Statement before the Senate Committee on Homeland Security and Governmental Affairs
On Protecting the US from Global Pandemics

Are we prepared? Protecting the US from global pandemics

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The epidemic spread of coronavirus in China -- along with community transmission in Singapore, Hong Kong, and Japan – sharply increase the chance that we endure pandemic spread. Worse still, the novel coronavirus may become endemic. It could take a new position as a more sinister member of the seasonal pathogens that circulate each year and infect humans.

The next month is critical. We must prepare for the prospect that the virus evaded our border protections and was already introduced into the U.S. in late December or early January – when it first appears to have become epidemic in China's Hubei province. Those index cases could have seeded community spread, and eventually, outbreaks could emerge in America. We have the capacity to contain small outbreaks. But we need to be vigilant and ready.

Models suggest that from the time of first introduction of the virus into China – which we now suspect occurred sometime in November – to the time of epidemic spread in China, was about 10 weeks.[i] The experience in the U.S. is likely to be different, not least because our awareness of this risk is prompting collective action that can limit spread. But China's experience shows that if cases were imported into the U.S. in early January and remain undetected, then we could still be early in our own evolution toward broader outbreaks. Right now, we're depending largely on clinical surveillance as our primary tool for identifying potential outbreaks since we're just now deploying diagnostic tools to the Laboratory Response Network. Moreover, we still haven't broadened our screening criteria to include patients who don't have a connection to recent travel to China. This limits our ability to identify secondary spread. So, we may know we're experiencing outbreaks of this disease only when a cluster of cases of atypical pneumonia present to a hospital and trigger closer scrutiny by health officials. By that time, there could be dozens or even hundreds of cases in a local community. Controlling broader spread could become a challenge.

There are many steps we can take to address these risks, both in the setting of this current public health crisis, as well as in preparing for the next one. There will always be a next one.

Among many components of preparedness, we're dependent on the robustness of our 3,000 local health jurisdictions; the technology to rapidly deploy point of care diagnostics and develop safe and effective therapeutics and vaccines; local surveillance; federal tools to track outbreaks and contain spread; collaboration with international health partners; and sound leadership.

First and foremost, we must observe the human tragedy, and take steps to mitigate human suffering. While we don't fully understand the spread and severity of this virus, it has already caused a lot of death and suffering, and the full scope of its impact is far from finished.

Today I want to talk about another aspect of risk and response – our global supply chain for key healthcare products, and how it can become stretched in times of public health emergency.

I want to focus my observations on the vulnerability of our supply chain for drugs and medical devices. Some shortages or near shortages may be inevitable in U.S. as a result of crisis in China. Our drug and medical device supply chain is pointedly and precariously dependent on production in China for our finished goods. In many cases it isn't the finished drugs or medical devices that

are being manufactured largely or exclusively in China. Nor is it the intermediate products like the active pharmaceutical ingredients (API). It is lower margin, low technology starting materials and components that – over time – have become sole sourced in China.

Securing alternative supply in the setting of a crisis takes time. But here are steps U.S. regulators can take in the near term, working with Congress and other partners, to lessen the potential impact of supply disruptions on Americans by identifying vulnerabilities and bringing substitute supply online. There are also longer-term policy steps that we could take to reduce the vulnerabilities created by these choke points in the supply of critical public health goods.

I want to address in greater detail these issues as they relate to drugs and production in China.

About 40 percent of generic drugs sold in the U.S. have only a single manufacturer. A significant supply chain disruption could cause shortages for some of many of these products.[ii]

Last year, manufacturing of intermediate or finished goods in China, as well as pharmaceutical source material, accounted for 95 percent of U.S. imports of ibuprofen, 91 percent of U.S. imports of hydrocortisone, 70 percent of U.S. imports of acetaminophen, 40 to 45 percent of U.S. imports of penicillin, and 40 percent of U.S. imports of heparin, according to the Commerce Department. In total, 80 percent of the U.S. supply of antibiotics are made in China.[iii]

While much of the fill finishing work (the actual formulation of finished drug capsules and tablets) is done outside China (and often in India) the starting and intermediate chemicals are often sourced in China. Moreover, the U.S. generic drug industry can no longer produce certain critical medicines such as penicillin and doxycycline without these chemical components.[iv]

According to a report from the US-China Economic and Security Review Commission, China's chemical industry, which accounts for 40 percent of global chemical industry revenue, provides a large number of ingredients for drug products.[v, vi] It's these source materials --- where in many cases China is the exclusive source of the chemical ingredients used for the manufacture of a drug product -- that create choke points in the global supply chain for critical medicines.

Moreover, when it comes to starting material for the manufacture of pharmaceutical ingredients, a lot of this production is centered in China's Hubei Provence, the epicenter of coronavirus. Most drug makers have a one to three-months of inventory of drug ingredients on hand. But these supplies are already being drawn down. Among big API makers in Wuhan are Wuhan Shiji Pharmaceutical, Chemwerth, Hubei Biocause, Wuhan Calmland Pharmaceuticals.[vii]

There are steps that we can take – both in the short term as well as the long run – to expand our supply chain for making these raw and intermediate components of drug production and mitigate risks to our supply chain. In the setting of the current public health crisis related to the novel coronavirus, I want to focus my remarks today on some of these potential actions.

We're facing the potential for unprecedented supply chain disruptions. You can't easily switch component part suppliers — either starter material for the manufacture of drugs or components for device devices. You have to qualify those alternative sources, make sure they meet regulatory standards for Good Manufacturing Practices (GMPs), and meet the conditions set by those incorporating these materials into their finished goods. Even if FDA is able to offer manufacturers flexibility in making these component changes, substitutions are often complex.

Right now, we may not even be aware of the full scope of these vulnerabilities. In many cases, we don't have established systems for tracking down to the level of these components, to easily identify the choke points. This is true even when it comes to where API is sourced. We rely on our ability to track the finished products. This isn't just a coronavirus challenge. An earthquake or political unrest in a major manufacturing region could present the same problems.

How can we take steps to try and address some of these significant challenges?

First, we can work to bring on alternate supply. After Hurricane Maria devastated Puerto Rico, and took offline fully 10 percent of the manufacturing capacity for drugs intended for the U.S. market, the FDA took proactive steps to restart facilities that manufactured key products, and identify alternative suppliers for some products where significant and potentially harmful disruptions were believed to be unavoidable owing to the damage.[viii] There's idle manufacturing capacity that can be developed to address some of the immediate needs. India, for example, has about 1,500 plants that manufacture APIs and are running at 40 percent capacity.[ix]

Second, we also need a better system for identifying these supply chain choke points.

When it comes to the kinds of starting materials that may have been disrupted by the crisis in China, FDA would be dependent on manufacturers to identify these supply choke points. This is challenged by the current shortage framework. It relies on a passive reporting system from manufacturers, where we might find out too late of impending shortage. It may not work in a crisis situation like this where information and reporting are imperfect.

In the near term, FDA can issue a solicitation for such information. U.S. officials should already have some awareness of the key components that are manufactured in China, and in the Hubei Province particular. But in the longer term, we need a more systematic process for collecting this information. This is where Congress can help, by giving the FDA authority to look not only at the supply of finished products but to also identify circumstances where key components may have only a single source across an entire category of products. This may take the form of a requirement that manufacturers develop risk management plans that explicitly surface critical supply chain choke points. In turn, we could require companies to take steps to identify alternative sources in the event of a major disruption. It isn't just supply disruptions we need to be fearful of. In the setting of a public health crisis in a country that hosts the manufacture of critical components, a government may seek to withhold supply or even nationalize key facilities if the components are essential to their own relief efforts. A nation could seek to satisfy its in

country needs before they ship outside their borders. Such a circumstance arose with respect to the manufacture of flu vaccine after the H1N1 pandemic.[x]

Standing up new sources of supply is not as complex as creating new facilities for manufacturing intermediate and final drug products. That's because these starting components and ingredients fall under the GMP requirements of the finished manufacturer's supplier controls. This means that the ingredients and parts are not independently subject to GMP requirements if they're not themselves the drug product or finished device. So, this flexibility can make it easier to more quickly establish alternative manufacturing sites for the production of source material and other inputs. It doesn't require that these new facilities undergo all of the more time consuming GMP requirements as the finished drug. Only finished products need to meet these standards.

It's clear now that we are also going to have significant delays in FDA inspections of facilities in China, and maybe in other foreign locations. This could make efforts to identify new manufacturing sites more challenging if those facilities are required to be inspected by the agency. The falloff in inspectional capabilities could also create some immediate consumer risks.

There are steps we can take to offset these challenges. For example, Congress can support efforts by FDA to increase import sampling and testing of regulated goods coming from China, since the agency will be hard pressed to make up for the lost inspectional activity, even after the current crisis has subsided. This will require additional resources for FDA's inspectional program.

The FDA could also consider revising its risk-based inspection model and plan for 2020. Based on the shutdown in Chinese manufacturing and the need for alternate supplies, the agency might need to redefine the highest risk facilities and shift some of the focus of its inspection resources once facilities are brought back online. These efforts can be supported by Congress. The FDA's inspectional activities and its field force are on the front lines of the agency's historic consumer protection mission. The agency has the expertise to adapt to these challenges, but it can benefit from focused resources and authorities that support these efforts in both the near and long term.

It's not just generic drugs that could fall into shortage. Brand drugs use contract research organizations like WuXi in China for development work, and global clinical trials enroll patients China.[xi] There are 16,490 studies registered on Clinicaltrials.gov in China and 5,086 studies are currently recruiting. This is about 10 percent of all of the actively recruiting studies. The clinical trial work, as well as the work conducted by China CROs has -- in many cases -- has stopped.[xii]

As a consequence, some new drug programs could be delayed as innovators are forced to change clinical trial enrollment plans, amend protocols, or shift certain critical development activities to other CROs located in other regions. This could delay regulatory filings on new drugs.

We also must address potential device shortages. Medical devices operate under different framework than drugs. It may be harder to identify and mitigate potential shortages. We should adopt the same practices we've implemented for drugs – which requires manufactures to give

FDA early notification of potential shortage situations. More than a year ago, FDA first put forward such a proposal. That proposal was incorporated into the President's current budget.

Finally, we should also contemplate for medical devices a similar framework to the one I believe we need for drugs. It would require manufacturers to report to FDA when there is a key component that is sole sourced and where alternate supply cannot be easily obtained.

While we hope no shortages will result from the tragic epidemic, given the concentration of production work in Wuhan, the risk is real. Those risks can be reduced through careful planning.

In the long run, there are structural changes we can make to reduce these risks for when next global crisis arises. It starts with shifting our emphasis. We've been focused on the risk that finished goods can fall into shortage owing to a supply disruption. In a world where the manufacture of components and source material has become highly centralized around a small number of regions and facilities, we need to pay equal attention to identifying these other choke points and taking steps to make sure that critical production doesn't hinge on a single location.

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