceutical companies to do business inside the United States, those needs are going to be met for the American people by someone. Someone is going to fill that gap in. And this is kind of the dangers in my opinion that we face when we overregulate any industry, because

we can regulate them to death, where it is not conducive for them to continue working inside the United States, and then we lose control over being able oversee it.

Dr. Woodcock, you have a very difficult job, when you are trying to regulate industries outside the United States. We only have that ability to regulate them if we have a partnership with the government. But when you are talking about China, who is neck deep in corruption, that inspection only goes so far. So I really don't have a question for you. I just commend you for the work that you are trying to do. It is difficult. But I do think Congress plays a role in this thing too. We have kind of stepped on our own tail, and we find ourselves in this situation. So thank you guys for both being here.

Ms. Eshoo. The gentleman yields back. A pleasure to recognize our resident pharmacist, the gentleman from Georgia, Mr. Carter, for his 5 minutes of questioning.

Mr. Carter. Thank you very much, Madam Chair, and let me clean up a few things from the hearing today. Dr. Woodcock, we were talking earlier about Vincristine and about the fact there has just been a shortage because Teva stopped manufacturing. Teva was only manufacturing 3 percent, and Pfizer was notified that they were going to stop the production of it. Yet we still ended up with a shortage that reached to the level where I was getting phone calls in my office, reached to congressional level. How could a drug that a company that is only providing 3 percent of the market share, how could that have happened?

Dr. Woodcock. That didn't -- wasn't the cause. All right? Pfizer became the single source and developed a problem with finished dosage for manufacturing, and that is -- they stocked out. They were not able to make -- to supply the --

Mr. Carter. So it was just coincidence that both of those things happened at the same time?

Dr. Woodcock. Right. Well, Teva notified us properly that they were going off the U.S. market --

Mr. Carter. Right.

Dr. Woodcock. -- and gave us the advance notification that Congress asked for. So we knew that was happening. That was known. We didn't hear from Pfizer about their -- that they were going to stock out. We heard about this from MD Anderson.

Mr. Carter. Okay. Let me get into some other stuff here. First of all, I want to talk about compounded drugs and how they factor into this issue as well. We have been talking about finished manufacturer drugs, but what about bulk API products that a compounder here in America may purchase? Can any manufacturer register themselves with the FDA and begin selling bulk API products?

Dr. Woodcock. Well, we feel that there are -- we would like to talk to you about this, because we feel there is a -- there is sort of a loophole here --

Mr. Carter. Yeah.

Dr. Woodcock. -- to register, but you can ship -- you can ship the product.

Mr. Carter. So what you are telling me, that it is possible that, you know, for repackagers of API bulk products, that they could register and sell an API in bulk product without first being inspected by the FDA?

Dr. Woodcock. That is correct.

Mr. Carter. Wow. We need to fix that. We need to fix it. Because essentially it would be possible for a repackager to sell into the supply chain, and to then

go out of business, without ever being inspected by the FDA?

Dr. Woodcock. Right. And we have seen some APIs that were mislabeled. They had a correct -- a different certificate of analysis, but they were actually a different drug --

Mr. Carter. How do we fix that ASAP?

Dr. Woodcock. That would probably -- the fastest way would be Congress to get involved.

Mr. Carter. Wow. We need -- that is -- okay, well, we are going to get involved, okay?

Talking about compounding and the important role that compounders play in the broader supply chain. What about your MOU? I know that you are coming up one. Can you give me an update on where we are at with that?

Dr. Woodcock. Yes. Well, as you know, the MOU process has been attended with a lot of controversy. We recently had an agreement, cooperative agreement, with NABP, and we were able to provide them funding because much of the concerns of the States were about, how are we going to do this reporting to FDA?

Mr. Carter. Right.

Dr. Woodcock. And so what we would like is, they can report to NABP, which is something they do already, and if we can make a system that is very easy and seamless to you, so there wouldn't be a lot of paperwork making --

Mr. Carter. Right.

Dr. Woodcock. -- IT systems, and we hope that will then make States, once that is apparent to them, happy to sign on to the MOU.

Mr. Carter. Okay. Because your intention and your hope is that all States are going to sign on to it?

Dr. Woodcock. Absolutely.

Mr. Carter. Do you expect that to happen?

Dr. Woodcock. Not initially, but we hope eventually.

Mr. Carter. Okay. Well, that is very important, because as you well know, I am one who believes that patients should be able to get the medication of their choice at where they want to get it from. So that is just something that is very important to me.

While I am on this, let me ask you this. You talked about the inspection of manufacturers and how that was scheduled. What about 503B pharmacies, are they scheduled, or are they just surprise inspections?

Dr. Woodcock. They are domestic, so we don't need to schedule. We don't need to, like --

Mr. Carter. So what you are telling me is, with the mass manufacturers, you schedule the inspections, but with the 503B pharmacies, you do that by surprise?

Dr. Woodcock. Domestic manufacturers, we do not -- we do by surprise, too, or we can. Okay?

Mr. Carter. That is even worse.

Dr. Woodcock. However, foreign, because of the logistical problems, we can do surprise inspections, and we do do unannounced inspections, but typically the field organization does announced inspection.

Mr. Carter. Okay. Let me shift real quick to counterfeit drugs because that is

something that is very important as well. What about the FDA's role in protecting Americans from counterfeit drugs, which we know that the cartels are producing this now?

Dr. Woodcock. Well, since Congress passed the DCS -- DSCSA and the track-and-trace provisions are being put into place, I think what I call the distribution chain is getting a lot safer, right, because we are tracking it from distribution. However, of course, there is still come through mail facilities, small packages and so forth, and other ways of entry into the drug supply.

Mr. Carter. Madam Chair, if you will indulge me for just another second. You know, this committee is working on prescription drug pricing, and one of the things that has come about during this discussion has been the reimportation of drugs. Does that concern you when we are talking about counterfeit drugs?

Dr. Woodcock. Well, of course, that is one of the main concerns about importation, is that a lot of the people who order drugs on the internet now, they are getting counterfeits, right? Canada Drug Pharmacy, right, and they are getting it from who knows where, and it isn't what they think it is.

Mr. Carter. It is not -- and, you know, this committee, which, you know, I am just proud to be on it and proud of the work that we do, we are attacking it from two angles. Not only are we attacking it from the reimportation of drugs, but we are also attacking it from the technology part and with the internet, with the servers -- not servers, but the internet providers making sure that they are helping us in curtailing that.

Dr. Woodcock. Right.

Mr. Carter. Good. Thank you, Madam Chair. I appreciate your indulgence,

and I yield back.

Ms. Eshoo. I thank the gentleman. I just want to -- I think that this is correct, and you can say yes or no, Dr. Woodcock -- on the children's cancer drug, from 2015 to 2018, Teva had between 10 and 15 percent of the market. They then dropped it to 2 percent, and then they informed you that they were dropping the U.S. market and -- that's correct?

Dr. Woodcock. That is my understanding, correct.

Ms. Eshoo. And they were dropping the U.S. market or what was left of it because they wanted to go to foreign markets where it was more profitable. Now, we are talking about lifesaving drugs. These are -- it is an injectable, isn't it?

Dr. Woodcock. Yes.

Ms. Eshoo. Yes. Okay, thank you. Now we are going to our -- well, are those that waved on, don't they -- oh, Mr. Sarbanes is here, right. The chair recognizes the gentleman from Maryland, Mr. Sarbanes, for his 5 minutes of questioning.

Mr. Sarbanes. Thanks very much, Madam Chair. I just want to say as an aside, I enjoyed the clinic between Dr. Woodcock and Congressman Carter, which I think is probably a testament to the expertise and experience both of you bring to this topic. So thanks for bringing me up very quickly on a lot of the issues as I walked into the room.

I wanted to talk with you, Dr. Woodcock, about these shortages. And as I am going through my district, I hear much more frequently than makes me comfortable from providers and hospitals about this difficulty they are seeing in getting access to products they need, because of these ongoing and persistent drug shortages. It is actually shocking sometimes when you have those conversations because you don't expect it.

And then to hear about it and the constraints it is placing on these key providers is very worrisome.

Getting access to, in a reliable way, to critical medicines, is obviously imperative to ensuring that we can deliver high-quality and impactful healthcare to patients in this country. You have talked today about that impact, and we certainly appreciate it. And you have spoken as well or alluded to the benefits that advanced manufacturing technologies can offer in increasing the quality and safety while managing and mitigating those shortages. Can you discuss a little bit more about the emerging technology program and how it incentivizes the approval of these advanced manufacturing processes?

Dr. Woodcock. Certainly. We have been working on advanced technology pharmaceutical manufacturing since the early 2000s, and we have tried to be -- first, we tried to remove regulatory barriers. A number of years ago, we put together the Emerging Technology Team, which is a group of people from our quality organization who kind of provide a concierge service to people who are trying to bring about advanced manufacturing. And they help them through all points of the regulatory process. So that people, you know, who are used to regulating one type of manufacturing don't, you know, recoil from some really novel idea. As a result, we have approved five different applications that use different kinds of advanced manufacturing, and we have also approved a 3D printed product, but I really think this is just the tip of the iceberg. And in my opening remarks, I talked about some of the announcements that have been made by firms that they are getting really big into advanced bioprocessing, which means they would make biological products this way, in a way that is much more efficient and will --

Mr. Sarbanes. Since I have -- I still have 2 minutes. Maybe you could just give me an example of one of those five applications that you approved so we can get a better sense of what we are talking about here.

Dr. Woodcock. Well, we have approved actually a couple applications from Vertex Company, which is in Massachusetts. They make drugs for cystic fibrosis, and they are making their finished dosage form with a continuous process. This is a rare disease, cystic fibrosis, and this allowed them to scale up to their commercial product without going through many, many months or perhaps a year and a half of scale-up activities. They could just run their machine faster. So that is an example of advanced manufacturing that is actually operating in the United States.

Mr. Sarbanes. And before you put in place the procedures and the processes through this program at FDA to facilitate approval of that kind of technology, can you give me a sense of what it would have taken, how long it would have taken, the hoops that they would have had to jump through then versus what you have been able to create as a different pipeline now, just to get a sense of that?

Dr. Woodcock. Sure. I don't think it would have happened. This is a highly regulated industry who operates at risk in the new drug side.

Mr. Sarbanes. Yeah.

Dr. Woodcock. And so they are not going to risk an important asset to some experimental technology, right? We have had a couple where the people have taken very high volume new-drug products, you know, that have been huge commercial successes, and switched them over to advanced manufacturing. Because it is more cost-effective and, you know, it is better to do that. But in general, I don't think this

transformation would have happened because the industry is so regulated. Now, the concern is that the generic drug industry, which really is a commodity type of product, that they don't basically have the resources to move to this new paradigm, and other people are going to have to lead the way.

Mr. Sarbanes. Right. Thanks very much. I yield back.

Ms. Eshoo. I thank the gentleman.

I now would like to recognize Mr. Flores of Texas who has requested to wave on today to participate. Welcome, and you are recognized for 5 minutes for your questions.

Mr. Flores. Thank you, Madam Chair, for allowing me to wave on today.

Dr. Woodcock, you know historically that the production of medicines for the U.S. population has been domestically based. However, in recent decades, drug manufacturing has gradually moved out of the United States. I agree with the rest of the panel that this is concerning in part because of the safety implications that we have discussed today.

One policy would be to change the factors that influence a drug company's decision to source its API from overseas. So I would like your thoughts and feedback on a policy where, if we did it, we would expand the definition of a banned foreign facility to include one where a class 1 or class 2 recall was issued for a drug that was manufactured or processed at that facility, and then we make the importation of a drug that was manufactured at such facility a prohibited action under section 331. So would such a policy, if implemented, be an effective tool that FDA could use to protect patients from the risk of imported drugs that contain adulterated API?

Dr. Woodcock. Well, it would be a tool we have to use very carefully because as a witness in the next panel is going to talk about, you know, we can't cut off the drug supply in the United States for certain products in order to, you know, enforce a certain level of, what, domestic production or whatever. So we have to -- we don't let facilities that have OAI that are very poor, we don't let them import drugs into the United States now. We are able to do that unless if they are making critical drugs and they are the sole source, then we have to figure out how we are going to get drugs -- good drugs to the patients. So --

Mr. Flores. I think the issue is here, to start, if we had a policy like that, again not to cut our nose off with respect to critical drugs but to begin to influence the companies that are offshoring production of these drugs, so that they change their behavior so that they don't get offshored in the first place. That is what I think we need to look at.

Dr. Woodcock. I see.

Mr. Flores. So I would like you to continue to think about that. Dr. Woodcock, you also -- well, let me say this. This question is also directed at Dr. Woodcock, but Mr. Wessel, feel free to weigh in as we go through this. In Mr. Wessel's written statement, he references testimony given before the U.S.-China Economic and Security Review Commission concerning FDA's ability to address safety violations in China. That testimony was as follows: According to FDA's own data from 2013 to 2018, out of 864 inspections of facilities in China that FDA investigators recommended as official action indicated, FDA officials downgraded 78 of those. By contrast, in the same period, out of 11,642 inspections that the FDA investigators conducted in the U.S. and recommended as official action indicated, only one inspection was downgraded at that time. It was then

stated that this reflects FDA's willingness to give foreign plants, particularly in China, an opportunity to reform without sanctions.

Dr. Woodcock, first, would you agree with that assessment?

Dr. Woodcock. Well, I don't agree. Our most recent data over the past 5 years shows that domestic downgrades are 16 percent and foreign overall are 27 percent. So there is a difference, but I don't agree that it is due to our willingness to grant foreign entities some kind of pass or something like that.

Mr. Flores. Okay.

Dr. Woodcock. These are technical reasons.

Mr. Flores. When an investigator recommends official action indicated after inspecting a facility, what does that mean?

Dr. Woodcock. Officially, that is -- the investigator is simply putting observations in the 483. Those are investigator observations. They don't have official weight. Then we have an agreement on concept of operations, we call it, with the field organization, Office of Regulatory Affairs, on who does what, when, and how this process goes, and it is all very clearly laid out. Then the field organization looks at these recommendations. They have compliance officers who then they make an overall recommendation, and they get more information from the firm. The firm must respond within a very short period of time, to the observations, and talk about their corrective actions or explanations or so on. At that point, then all of this goes to the Center for Drugs Compliance Office, where we take into account the legal issues and everything and make a final determination. And we do have other authorities that we can do that don't necessarily require an OAI, but also ensure the compliance that we are seeking.

Mr. Flores. Okay. Thank you. I have an enforcement question that I will submit for the record, and I thank the chairman, and I look forward to working with you as we protect our Nation's drug supply. I yield back.

Mr. Wessel. If I could just add very quickly, I think as has been talked about here, that you are looking at potentially updating the earlier GAO study at the question of what happens in this, to follow up on your question, merits further attention, there have been instances where there have been questions raised by inspectors, but where there is a critical nature of a drug, and, therefore, whether it is limited sourcing, et cetera, it has been allowed in. How often that has happened and what the entire process is, I think deserves greater attention.

Mr. Flores. Thank you.

Ms. Eshoo. A point very well taken. I would like to thank our witnesses. You have been really excellent.

Mr. Burgess. Will the chairman yield for a unanimous consent request?

Ms. Eshoo. Certainly.

Mr. Burgess. I just have unanimous consent to ask that this report from Mylan Pharmaceuticals about their voluntary, nationwide recall of alprazolam tablets, and I misspoke when I said Ativan. It is alprazolam, the generic, and I would like to put that for the record and --

Ms. Eshoo. So ordered.

Mr. Burgess. ~~--~~ if that ~~you~~ will help you get the information back to us.

Ms. Eshoo. So ordered. Again, thank you to the witnesses, Dr. Woodcock, Commissioner Wessel, you have been outstanding. It won't be the last time on this.

We have a lot of work to do. I think that the whole issue of how much, in terms of America's drug supply is manufactured elsewhere, and our country's dependence on foreign countries for such a critically needed -- our drug supply, that this just really can't stand. And we are going to have to work very hard to come up with the United States of America plan for our drug supply, and we are going to have to work with industry, with FDA, with the stakeholders, but my ultimate goal is that we have an American supply. We have an American supply. So thank you very much.

And we would now like to bring up the second panel of witnesses. At 1 o'clock, there is going to be a secured briefing for the entire House of Representatives on Syria. So we want to move and get our witnesses to the table as quickly as possible.

Are you going to stay, Susan?

Mrs. Brooks. Yes.

Ms. Eshoo. Okay, wonderful.

All right. Now we will hear from our second panel of witnesses. Thank you for your patience. But I think you must have found from 10 o'clock on interesting because of, you know, where you sit in terms of this issue. So I just want to say, for the record, that Teva was asked to provide a witness today for this panel, but they declined. And they referred my staff to the Association for Accessible Medicines, and I am pleased that they are here today to testify.

So let me introduce, starting with Rosemary Gibson, she is the senior adviser at The Hastings Center and author of the riveting book "China RX." She is a hero to me, and I thank her for the time that she has spent with myself and my staff to walk me through so many of these issues earlier this year. Welcome. Thank you for agreeing to

testify today.

To Mr. Ed Price, the president and CEO of Seqens, thank you for being here, and to Dr. David Gaugh, the senior vice president for sciences and regulatory affairs at the Association for Accessible Medicines.

So, with that, let's begin with Rosemary Gibson. You have 5 minutes for your opening statement and thank you again.

STATEMENTS OF ROSEMARY GIBSON, SENIOR ADVISOR, THE HASTINGS CENTER; ED PRICE, PRESIDENT AND CEO, SEQENS CDMO; AND DAVID GAUGH, R.PH., SENIOR VICE PRESIDENT, SCIENCES AND REGULATORY AFFAIRS, ASSOCIATION FOR ACCESSIBLE MEDICINES.

STATEMENT OF ROSEMARY GIBSON

Ms. Gibson. Thank you, Madam Chair, and members of the committee for this very important hearing on a subject of great import to our health security and our national security.

I have three points. The first is that China is deeply embedded in our medicine supply. We have to look beyond the API facilities. Where does API come from? It is made from raw materials and chemical building blocks. We have to look at where they come from. My understanding is that the FDA typically doesn't inspect that; they are not part of GDUFA. But that is what is really important.

So what role does China play in going upstream in those other materials to make the API? It is not a state secret that India is a huge generic drug maker. Its industry will collapse in weeks, not because of API coming from China but because it needs the raw material. It needs the chemical building blocks to make API, and China is the source.

Second, if you ask, because I have CEOs of three different generic manufacturers who have more than a hundred years of experience -- these are the guys and gals that

have to go out and find the material to make API, and you ask them, where does it come from, the raw material, and the chemical building blocks, and they say China. So we have to look beyond API to the raw material and chemical building block plants to know our vulnerability.

Let me tell you the story of penicillin, which will illustrate this. The United States can no longer make penicillin anymore. And how did that happen? It just wasn't because of lower labor costs and, you know, less regulation. This is a slide that came from the European industry, and we can talk more in the Q&A. Just briefly, a handful of Chinese companies dumped penicillin product, not the API, the raw material, on the global market at below market prices beginning in 2004. And they kept the price low for 4 years. During that time, all the U.S., European, and even Indian penicillin fermentation plants were driven out of business. So this is not just the market operating and it is cheaper -- this is a deliberate strategy to drive out and take control of the global supply of penicillin. This is the playbook for other generic antibiotics: cephalosporins, doxycycline. Again, get control of the raw material. I ask people in the industry, do you know any antibiotic fermentation plants in the continental United States? We used to have these plants all over this country. They can't name one. Maybe there is one; we should know it. So we can't -- we are dependent on China for, I would say, most, virtually all of our antibiotics, for that raw material and chemical -- there might be others, but China is the dominant source globally. There was one -- and talking about API facility, there was one plant in China that exploded. And there was a global shortage of a really important antibiotic to treat sepsis. And doctors had to substitute, and some of those patients got a terrible infection called C. diff. So we have a really serious problem. China is deeply

embedded, and it is a very concerted strategy.

This is why we have shortages. If you narrow the supply chain into a single country, we are going to have shortages just because. We wouldn't have all the oil of the world from one country. You would have shortages. There would be problems.

The second thing I want to address is finished drugs. We will hear today that about 8 percent of our generic drugs, finished drugs, the pills we take, are coming from China. Let's make this real. These are some of the generic drugs made in China by Chinese companies that comprise an 8.5 market share. This is doxycycline for anthrax exposure. And China gained 8.5 percent market share, if that is true, just within 10 years. Where are they going to be in another 10 years from now and another 10 years from now? Doxycycline, birth control pills, made in China by Chinese domestic companies. HIV-AIDS medicine, this was the one that had rocket fuel in it, made by a Chinese company. Antidepressants made in China by Chinese companies. Chemotherapies. Alzheimer's medicine. And we could go on. Diabetes medicine, epilepsy, Parkinson's. So China is gaining a foothold in our finished generic drug industry as our Western generic companies, like Teva, Sandoz, they are collapsing. And we are already spending -- I did a really rough back-of-the-envelope calculation, 8.5 percent of generics. We are already sending $6 billion of our American money -- seniors, hardworking families, our military, veterans, our taxpayer dollars are going to support China's generic industry as ours is collapsing.

I love country-of-origin legislation, but you know what, by the time that happens, by the time we get it done, China will have it. And I predict in "China RX: Exposing the Risk of America's Dependence on China for Medicine," which I wrote in the public

interest -- no one paid me to do it; I do it because I care about the health of our country -- I predict that China will overtake India in generic drug production because China has a plan, and nobody else does. It is just a matter of time.

And even you look in the Indian media, the senior government officials in India, and they call it a national security risk, their dependence on China. China can use that leverage against India.

National security risks, China is rolling out its social credit score for businesses operating in China, including U.S. and other drug manufacturers. I have no doubt, in the event of a global pandemic or whenever China wants to, it could order those companies not to send medicines to the United States, to keep them in China.

I have three recommendations. We really do need a point of accountability in this country, in our national security apparatus, to know who controls our medicine supply, to do what the FDA can't do, which is to conduct risk assessments of countries, to track market intelligence on what is happening. We need that capability. Somebody needs to be in charge. Because I was shocked when writing "China RX," it is nobody's job in the Federal Government to do that. We just cannot rely on the FDA, and we have to work in a whole-of-government approach.

A second recommendation -- this was talked about -- we need to begin immediately -- Strategic National Stockpile -- I am sorry. This is such an important topic. We need to use our Federal procurement dollars differently and start buying here in the U.S. And we need the advanced manufacturing for generic drugs, not just brand-name.

And, finally, we need Consumer Reports type testing of every batch of every generic drug. Valisure, the online pharmacy, they test. Whatever they have tested, 10

percent of generics have not met the standards for API or dissolving in the body properly or active ingredient. Sorry to go over. Thank you very much.

[The prepared statement of Ms. Gibson follows:]

******** INSERT 3-1 ********

Ms. Eshoo. Thank you, Ms. Gibson, very much. I wanted you to be able to get as much as you can in. You waited a long time to do it, and it is really high-value information.

Mr. Price, you are recognized for your 5 minutes of testimony, and thank you for your patience in waiting to speak on the second panel and being willing to testify today.

STATEMENT OF ED PRICE

Mr. Price. Madam Chairwoman, Ranking Members, and members of the committee, thank you very much for your invitation today. It is encouraging to hear that this committee is considering this issue a crisis and is willing to take the action that is appropriate.

My name is Edward Price. I am the president and CEO of Seqens North America, a fully integrated pharmaceutical contract development and manufacturing organization. We are headquartered in Newburyport, Massachusetts, and before 2018, Seqens North America was known as PCI Synthesis, a firm I founded in 1998 and then subsequently sold to Seqens, which is a global pharmaceutical ingredients manufacturer headquartered in Leon, France.

My firm is a developer and manufacturer of active pharmaceutical ingredients, APIs, doing it here in the United States. We have two sites in Massachusetts, and we have 130 employees. As a manufacturer of APIs, we thus produce the key raw material for our customers, for use in drug products and therapeutics that may be looking to bring to market, and we have three main areas of activity with our organization.

First, we develop and supply clinical API material for use in clinical trials for new drugs. We are a commercial manufacturer of active ingredients for generic products, and we are a commercial manufacturer of new chemical entities for therapies that are still covered by patent, also known as branded drugs.

I think it is important that the committee understand that any drug that is approved by the FDA is essentially the combination of two things -- the drug substance, which is the active ingredient that my organization produces, and the drug product, which, of course, is the vehicle in which it is delivered to the body, may that be the pill or cream or ointment or other delivery mechanism formulated with the drug substance.

These two activities require vastly different skill sets, they require different science and technology, different equipment, and very different facilities. The reality of today's pharmaceutical supply chain, especially in the generic sector, is that the overwhelming majority of drug product manufacturers are not drug substance manufacturers and vice versa. If you add in globalization and the ever-increasing trend of outsourcing of both of these activities by pharmaceutical firms, you have an ever-increasing intertwined global industry in many countries around the globe.

Considering that there is nearly a billion and a half dollars of pharmaceutical products consumed in the United States each and every day, produced by thousands of fragmented manufacturers around the world, the competing goals of reliable supply, safety and high-quality products, and low cost, are truly going to be very difficult to achieve in the long term.

The FDA has steadily increased the bar on manufacturers throughout the supply chain, most notably over the last 10 years. The industry accepts that this is the way it is

and assumes this will be the case, and it has responded appropriately. Pharmaceuticals, however, is a business like any other. So increased oversight and increased regulation increases costs. And increase in costs forces business decisions. In the last 5 years, due to consolidation, most of the recognized U.S.-based independent API manufacturers have been acquired by multinational firms, my own firm included. The manufacture of smaller volume products with modest sales volumes are harder to justify and to continue when you become part of a large, multinational firm. As an independent, you have more leeway on products you can develop. And I can tell you that from personal experience, we decided to be acquired by a European manufacturer rather than an Asian manufacturer, for some of the issues that were brought up today.

Ms. Eshoo. Thank God for that.

Mr. Price. In the meantime, our clinical supply business, I have to tell you, is very robust and has grown steadily over the last few years. Due to both perceived as well as published quality issues with overseas suppliers, many early stage, emerging pharma companies want to work here in the U.S. They prefer to work with entities like myself that are regularly inspected, they can visit easily, they can work with closely on very complex and technology advanced programs and manage them closely. This ultimately can be more efficient and outweigh any potential savings by working with an overseas supplier.

The problem is that many of these overseas suppliers that they don't want to work with and prefer to come to me are also commercial suppliers supplying into the United States. This is a complicated situation. For the benefit of U.S. patients, we shouldn't broad-brush positively or negatively any particular country or region of the world. But

pharmaceutical suppliers should be judged on their own merits after robust inspections and only should appropriate restrictions be put in place.

It costs millions of dollars to bring a generic drug to the marketplace. You have to -- and the business case for doing so can be very complicated because a good program today could be a disaster 3, 4 years from now if there is multiple approvals and the business opportunity evaporates after you make that investment. Just this calendar year alone, my firm had to contend with EPA, OSHA, IRS, DEA, and FDA, all simultaneously while trying to run a business. And in a number of instances, we were dealing with issues brought about by activist agencies critical of our operations that they previously approved of or, in another instance, changed their interpretation of existing rules or simply that our number came up.

In short, we are an overregulated industry, and it would be impossible to start my company today as I did in 1998. At the same time, I have 10 job openings I cannot fill because I can't find enough qualified employees to do so.

What can the government do? First, beyond the FDA, the scope and scale of regulation in my sector is unwarranted, overreaching, and unprecedented in the last 5 years. Common sense has to be brought back into the system. We need to encourage the FDA to further expand inspection of overseas facilities and making sure facilities are adhering to GNPs and only allow into the U.S. products from inspected facilities.

We need to target at-risk and sectors of the industry to address existing shortages, have the FDA partnering with companies to develop and make sure there is adequate, safe and supply; limiting approvals, maybe giving exclusivities or expediting reviews.

Promoting STEM education so that the industry can have a steady stream of

qualified workers here in the U.S.: Eighty percent of my technical staff is foreign-born, and when H-1B visas are limited, it is very difficult for us to expand both our business and the activities that we do.

And, additionally, State and Federal authorities need to partner with industry and the FDA to be able to allow facilities like mine to expand their capacity and do more manufacturing here, but more essentially, we need the business climate to be able to do so successfully. Thank you.

[The prepared statement of Mr. Price follows:]

******** INSERT 3-2 ********

Ms. Eshoo. Thank you, Mr. Price.

Mr. Gaugh, thank you for agreeing to testify today. You have your 5 minutes for your opening statement.

STATEMENT OF DAVID GAUGH, R.PH.

Mr. Gaugh. Thank you, Chairwoman Eshoo and Ranking Member Burgess, and the rest of the members of the Subcommittee on Health. Let me start by making one point clear: Patient safety is the number one priority of AAM and our member companies who manufacture FDA-approved generic and biosimilar medicines. FDA ensures generic and biosimilar medicines are just as safe and effective as their brand-name drug counterparts. Patients should know and be confident in the quality of the generic medicines prescribed and picked up at the pharmacy because of FDA's rigorous approval and inspection processes.

And it is critical the patients take their medication as prescribed by their physicians. As the FDA has emphasized and stated here earlier this morning, not taking one's medications as prescribed could have the undesired effect of exacerbating a patient's illness and lead to worse health outcomes.

Now, we understand why the subcommittee would be concerned about the recent reports that paint a distorted picture of the global supply chain that it is heavily reliant on China and other countries of API. Our generic and biosimilars are part of the same global pharmaceutical supply chain as the one brand-name drug and manufacturers use.

And as the FDA noted earlier in Dr. Woodcock's testimony, the agency looks at the supply chain comprehensively, inclusive of all drugs on the U.S. market, such as brand-name, generic, over-the-counter, and compounded medicines. With this said, let me provide the subcommittee with AM's analysis of the global location of where generic, finished dose, and API facilities are located.

We conducted this analysis of data publicly available on the FDA's website, and our analysis for 2020 data shows that, for generic API facilities, 31 percent are in the European Union, 31 percent in India, 17 percent in China, 13 percent in the U.S., and 8 percent in rest of world.

For the finished dose facilities, we found 40 percent in the United States, 24 percent in India, 17 percent in European Union, 8 percent in China, and 11 percent in the rest of the world.

Considering this analysis of FDA's data, it is important to accurately depict and not overstate where generic API and FDF facilities are located. It is also important to note the robust, regulatory environment that is in place today to ensure safety and efficacy of prescription drugs. All pharmaceuticals, whether brand or generic, must be manufactured in accordance with rigorous regulatory standards that require high levels of diligence and accompanying documentation.

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[12:57 p.m.]

Mr. Gaugh. And when the FDA finds the deviation from the strict standards of production, FDA takes swift action. The FDA also utilizes a risk-based inspection strategy to maintain a robust inspection footprint around the world and the number of inspections, both domestically and internationally as we heard earlier, have increased over the last 5 years. All this is in place in no small part due to the significant financial investment and commitment from AAM and its member companies through the GDUFA fees. GDUFA, that was passed in 2012 and reauthorized in 2017, includes a $4 billion commitment to the generic drug industry alone. The FDA uses this funding for its rigorous approval process, to develop and uphold manufacturing regulations and to conduct inspections of manufacturing facilities globally. This ensures FDA-approved medicines are at a level of the supply chain from active pharmaceutical ingredients to the finished medicines sold to the consumers at the pharmacy counter are safe, effective, and high quality. This, combined with a daily commitment to quality from AAM's member companies, ensures the U.S. has one of the safest drug supply chains in the world.

Thank you for the opportunity to testify, and I am glad to answer any questions now or separately after the hearing is over.

[The prepared statement of Mr. Gaugh follows:]

******** INSERT 4-1 ********

Ms. Eshoo. Thank you very much.

I now recognize myself for 5 minutes of questions. Dr. Gaugh, what percentage of American generic drugs are manufactured in the United States?

Mr. Gaugh. The finished dose? Roughly 40 percent of finished dose are manufactured in the United States.

Ms. Eshoo. So, of the world's API, how much is manufactured in the United States?

Mr. Gaugh. That is a smaller number of 13 percent.

Ms. Eshoo. Facilities, not volume.

Mr. Gaugh. Thirteen percent facilities, yes.

Ms. Eshoo. How many?

Mr. Gaugh. Thirteen percent.

Ms. Eshoo. Thirteen percent.

Mr. Gaugh. As Dr. Woodcock mentioned this morning --

Ms. Eshoo. Of all facilities, 13 percent in the United States?

Mr. Gaugh. Yes, ma'am.

Ms. Eshoo. That is a really small number.

Mr. Gaugh. Yes.

Ms. Eshoo. Now the FDA yesterday published a report on drug shortages that I think really speaks to the challenges that we have that are facing the generic drug industry. Do you agree with the FDA's findings that generic companies are discouraged from manufacturing older prescription drugs? Yes or no?

Mr. Gaugh. So discouraged in the fact of, at some point in time, the pricing of

those --

Ms. Eshoo. Do you agree, yes or no, with their findings? Did you read the report?

Mr. Gaugh. Yes, I have.

Ms. Eshoo. Okay. Do you agree or disagree?

Mr. Gaugh. With many parts of the reports, yes, I do.

Ms. Eshoo. Yes, you do, what? Agree?

Mr. Gaugh. Agree with many parts of the report, yes.

Ms. Eshoo. Do you agree that this leads to shortages?

Mr. Gaugh. Yes, it can.

Ms. Eshoo. Do you agree with the FDA's findings that generic companies may not be investing in manufacturing quality for older low-priced prescription drugs?

Mr. Gaugh. I do not.

Ms. Eshoo. You do not agree?

Mr. Gaugh. I do not agree.

Ms. Eshoo. Could minimizing the investments in manufacturing quality lead to quality problems?

Mr. Gaugh. It could. I am not aware.

Ms. Eshoo. Well, if you minimize investments in manufacturing quality, it seems to me that that leads to quality problems. It kind of answers its own question, but you may not agree. Based on this, is it true that the generic's industry is facing three overlapping crises, shortages, which is what we have talked about this morning, quality problems, and foreign reliance?

Mr. Gaugh. So, to answer your question for number one, yes; number two and number three are the same for the brand pharmaceutical companies: reliance on foreign market.

Ms. Eshoo. Mr. Price, you said something about, you know, the cost for generics and much of what you said I am really taken by because we have to take this into consideration in order to resolve the problems that we have heard about, and there are many of them this morning, but I am also struck by the following, that the generics industry gets something for free. They get the recipe. Once the patent expires from the pharmaceutical companies, you get the information, and then you start manufacturing those pills.

Mr. Price. That is not entirely accurate.

Ms. Eshoo. It is not entirely accurate. What isn't accurate, and what is?

Mr. Price. Because --

Ms. Eshoo. You don't buy it from them; you get it from them.

Mr. Price. When a product becomes off-patent, what they have access to is the clinical data that was done, and they don't have to perform the clinical trials.

Ms. Eshoo. Right.

Mr. Price. They don't get necessarily access to the actual formulation of the drug. They are afforded samples. They can reverse engineer it, but they have to come up with their own formulation, which then has to go into bio-equivalence studies to prove that its equivalent. My part in this whole process is the drug substance, the API. We have to prove chemical equivalence.

Ms. Eshoo. How much of the U.S. market do you dominate in API?

Mr. Price. Me personally? We are a 130-person organization. We are a fraction of a fraction, but, anecdotally, I can tell you that from 2005 to 2015, we developed about a dozen generic products. We have developed nothing new in the last 3 years because none of our generic partners can afford to help work with us to cover the cost of development and I will subsequently introduce new products.

Ms. Eshoo. And that is based on the API?

Mr. Price. And that is based on the API. Because we don't get any formula of an off-patent drug, I have to put a whole team together of roughly a dozen people to develop the chemistry, scale it up, develop all the analytics. Costs my organization alone upwards of a million dollars to develop an active ingredient.

Ms. Eshoo. I wish we had more time with you.

To Rosemary Gibson, I am just going to squeeze this in. We have heard from other witnesses' testimony today that cheaper labor and lower environmental standards contribute to China's dominance of the pharmaceutical ingredient manufacturing, but you disagree. Can you just very quickly explain why you disagree on that?

Ms. Gibson. Sure. U.S. and Western companies are not just competing with other Chinese companies; they are competing with the Chinese Government, which is willing to subsidize its domestic industry. It was the Chinese Government that invested in all the infrastructure to make antibiotics for the world. That is the challenge that we are facing. It is not just lower labor costs and weaker regulatory regime; it is the Chinese Government subsidies and, frankly, their violation of antitrust rules, stealing of intellectual property through all legal and illegal means. China is advancing to become the global pharmacy of the United States and for the world.

Ms. Eshoo. This is chilling testimony, and I thank you for it.

I now would like to yield to the gentlewoman from Indiana, Mrs. Brooks, for her questioning.

Mrs. Brooks. Thank you, Madam Chairwoman.

I would like to start with you, Ms. Gibson, because I am very interested and because of the work that we have done in the Biodefense Caucus, very interested in the notion of having a position at the National Security Council focused on biodefense. And it has been a recommendation of the blue ribbon study panel, one of their top recommendations, but I think what you are recommending is going even further than that in that you are recommending a national security review of all medicines, not just what we were focused on on biodefense. Who would you have oversee that type of position or where would that -- is it the ASPR? Is it DOD? Is it FDA? NSC?

Ms. Gibson. I would have to engage with you in conversation to figure out what the right locus of responsibility is, but I can tell you what some of the functions should be. This should be an entity that should collect market intelligence way beyond what an individual private citizen does as I have done. Collect the market intelligence, the environmental intelligence about China and its plans -- and this is an ongoing function -- conduct country risk assessments, conduct supplier risk assessments, think about the risks of natural disasters, like there is a lot of pharmaceutical plants in Italy where there were earthquakes. What about natural disasters that could hit China? This is the type of ongoing risk assessment function -- tracking global supply and demand. Just not look now, but where are we headed in the future, where are we headed in the future with Heparin as China grows its healthcare industry, and we do have to move

beyond pigs because there is just only so many pigs, so those are some of the functions.

Mrs. Brooks. And so, while we might not have that position currently, is there an entity in the world that does that now?

Ms. Gibson. I am not aware of it, no.

Mrs. Brooks. And would you -- would all medicines essentially be subject to the review that you would like to see?

Ms. Gibson. I would like to see this done for the medicines that are essential for the business continuity of our healthcare system, that are essential for life, that if we don't have, our society would collapse.

Mrs. Brooks. And have you studied, yes, what our Department of Defense does relative to this issue?

Ms. Gibson. Well, I have recommended a whole-of-government review with the DOD just because they are very proactive. They have a real vested interest just like they did with the review of their defense industrial base which was really stellar. They had a terrific methodology for how to do that, a framework; that is the kind of framework we need to assess our vulnerability when it comes to China for our medicine supply.

Mrs. Brooks. Thank you. Switching gears briefly, Mr. Price, thank you so much. You are one of the very few API producers in the country, correct? There are --

Mr. Price. Just a handful.

Mrs. Brooks. What is a handful roughly? About how many really that you are aware of your competitors?

Mr. Price. Dozens, probably number in the dozens, and, frankly, most of my competitors have disappeared over the last 4 or 5 years as the industry has gone through

a tremendous amount of consolidation.

Mrs. Brooks. And I know you have certainly talked about all of the agency regulations that are involved, but yet I am also concerned what you were just talking about relative to the workforce. You are a relatively small company but yet you have 10 openings, and can you talk about what are those -- what are the kinds of jobs that you have openings for because we keep talking about the workforce issues, and this is highly technical, correct? And so can you just share with us a little bit about that workforce issue because if we are going to try to invest and try and get more government investment in some way or incentivizing companies to invest in this, it still doesn't mean that they have the people to do the work?

Mr. Price. It is a significant threat, and it is a significant issue that we deal with on a daily basis. As a manufacturer and a technical organization, our workforce runs the gamut from high school educated working on the plant floor all the way to Ph.D.'s with multiple degrees and very sophisticated science, as well as business people, financial people. We really are a broad cross section of the talents that you need in the workforce, and it is a significant issue across the board for us to find people at all levels. It is not any one in particular.

Mrs. Brooks. I have one last completely unrelated question, the types of raw materials that you focus on, are these raw materials found only in China?

Mr. Price. I would say that better than 90 percent of the key raw materials that we purchase and use to synthesize our APIs come either from India or China.

Mrs. Brooks. So the actual raw material comes from India as well?

Mr. Price. The building blocks that Ms. Gibson was referring to, the raw

materials, there is almost no fine chemical manufacturing left in the United States.

Mrs. Brooks. But at some point --

Mr. Price. I actually began my career in the fine chemicals industry but migrated into pharmaceuticals because the fine chemical industry was disappearing.

Mrs. Brooks. But are the actual raw materials for -- and maybe I don't know the terms well enough -- at one point, were they in the United States?

Mr. Price. Yes. Oh, sure, absolutely.

Mrs. Brooks. Okay. Thank you. I yield back.

Ms. Eshoo. Recognize the gentlewoman from California, Ms. Matsui.

Ms. Matsui. Thank you very much, Madam Chair, and I find this all very fascinating as we get into this.

When you are a generic manufacturer, you depend on reliable access to APIs to produce affordable treatment options for patients. I understand that between navigating global regulations and various delivery systems, sourcing ingredients can be a complicated, time-consuming process for generic manufacturers looking to quickly scale up production.

Dr. Gaugh, at what point in the generic drug application process does a prospective generic drug developer need to scale up its manufacturing to prepare for a commercial launch?

Mr. Gaugh. So you first go through the development stage for that product. That is done on what we call bench development. Once bench development is complete, it goes into the manufacturing floor and developed in the manufacturing floor. So it is all done prior to the application being submitted to the FDA.

Ms. Matsui. Okay. Now, after obtaining approval, what steps do generic drug developers need to take to ensure that they will be able to meet the demand for their product?

Mr. Gaugh. So that is portfolio management, if you will, and in the brand world, you know that your product is 100 percent of the market and you know what that is going to look like. In the generic world, you look at how many applications have been approved by the FDA, and then you start the contracting process with a third-party contractors. It is very difficult to tell what your market share is going to be from time to time.

Ms. Matsui. Okay, but this is a certain time frame that you sort of do this in, right? I mean, I am just looking at this as a scale-up process.

Mr. Gaugh. So, in general, I would say that when a company looks at a product, they usually know who their competitors are going to be in the market, and so they are going to develop their market-share analysis based on that competitors. If it is two or three or four, that would give you one percentage to look for for production. If it is 13 or 14, which you would find in the oral solid market, that would give you a different percentage. So that number can be anywhere from 10 percent to 40 percent that you might think you would capture the market share or if you are the only product, 180-day exclusivity, you know you have potentially most of the 100 percent.

Ms. Matsui. Okay. A concern I have is how downward pressure on prices in the drug supply chain may influence generic drug makers to exclusively rely on cheaper foreign API manufacturers.

Dr. Gaugh, what tradeoffs, if any, do you see generic manufacturers making

between quality and price when it comes to sourcing APIs to meet production goals?

Mr. Gaugh. I don't see any difference quality and price. We don't cut back quality to get a better price. Most of the reasons going to foreign countries is because it is not available as we have already said in the United States. If you look at API manufacturers, our numbers show that there are 105 generic API manufacturers in the United States. If you look at Dr. Woodcock's numbers that would tell you there is probably roughly 210, 215 API manufacturers in the United States. Companies that produce products, specifically generics, have several hundred products in their portfolio. They don't have the capability of producing the API themselves, and, in general, you can't get the same -- you can't get APIs from the same manufacturer. There is different technology, different chemistry, different expertise, different manufacturing facilities, and, therefore, you have to go to the company that will make that and can make that for you. Many times you go to Europe, foreign, China, India, et cetera, yes.

Ms. Matsui. Well, how do we -- what can we do to incentivize the use of high-quality products, particularly for generic manufacturers limited by smaller operating budgets? There is --

Mr. Gaugh. Again, I don't see that budgets and quality have anything to do with each other. We still produce high quality and the FDA guarantees that we will produce high-quality products. And we are ourselves as companies all have quality systems. Dr. Woodcock in the drug shortage document that she put out yesterday -- or the FDA put out yesterday -- talked about mature, quality systems and having a potential rating system around those. She wasn't talking about the general approval of inspectional facilities; she is talking about steps above and beyond.

Ms. Matsui. Do you have a comment, Ms. Gibson?

Ms. Gibson. When I read what is going on in some of the plants in China, the one that sent the Valsartan, this is a company that knowingly sent a substandard product to the United States. It reprocessed a batch rather than doing a root cause analysis to find out what was wrong. So it knowingly sent a really important medicine to this country with a genotoxic impurity. This is unthinkable from what we used to do 20, 30 years ago.

Ms. Matsui. Okay. Thank you very much.

And I yield back.

Ms. Eshoo. I thank the gentlewoman for her examination.

Pleasure to recognize Mr. Guthrie from Kentucky for his 5 minutes of questioning.

Mr. Guthrie. Mr. Gaugh -- actually, I wanted to start -- I am not clarifying Mrs. Brooks' question because she was pretty clear, but it piqued something in my mind. And I don't know the ingredients -- I mean, the raw ingredients. You said fine chemicals, such as Birmingham, Alabama, existed as a steel town because it is set on a mountain of iron ore, and so it made sense to make iron -- or steel in Birmingham. I guess the question that piqued my interests are the raw materials for pharmaceuticals in China or India, or is it only we are sending the raw materials through China and India? Because what you are saying is that it is a manufacturing issue. They manufacture the ingredients, therefore, that you use in your process? It is not like they have a natural advantage.

Mr. Price. I think you need to appreciate that an active pharmaceutical ingredient is the results of multisteps -- sorry -- an active pharmaceutical ingredient is the

results of multisteps of chemistry, so you have to start with something and you can't start with water and tree bark and dirt. You have got to start with some organic molecules that you can build upon, so those are the raw materials.

Mr. Guthrie. Is what you are talking about as the fine chemical?

Mr. Price. That is what I am talking about.

Mr. Guthrie. And not much of that is done here?

Mr. Price. Not much of that. We resource all over the world, but some of the more advanced molecules which we then take as raw materials to make the final active ingredient are in many cases sourced in India and China. And we suffered severe shortages, even for some of our commercial products, when the Chinese started to shutdown facilities over the last couple of years because of environmental issues and other regulatory concerns that they had over in China.

Mr. Guthrie. So there is really not a mined product or anything that is the beginning of your process? It is the molecule itself as the beginning --

Mr. Price. Exactly.

Mr. Guthrie. Mr. Gaugh, thanks for being here today. So I am just kind of getting back to the continuous manufacturing issues that Chair Pallone and I have talked about. I am just trying to understand -- I used to be in manufacturing -- so the root cause analysis and so forth. So when a problem occurs and the manufacturer is required to notify FDA -- so you say, "Here is the problem"; this is one to the level of notification -- how does that -- could you walk me through that process, like what is the timeline, and what is your root cause analysis you are required to submit to FDA for the resolution?

Mr. Gaugh. So that is a depends question.

Mr. Guthrie. So we are not clear, or the FDA is not clear?

Mr. Gaugh. No. To answer your question, it depends on the product and the situation and what was the quality issue that occurred. Not all are equal, so there wouldn't be one --

Mr. Guthrie. Just any that rises to this --

Mr. Gaugh. There is a bracketed process, yes, that each company goes through once a quality issue is uncovered, and they go through that issue, work through that, and then send a report in to the FDA. That could take days, or it could take weeks to accomplish. It depends on the situation.

Mr. Guthrie. And in the meantime, what, the products are produced? The products -- depends on the level --

Mr. Gaugh. Again, it depends on the level of what the issue is that was found. It could stop production immediately because of that, or production could continue while the investigation is ongoing. The companies work with the FDA through that.

Mr. Guthrie. Okay. What role do you think the AAM companies have in securing the global supply chain?

Mr. Gaugh. I am sorry. Say again?

Mr. Guthrie. What role do the AAM companies have in securing the global supply chain?

Mr. Gaugh. So each company secures its own products for its production, and, again, if you are looking at the large manufacturers of generics, there is usually somewhere in the realm of 500 to 1,000 products in their portfolio. Smaller companies

could be one to five. In fact, when we did GDUFA, we based that on small, medium, and large companies, but they all sourced their own.

Mr. Guthrie. So, just on generics, I thought since you are here, I would ask you just on generics in general. A lot of times I hear from people who are concerned about their health insurance or what is being provided to them, and you will say: Well, this costs X amount of dollars, but I can take the generic if that is what is on my formulary, but if I take the generic, it my understanding is a generic -- a chemical generic is the same as a branded generic?

Mr. Gaugh. That is correct.

Mr. Guthrie. But people will say, this one doesn't work for me, but I still have to pay out of pocket for the other, but generics are essentially the same --

Mr. Gaugh. Yes.

Mr. Guthrie. -- in the chemical part? Do you want to talk about -- you must hear that too?

Mr. Gaugh. As a patient and a pharmacist, that is a very true statement. So not every human or no human reacts the same as a human sitting next to them when they ingest a drug. So there is going to be a difference in absorption. There is going to be a difference in the way --

Mr. Guthrie. But they should react to the -- the same human, if they have this drug that is branded and this drug that is not if it is identical? The same human should have the same reaction?

Mr. Gaugh. Except that the API is identical, yes, but the excipients used to --

Mr. Guthrie. So there is a difference?

Mr. Gaugh. -- that product can be different and can make a difference.

Mr. Guthrie. Okay. That is fair. The generics supposedly -- so I learned something here today as well, so thank you. I appreciate it.

And I will yield back.

Ms. Eshoo. The gentleman yields back.

Pleasure to recognize Mr. Schrader of Oregon for his 5 minutes.

Mr. Schrader. Thank you, Madam Chair.

I apologize to panel for not being here for your remarks. I was in another hearing, but very interested in this area.

I read, Ms. Gibson, I read your book and found it very compelling, very disturbing; hence the earlier line of questioning about what has FDA done, so to speak, since then. They have obviously made some improvements, tried to broaden their inspection overseas. There is apparently a manpower issue, and you detail in your comments, you know, other recommendations, what would be the top two or so that FDA should pursue that they haven't done quite at this point in time that we have been most helpful?

Ms. Gibson. With our medicine supply chain being so complex and so many challenges, I think -- I have come to the conclusion it is almost out of the hand of the FDA to really ensure that every pill from every manufacturer is what it should be. That is why I recommend, and this isn't for the FDA, but we are beginning to see a private entity, this company in New Haven, that is beginning to test before it sells it as an online pharmacy, they are testing every generic product before it sells it, three batches. And they found that more than 10 percent of what they tested did not meet standard. The API wasn't what it was supposed to be. The disillusion in the body -- so say if you have

an extended release pill -- there was one in epilepsy medicine, which is really important. You have to have that consistently in the body to prevent seizures, but if it is not really extended release, that is a huge risk to patients.

Mr. Schrader. Do you think that is beyond FDA's ability to test for those sort of things?

Ms. Gibson. I think that we need a market-based approach in real time, and I would love to see -- and I would love to see companies crop up, every pharmacy that sells it, says we have tested everything independently and even have third-party verification because I think we really have to restore trust in our medicines -- I think there is a crisis of confidence in our medicines among the American people and physicians.

Mr. Schrader. So that gets to your comment, I think, that we need some central repository where at least different people, different organizations could bring to the attention of the FDA and others where there are serious problems and be able to move beyond there.

Ms. Gibson. That is right. We need a national security apparatus attention here at a very high level, which is really outside the purview of what FDA's mission is. This is, again, from a national security perspective, what is going on in China, the trends, and what we are facing.

Mr. Schrader. Again, I missed some of the hearing and I apologize, but what -- is there a room then for the United States either to incentivize some of the API or generic manufacturing that Mr. Price and others are trying to do or things we should do to go after China for the marketplace manipulation that they are doing right now?

Ms. Gibson. I think we got to start rebuilding our own manufacturing capability

here. I visited a biotech place at Virginia Commonwealth University a couple months ago, and they have an incredible capability. They want to start tomorrow making, you know, the API using continuous manufacturing, stockpile that, and then there is private -- Civica RX is out there. They said: If these folks can make the API, we will buy it, and we will set up a manufacturing plant next door to make the finished drug.

The challenge and the limitation is what we have talked about. These folks need a little capital investment to refurbish an existing plant in Petersburg, Virginia. We got a lot of, you know, plants that is lying fallow. A little bit of money to refurbish that, and once we begin to use continuous manufacturing, I am told that you can make it at 40 cents less than our traditional way of manufacturing. Once we make the investment, we can actually make them cheaper than what we are making them now.

Mr. Schrader. Mr. Price, do you have a comment on continuous manufacturing?

Mr. Price. Yes, I do. I think continuous manufacturing is extremely exciting and extremely promising. However, the testimony by Ms. Woodcock from the FDA, whenever she spoke about continuous manufacturing, she mentioned the name Sanofi and Genzyme and Vertex, which are all multibillion dollar companies, okay?

Mr. Schrader. Okay.

Mr. Price. So to think that continuous manufacturing is going to solve the issue of a small volume oncology cancer drug that is an older product that is in short supply, I think, is wishful thinking.

Mr. Schrader. I just think there is -- I am sorry to interrupt -- final comment is this Civica RX came to visit me. It is a nonprofit made up of a variety of folks around the country that see the shortage that Mr. Price is trying to address and be very important, I

think, for United States Government to step in and help small enterprises like Mr. Price's and others to incentivize that production, the continuous manufacturing so its nimble. It is not just one drug; it is drugs that are needed at a given point in time in different regions of our country. So something for us to pursue, Madam Chair. Thank you very much.

Ms. Eshoo. I thank the gentleman.

This is all about our taking a decision that we are going to make this a top priority in our country, that we are going to bring this back to the United States of America, that we can and how we work with industry to make sure that the resources are there, that the underlying resources relative to developing this through university system, the advanced manufacturing. We have people that are here today relative to Zantac and the assurance that that was actually -- it was their work that brought about the attention of the FDA and its efficacy, so these are things we can do, but we have to take a decision that it is a top priority for our country and develop a plan and stick to it. So let's see, whose next? Dr. Burgess?

Mr. Burgess. Go to Mr. Griffith. Morgan's been sitting here quite a while.

Ms. Eshoo. Oh, he has been waiting. You don't have to be waived on, you are a member of the committee. There was one more member -- who was it that didn't come back that had waived? Anyway, Mr. Griffith, you are recognized. Thank you for your patience.

Mr. Griffith. Thank you very much. And I would just say, based on some earlier testimony, Mr. Gaugh, is that correct? I am sorry. I was in another committee hearing earlier when you were introduced.

Mr. Gaugh. Gaugh.

Mr. Griffith. Gaugh. When you were talking about different people reacting differently, I am one of those people, and some of my generics work just fine, but I take Synthroid. And I tried going to the generic, just because I was trying to figure out ways to save money. Don't think it would have saved me any money, but the insurance company, if we all work together, we can make a difference. Oh, my goodness. I had a terrible time with the generic, and I went into my pharmacist and said: I don't care what it costs. Give me the brand name. This is driving me nuts.

So everybody does react a little bit differently, and sometimes the generics are fabulous and many -- I use many generics for that reason. Sometimes they just don't work with your body chemistry because of the excipients? Did I say that correctly?

Mr. Gaugh. Correct.

Mr. Griffith. So we have to try and work on that.

Ms. Gibson, I found your testimony very interesting, and I am just curious, what makes pig guts the rare earth of medical care?

Ms. Gibson. So I was trying to find a way to communicate how dependent we are on a single country for a really important component, and there has been a lot in the media about rare earths in our consumer products. You can't make your iPhones and hybrid cars and wind turbines. So I was trying to reach out to sort of a broader constituency to understand that really our medicines. They are like the rare earths, in quotes, for the continuity of our healthcare system. If we don't have them, it will shut down.

Mr. Griffith. And you were specifically referencing Heparin and pigs and so forth

and raised concern about Smithfield having been acquired, I think back in 2013, by a Chinese company, but the pigs are still, even though not part of my Virginia, they are still Virginia and North Carolina pigs predominantly. And so I am just wondering, was your concern more about the way that a Chinese company could affect the production amounts of the distribution locations? It is really not about the pigs being grown in Virginia or North Carolina or the pig guts raised that are produced there?

Ms. Gibson. It is about where those pig intestines that are the raw material for Heparin where they are going. Do we have any information? Smithfield is a private company. Are they willing to tell Congress and our national security apparatus where those pig guts going? Are they going to China to make for that population? Are they going to Europe? Or they staying here in the United States? I understand we slaughter 15 million pigs a year in this country, and if there is a shortage of Heparin because of what is happening in China with the pigs, that would be good information to know so we can ensure a supply of Heparin here.

Mr. Griffith. All right. And I do appreciate that.

I mean, Smithfield tells me that they are continuing to invest in expansion, and it is a beneficial practice even when that process occurs in the United States, but what you are saying is, is that you want more of that staying here in the United States and being able to track it. And how do we get other pork producers in the United States to allow their rare earth pig guts to be used in the United States for the production of medicine here?

Ms. Gibson. To create demand for API in the United States, and that will happen -- we are facing already -- a shortage of Heparin is going to be really severe, and

then prices go up when there are shortages. So that could incent certain companies here in the United States from wanting to make Heparin closer to home and not rely on China, but we have to think of this in the long term. That is why we need a national security long-term view here, but that is one thing that could be done to incent some manufacturing here.

Mr. Griffith. Now, let me side step just a little bit. So Heparin is made from the pig guts, and I don't know if it creates a reaction, but I have read reports that say 20 percent of the American population in the Southeast United States now has some sensitivity to the alpha-gal protein found in all mammals, including pigs. Is there any research going on on that, and is that a part of the problem if there is not research here -- this is not a problem that China is facing. It is the Southeast United States that is facing the largest outbreak of this alpha-gal condition.

Ms. Gibson. I am sure there is some fine experts that we can identify to answer that important question.

Mr. Griffith. I understand. I appreciate it.

And, Madam Chair, I yield back.

Ms. Eshoo. The gentleman yields back.

Now, I would like to recognize the ranking member of the subcommittee, Dr. Burgess, for his questioning.

Mr. Burgess. Thank you, and thanks for the recognition.

Ms. Gibson, I haven't read all of your book, but I have read some of it. I got to the part where you described an indolent Congress in 2008. Well, we were in the minority then, so if there was indolence, it had to be on the part of the other side of the

dais.

Ms. Eshoo. Thank you, Dr. Burgess.

Mr. Burgess. You are welcome. Let me just make sure I understood your answer or your discussion with Mr. Griffith. On the farm that is raising the pigs in this country, were you leading us in the direction that, since that company is now owned by Chinese interests, that they might just discard this raw material so that it didn't interfere with the API product stream coming from China?

Ms. Gibson. I think the question is, do we know where it is going? Is it going to support Heparin production in China, or is it going to support Heparin production for the United States and for the hospitals in our country?

Mr. Burgess. Well, that obviously is the critical question, and I will -- I think it was Dr. Woodcock when we had the hearing in 2008 made the observation, well, what are we going to do? Just go without Heparin, and as a practicing physician, I was like, yikes, that would not be a good day. We do have some other things we can do as far as anticoagulation, but Heparin is the gold standard.

You state in your written testimony that the current approach of hammering down on manufacturers on price is the root cause of contaminated and lethal drugs in the legitimate supply chain and rationing and shortages of lifesaving medicines. Do I have that substantially correct?

Ms. Gibson. That is right.

Mr. Burgess. And I don't know if you are aware, but 2 weeks ago, we had a lengthy markup in this committee. Everyone is concerned about the cost of pharmaceuticals. So some of the tools that were proposed to use to control the price of

pharmaceuticals was a fairly significant excise tax. What kind of effect would that have if your concern is the hammering down on manufacturers?

Ms. Gibson. There is a difference between the price that is paid to manufacturers and the price that you and I would pay when we go to the drugstore to get a medicine. So I asked someone recently, what does a bottle of pills cost -- how much would a manufacturer be paid for a bottle of 30 pills? They said maybe a penny a pill. What I think is very important for us to understand is transparency and the difference. Where does all that money go from what the manufacturers pay to the price that we pay when we go to pick it up at the drugstore? There is no R&D. There is no marketing. I think transparency for us to understand that differential will help us know whether we are actually getting value from the money that we are spending.

Mr. Burgess. Well, on this, I think if I understood correctly, was the administration's position with proposing the rebate rule so that there would be more transparency on the dollars that go into the purchase of a compound and how they are distributed throughout the supply chain. For whatever reason, Congressional Budget Office considerations, completion of that rule or the promulgation of that rule did not occur because of the concern that removal of the rebate or visibility transparency of that rebate would somehow in turn drive up prices in other parts of that ecosystem, insurance premiums or hospital charges. I am not sure about that. I don't think that is the case, but in any event, that was the concern voiced by the Congressional Budget Office, and the administration backed off from promulgating the rule because it had some other budgetary implications if they had gone forward and then had to withdraw it, but it is a concern to me that people don't know. And for years, I had a health savings account

where I had a very high deductible, and I go into the pharmacy and I just pay the list price. Kind of a shock to me later on to learn that, at some point along the line, there is a rebate paid, but I don't get to participate in that. In fact, I had an amendment during that lengthy markup 2 weeks ago that two of the things that have really driven this discussion on pricing of pharmaceuticals has been the cost of the EpiPen and the cost of insulin. So I recommended that, for insulin, in Medicare and Medicaid and CHIP, that that rebate just be given to the patient at the point of sale. Unfortunately, that was not accepted, but I think it is an idea that we should still continue to pursue because relief for the consumer is really where we were headed.

I am concerned about, yes, we can all make the argument that prices are just too high for pharmaceuticals, but on the other hand, as we hammer down, your words, as we hammer down on the manufacturers, there is going to be, whether you want it or not, there is going to be an effect and one of those effects may be shortages or some other problem. So, anyway, I appreciate the indulgence.

I will yield back.

Ms. Eshoo. I thank the ranking member, and he yields back.

I can't help but observe that when it comes to our military and what we need to defend our country, we don't outsource it to China or any other country. We don't have our jets, we don't have our carrier ships, our submarines, we don't outsource that, and we don't for a very good reason. We depend on American ingenuity, American IP, American manufacturing for our own national security, and I believe that the testimony that we have had today, underlying it all is that the drug supply for the United States for the people of our country is part of the security of our country. So we have, I think,

really been blessed by the testimony we have received today from experts from the first panel, the second panel. We have big decisions to make, and they are political decisions. We have to collectively make a decision to develop a plan that is for the security of the United States of America and its people. So I want to thank this panel.

Ms. Gibson, thank you for your extraordinary advocacy, your thinking, your writing, your research. You have been a great asset to the committee and to myself and my staff, and I thank you.

Mr. Price, thank you. I would like to see a whole new U.S. market for API, and I will consider it, you know, a collective success of this committee to develop that market. We want to work with you on it.

Mr. Gaugh, thank you very much for your testimony.

And, with that, I would like to ask for unanimous consent to place the following documents for the record. The statement from the U.S. Pharmacopeia Convention, the letter from Valisure, and a statement from the Premier Inc. Healthcare Alliance.

Hearing no objections, so ordered.

[The information follows:]

******** COMMITTEE INSERT ********

Ms. Eshoo. And the Health Subcommittee will now adjourn. Thank you.

[Whereupon, at 1:43 p.m., the subcommittee was adjourned.]