House Committee on Energy and Commerce

Safeguarding Pharmaceutical Supply Chains in a Global Economy

October 30th, 2019

10:00 am, 2123 Rayburn House Office Building

Purpose

The purpose of this hearing is to understand the causes of drug shortages and quality concerns within the global pharmaceutical supply chain, and their effects on national security.

Members Present

Chairman Eshoo, Ranking Member Burgess, Rep. Pallone, Walden, Butterfield, Shimkus, Guthrie, Castor, Griffith, Schrader, Bilirakis, Blunt-Rochester, Walden, Gomez, Buschon, Kelly, Brooks, Engel, Mullin, Carter, Sarbanes, Matsui

Witnesses

Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research
U.S. Food and Drug Administration
Michael Wessel., Commissioner
U.S.-China Economic Security Review Commission
David Gaugh, R.Ph.., Senior Vice President, Sciences and Regulatory Affairs
Association for Accessible Medicines
Rosemary Gibson., Senior Advisor
The Hastings Center
Ed Price., President and CEO
Seqens CDMO

Opening Statements

Chairman Eshoo said that there is a hidden health crisis in this country. Generic drugs are commonly used in the United States due to how cheap they are. These products are supposed to be safe. However, the generic supply chain is broken. There are critical drug shortages, subpar manufacturing and an over reliance on foreign drugs. These problems should not be happening in the United States. The over reliance on China for drugs such as insulin threaten our national security. It is crucial for Congress to not only focus on problems but also on solutions. This problem has been ignored for too long and Congress much act quickly.

Ranking Member Burgess said that this committee has a long history of being engaged in the safety of the pharmaceutical supply chain. There is an increased need for an efficient and safe pharmaceutical supply chain. This committee should remember the United States faced a deadly contamination of the blood thinner Heparin in 2008. The suspected contaminated active ingredient in Heparin came from China. However, the FDA has never identified the true cause of the contamination. Investigating contaminations after a patient dies is too late, the global supply chain must be safer now. Furthermore, this uncertainty surrounding the safety of pharmaceuticals does not only impact patients, but providers as well.

Rep. Pallone said that American consumers rely heavily on prescription drug products. The FDA plays a crucial role in ensuring the safety of pharmaceutical drugs in the United States. This committee has a long history of empowering the FDA to have more oversight on the pharmaceutical supply chain. Many drug manufacturers are getting ingredients for their product from overseas. These ingredients often have quality concerns associated with them. Thus it is crucial to give FDA the authority to regulate and oversee the global pharmaceutical supply chain.

Rep. Walden said that it is crucial to ensure that US regulatory agencies have the ability to verify the safety and quality of imported pharmaceutical drugs. Historically, drugs used in the United States were manufactured in the United States. However, due to an increasing global economy many manufacturers have moved over seas. This has made it increasingly difficult to verify the quality of these drugs. Meanwhile, FDA inspections of overseas manufacturers have dropped over the last two years. The United States reliance on foreign drugs also represents a national security threat. Foreign countries such as China could restrict the supply of crucial drugs or dramatically increase the price. This would leave American consumers to in deep trouble.

Panel I

Testimony

Dr. Woodcock said that the lack of a safe pharmaceutical supply chain leaves the United States at a national security risk. Active pharmaceutical ingredients (APIs) are typically manufactured outside of the United States. Global disruptions threaten to limit the United States access to crucial pharmaceuticals. The FDA has been advocating for advanced pharmaceutical manufacturing to bring drugs back to the United States. It is clear that drug manufacturing is feasible in the United States, however it will take a serious commitment to improving current technology. The FDA feels it is also important to bring a high quality drug supply chain to the global economy.

Comm. Wessel said that citizens have a right to know what is in their medicine cabinet. However, confidence surrounding the safety and quality of drugs manufactured in China is not high. This problem demands action and bipartisan solutions. Consumers typically do not have an option of which drug to procure based on where the ingredients were manufactured. Furthermore, China has made drug manufacturing a staple of its economy and plan to continue these efforts. China already supplies nearly 80% of the world's APIs. China is prepared to weaponize its manufacturing capabilities in order to gain global political and economic superiority. The United States cannot trust the safety and efficacy of Chinese products. Inspectors from the United States need better access to manufacturing plants in China.

Questions and Answers

Rep. Eshoo asked if the FDA knows what percentage of American drugs have their active ingredient sourced from China. **Dr. Woodcock** said no. **Rep. Eshoo** asked if the FDA

knows the sources of these ingredients. **Dr. Woodcock** said yes. **Rep. Eshoo** asked if the FDA knows what percentage of antibiotics have their active ingredient sourced in China. **Dr. Woodcock** said no. But we know the locations of these plants. **Rep. Eshoo** asked if there is a capacity for the US to manufacture APIs. **Dr. Woodcock** said yes but there is no economic incentive. **Rep. Eshoo** asked what the nationally security implications are regarding the United States reliance on China. **Comm. Wessel** said that China can weaponized their manufacturing capabilities. China also plans on dominating the global economic market surrounding pharmaceuticals. They are attempting to price everyone out of the market.

Ranking Member Burgess asked if the FDA has a roll to play in ensuring products are not contaminated. **Dr. Woodcock** said yes. The FDA typically looks at the manufacturing process. **Ranking Member Burgess** asked if the FDA has a role in coordinating interagency efforts to recapture the manufacturing chain in the US. **Dr. Woodcock** said yes, but it is limited.

Rep. Butterfield asked if it is true that China controls close to 22 percent of the supply chain. **Dr. Woodcock** said no. It is closer to 13 percent. **Rep. Butterfield** asked if this number includes generics and brand name drugs. **Dr. Woodcock** said yes. **Rep. Butterfield** asked if the FDA knows what percentage of each ingredient comes from specific manufacturing plants. **Dr. Woodcock** said no. The FDA gets that information retroactively. Since the market is so dynamic these percentages always change.

Rep. Shimkus asked if the FDA is approving more facilities than they are capable of inspecting. **Dr. Woodcock** said the FDA cannot stunt innovation. However, the FDA has had trouble hiring inspectors and this is why inspection rates are dropping.

Rep. Matsui asked if drug manufacturers are minimizing investing in quality and if this leads to drug shortages. **Dr. Woodcock** said yes drug shortages are typically caused by manufacturing difficulties. **Rep. Matsui** asked how requiring manufacturers to release quality ratings will actually improve quality measures. **Dr. Woodcock** said that purchasers are typically blind to the quality of drugs. By providing transparency it is possible to incentive better manufacturing standards.

Rep. Guthrie asked if FDA has the authority to require up to date API data from manufacturers. **Dr. Woodcock** said that FDA can only get this information in annual reports. **Rep. Guthrie** asked if manufacturers should be required to report this API data. **Dr. Woodcock** said yes. **Dr. Guthrie** asked how to ensure that proprietary information is kept properly. **Dr. Woodcock** said the FDA already holds onto private data. Storage methods would involve block chain technology and other IT techniques.

Rep. Castor asked if FDA has access to facilities in China. **Dr. Woodcock** said yes. **Rep. Castor** asked why the FDA office in China has a hard time retaining staff. **Dr. Woodcock** said it is hard to get people to move to China. In general the FDA has had trouble hiring new employees. **Rep. Castor** asked what regulatory tools FDA has in the post market

space. **Dr. Woodcock** said that in general the FDA monitors the safety of all drugs and documents adverse effects associated with these drugs.

Rep. Griffith asked if Zantac was manufactured in the United States. **Dr. Woodcock** said yes, and some is manufactured in the EU. **Rep. Griffith** asked if Zantac is stable. **Dr. Woodcock** said there is one ingredient which may be of concern but the data is incomplete. **Rep. Schrader** asked how confident the FDA is regarding the percentage of APIs manufactured at certain sites. **Dr. Woodcock** said that the FDA only knows where the manufacturing plants are. The FDA does not know exactly how much of each ingredient comes from each plant. **Rep. Schrader** asked if enough is being done to incentivize manufacturing in the United States. **Comm. Wessel** said no.

Rep. Bilirakis asked how labeling country of origin improve patient safety. **Comm. Wessel** said that consumer awareness and information can help put pressure on manufacturers and distributors.

Rep. Blunt-Rochester asked why the FDA is having staffing issues. **Dr. Woodcock** said it seems to be a process issue. The FDA has put forth a plan to rebuild staffing. **Rep. Blunt-Rochester** asked if it is true that API manufacturers have to register with the FDA. **Dr. Woodcock** said yes. However there are some loopholes that the FDA is concerned about.

Rep. Walden asked if it is true that some contaminants cannot be identified during routine inspections. **Dr. Woodcock** said yes. **Rep. Walden** asked if there has been a decline in inspections of foreign drug facilities. **Dr. Woodcock** said yes, this is due to staffing issues.

Rep. Gomez asked how the risk –based inspection schedule works. **Dr. Woodcock** said the system works well. FDA choses which facilities to monitor based on risk. Risk can include inspectional history of the facility or active ingredients in the drug. **Rep. Gomez** asked if the risk based inspection model has helped the agency inspect the most risky manufacturers. **Dr. Woodcock** said yes. **Rep. Gomez** asked how the FDA is ensuring that all facilities get inspected. **Dr. Woodcock** said that time lapses are a part of the risk-based model.

Rep. Buschon asked what barriers exist to advance manufacturing in the United States. **Dr. Woodcock** said the primary barrier is that there is no academic base coming forward with ideas. There is also not a large workforce ready to transition into the industry. Finally, the proper economic incentives are not in place. **Rep. Buschon** asked how many drug shortages can be traced to quality issues regarding APIs. **Dr. Woodcock** said the data is not readily available but the FDA can work to produce it.

Rep. Kelly asked why simply increasing the productivity of traditional manufacturing is not enough. **Dr. Woodcock** said that the traditional method is very time consuming and takes up a lot of space. It has significant limitations when it comes to mass mixing and mass reactions. **Rep. Kelly** asked what the future of manufacturing looks like. **Dr. Woodcock** said it will be smaller more mobile manufacturing methods. **Rep. Kelly** asked if

the current state of advanced manufacturing in the US has been effective. **Dr. Woodcock** said there has been limited adoption of advanced manufacturing in the United States, however the future seems promising.

Rep. Brooks asked how to incentivize manufacturing in the United States. **Dr. Woodcock** said that it is necessary to figure out how to regionally produce certain drugs. The FDA is not in the incentive business. **Comm. Wessel** said that Congress should give priority to domestic products.

Rep. Engel asked if there are safety risks that arise exclusively because a product is manufactured overseas. **Dr. Woodcock** said it depends on the country that is producing the product. The EU does a better job than China. **Rep. Engel** asked if safety and quality issues associated with API are unique to generic drugs. **Dr. Woodcock** said no.

Rep. Mullin asked how China became the world's largest supplier of APIs. **Comm. Wessel** said they have been enhancing their chemical sector. They have also prioritized the development of the bio economy. **Rep. Mullin** asked if China can weaponized the drug system. **Comm. Wessel** said yes. They have already done it with Japan. **Rep. Mullin** asked if corruption in China leads to quality issues. **Comm. Wessel** said yes.

Rep. Carter asked if any manufacturer can begin selling bulk API products. **Dr. Woodcock** said yes. **Rep. Carter** asked if manufacturers can sell this product without being inspected by the FDA. **Dr. Woodcock** said yes. **Rep. Carter** asked how to fix this problem. **Dr. Woodcock** said the fastest way would be for Congress to pass legislation directly addressing the issue. **Rep. Carter** asked what FDAs role is in protecting consumers from counterfeit drugs. **Dr. Woodstock** said the distribution chain is getting a lot safer.

Rep. Sarbanes asked how the emerging technology program incentivizes the approval of advanced manufacturing processes. **Dr. Woodcock** said that the program is helping to eliminate technological barriers.

Rep. Flores asked if the difference between domestic and international downgrade rates is due to foreign entities receiving preferential treatment. **Dr. Woodcock** said no. **Rep. Flores** asked what it means when an investigator recommends official action. **Dr. Woodcock** said that it triggers a robust reaction of overview on the facility.

Panel II

<u>Testimony</u>
Ms. Gibson said that China is deeply embedded in the United States medicine supply. It is crucial to look beyond API facilities and find where the ingredients to make the API come from. Furthermore, it is suspected that almost all of the ingredients to make APIs come from China. China is also increasing its market share by pricing other companies and countries out of the market. They did it with Insulin and they will soon do it with antibiotics. This is where the danger of drug shortages come from. The United States

needs to assist the FDA with their duties, stock pile necessary ingredients and implement consumer port site testing.

Mr. Price said that as a manufacturer of APIs, his company produces key raw materials for manufacturers. It is important to understand that any drug approved by the FDA is a combination of two things, a drugs substance (active ingredient) and the drug product (delivery method). These two products require vastly different manufacturing techniques. Globalization and outsourcing has led to an intertwined web of global manufacturers. Pharmaceuticals still follow market forces, and consolidation has led to higher prices for consumers. It is important for Congress to ensure that regulations do not add undue costs or burdens to drug manufacturers. This will increase the price and slow down productivity.

Mr. Gaugh said that patients should be confident in the generic medicine prescribed to them. Recent reports have painted a distorted version of the global pharmaceutical supply chain. Generic API facilities are mostly spread across the United States, the EU, India and China. It is important to accurately depict where these facilities are located. Furthermore, there is already a robust regulatory environment in place. The number of inspections done both domestically and internationally have increased significantly over the last few years. Additionally, the approval process is also increasingly robust and ensures the safety of the pharmaceutical supply chain. The US has one of the safest drug supply chains in the world.

Questions and Answers

Chairman Eshoo asked what percentage of generic drugs are manufactured in the United States. **Mr. Gaugh** said about 40 percent. **Chairman Eshoo** asked what percentage of APIs are manufactured in the US. **Mr. Gaugh** said about 13 percent. **Chairman Eshoo** asked if generic companies are discouraged from manufacturing older prescription drugs. **Mr. Gaugh** said yes. **Chairman Eshoo** asked if this leads to drug shortages. **Mr. Gaugh** said yes it can. **Chairman Eshoo** asked if it is true that the generic industry is facing problems related to drug shortages, quality concerns and increased reliance on the foreign market. **Mr. Gaugh** said yes. **Chairman Eshoo** asked if lower labor standards are the reason that China is controlling the market. **Ms. Gibson** said no. The Chinese government subsidizes manufacturers in China.

Rep. Brooks asked who should oversee a new regulatory agency to ensure supply chain safety. **Ms. Gibson** said she is not sure what department would be the most appropriate. **Rep. Brooks** asked if there is an entity in the world that does the oversight Ms. Gomez is recommending. **Ms. Gibson** said no. **Rep. Brooks** asked how many API manufacturers are there in the United States. **Mr. Price** said dozens, but that number is getting smaller. **Rep. Brooks** asked where the building blocks of APIs come from. **Mr. Price** said most come from China and India.

Rep. Matsui asked what steps generic drug developers need to take to ensure they can meet the demand of their product. **Mr. Gaugh** said it comes down to portfolio management. It can be very difficult. **Rep. Matsui** asked what tradeoffs generic

manufacturers will have to make when it comes to quality and price. **Mr. Gaugh** said manufacturers do not cut corners on quality to bring down price. **Rep. Matsui** asked how to incentivize the use of high quality products. **Mr. Gaugh** said he does not see a link between cost and quality.

Rep. Guthrie asked if China and India have an inherent advantage due to the location of raw materials. **Mr. Price** said no. **Rep. Guthrie** asked what the process is for manufacturers reporting an issue to the FDA. **Mr. Gaugh** said it depend on what the problem is. Quality measures have different reporting measures than others. **Rep. Guthrie** asked if manufacturing has to stop when an issue is reported. **Mr. Gaugh** said not typically. Usually the FDA will work with a manufacturer to solve the issue without halting production.

Rep. Schrader asked what recommendation the FDA should pursue. **Ms. Gibson** said that the FDA should ensure that every pill and every manufacturer is what it says it is. There needs to be more rigorous testing. **Rep. Schrader** asked if the FDA has this capability. **Ms. Gibson** said she wants to see a market based approach. **Rep. Schrader** asked if continuous manufacturing is a good thing. **Mr. Price** said yes. But it is only feasible for large corporations with significant capital on hand.

Rep. Griffith asked why pig guts are the 'rare-earth' of medical care. **Ms. Gibson** said that the point she was trying to make is that medicine is the life line of our medical system. Additionally, Heparin is made from pig guts. **Rep. Griffith** asked how to get pork producers in the United States to sell their pig guts to US manufacturers. **Ms. Gibson** said there have to be market incentives. In order for that to happen there need to be buyers in the United States.

Rep. Burgess asked if Ms. Gibson was inferring that China is hoarding critical material like pig guts. **Ms. Gibson** said she was alluding to the fact that no one knows where these products are going.