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The Short- and Long-term Implications of a Global Pandemic on the World's Drug Supply Chain

(Sources: An Article by Neha Dasgupta Ludwig Burger for Reuters, an Article by Bowman Cox for Scrip, an Article by Avek Roy for Forbes, and an Article by Eric Palmer for FiercePharma)

As the Covid-19 virus spreads around the globe, it is painfully obvious what the short-term implications and challenges are for both local and federal governments. Countries struggle to keep the virus under containment with extreme measures that have many individuals under lockdown and businesses' doors closed until further notice. It is a frustrating and fearful situation that has caused widespread panic not seen on this scale in generations.

But more concerning are the long-term implications that will be felt in the months ahead. Countries such as India and China are limiting critical exports necessary for the manufacture of widely-used medicines, from acetominphen used in over the counter painkillers to other important ingredients used in lifesaving drugs. This curb on drug exports has caused panic everywhere and will severely impact the world's drug supply chain.

On March 3rd, India's Directorate General of Foreign Trade (DGFT) sent a notification restricting the exports of 26 active pharmaceutical ingredients (APIs) and formulations. According to industry sources, approximately 240 license application requests by exporters have been referred to the commerce and industry ministry and will face tough scrutiny before the licenses are granted.

The reasoning behind the tough restrictions was the need for India to ensure its own drug supply for the Indian population remains robust.

Pharmaceutical companies around the world depend on India and China for 80% of the chemical components needed to manufacture many widely-used drugs. Another major source of APIs is Italy but because the country has been so hard hit by the virus, India and China's imports have become even more critical.

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IMPORTANT NOTICE!

IFPW'S 2020 CEO ROUNDTABLE & IFPW FOUNDATION FUNDRAISING EVENT HAVE BEEN POSTPONED TO MARCH 24-25, 2021

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IFPW wishes its members and their families good health during this difficult time.

In Brief...

- **Walgreens** is proactively taking action to implement policies in support of its customers by waiving all delivery fees for eligible prescriptions. Walgreens pharmacists will be working with physicians and health plans, as well as state officials to ensure patient access to medication through 90-day refills and early refill efforts. The company is also highlighting **Walgreens Find Care**, a service which helps to connect patients to healthcare services from local providers and telehealth options that can be accessed online and through the Walgreens app.
- Brazilian pharmaceutical wholesaler and distributor **Profarma Distribuidora** reported a record gross revenue of R$5.6 billion (US$1.09 billion) for 2019, with a 12.9% year-over-year increase. The company's distribution unit rose by 18.7% to R$5.2 billion in 2019, while retail gross profit totaled R$345.4 million (US$67.2 million) with a 28.7% gross margin.
- **Teva** and **Celltrion Healthcare** are introducing *Herzuma (trastuzumab-pkrb)* for the treatment of HER2-positive breast cancer and gastric cancers as a lower-priced treatment option. "We are proud to make *Herzuma* available to patients in the

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First Human Trials of a Coronavirus Vaccine Have Begun

(Source: An Article by Berkeley Lovelace, Jr. for CNBC, and an article in Pharmaceutical Technology)

The first human trial testing of a potential vaccine to prevent Covid-19 began March 16th, a U.S. health official confirmed.

Finding a "safe and effective vaccine" to prevent infection from the new Coronavirus "is an urgent public health priority," Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, said in a statement Monday. "This Phase 1 study, launched in record speed, is an important first step toward achieving that goal."

The National Institutes of Health, the research and development arm of the Department of Health and Human Services, has been working with biotech company Moderna to develop a vaccine using the genetic sequence of the new coronavirus. The trial is taking place at the Kaiser Permanente Washington Health Research Institute in Seattle, Washington, where Covid-19 cases have surged and authorities have banned mass gatherings. The early stage, or phase 1, trial will test the vaccine on 45 males and non-pregnant females between the ages of 18 and 55, according to trial details on NIH's website.

To date, there are no known proven therapies for the treatment of the virus, which has killed nearly 7,000 and spread to more than 200,000 individuals worldwide since emerging form the Chinese city of Wuhan several months ago. The hope is to get a vaccine

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Short and Long-Term (cont.)...

Conversely, the Pharmaceuticals Export Promotion Council of India (Pharmexcil) has flagged many products which were not listed in the notification but fall under the group of products with the same tariff codes. These products are also on hold by the customs authorities. Dinesh Dua, chairman of Pharmexcil, noted that many of the restricted APIs and medicines are widely exported to Europe and the United States. Indian officials have stated that they do not expect the restrictions to be a long-term or a permanent measure.

The list of restricted medicines account for 10% of India's total pharmaceutical exports and includes several antibiotics. Adrien van den Hoven, Director-General of the Medicines for Europe Association of the region's generic and biosimilar drugmakers said "We are very alarmed that other countries would pursue other, more narrow strategies, which won't solve the issue."

The U.S. Food and Drug Administration said it was working to determine how the restrictions will affect the U.S. drug supply. Indian imports accounted for 24% of medicines in the U.S. in 2018.

In China, the virtual countrywide shutdown of its manufacturing sector only adds to the potential for global drug supply shortages and further magnifies the need for robust supply chain alternatives and regional supply chain redundancy. Covid-19 may turn out to be a stronger rebuke to globalizations than all the barriers to migration and trade that have become so popular in the hollowed-out economies of industrialized nations' manufacturing areas. It demonstrates the pitfalls of the highly interdependent system for the manufacture of medicines that is in place today, and the domino effect that can occur during a global crisis. Just as the 2008 heparin crisis (which caused dozens of U.S. patients to die due to economically motivated adulteration of heparin API) led to the FDA Safety and Innovation Act reforms in 2012.

Perceived hoarding of critical drugs by individual countries can only provide a temporary solution to shortages. Some pharmaceutical companies such as Sanofi are working diligently on a more permanent solution which involves spinning off an ingredient manufacturing unit to help reduce Europe's dependence on Asia for APIs. Sanofi's spinoff would be the second-largest maker of APIs in the world.

Another model for a broader solution is the approach used by Baxter International Inc. after hurricane Maria hit the island of Puerto Rico, paralyzing its production of small-volume saline mini bags. Baxter's response was to establish significant redundancy by obtaining U.S. FDA approval to import saline from its plants in Ireland, Australia, Canada, Mexico, England, Italy and Brazil. This helped mitigate the hurricane-related shortages.

In fact, decades prior, Puerto Rico was a leader in drug manufacturing, but lost its stronghold when companies moved their manufacturing operations abroad. There is a resurgent interest in Puerto Rico being given "favored nation" status with regard to pharmaceutical production in order to rekindle the drug manufacturing industry on the island. This would aid the U.S. with its unenviable dependency on foreign pharma manufacturers and strengthen the U.S. drug supply chain.

Now the U.S. FDA is proposing (as part of a legislative agenda contained in its fiscal year 2020 budget request) that Congress require pharmaceutical risk management plans. This would require manufacturers of certain critical drugs to periodically assess their manufacturing supply chain vulnerabilities and develop plans to mitigate the associated risks. This would result in a more resilient, global manufacturing infrastructure.

Could Telemedicine Be A Critical Tool During a Global Pandemic?

(Sources: An article by Judd Hollander, M.D. for The New England Journal of Medicine, and an article by Eric Wicklund for mhealthintelligence.com)

In this age of information and technology, there is a growing call for the use of telemedicine, particularly in light of the very fluid and uncertain Covid-19 global pandemic. Covid-19 is especially concerning for those over the age of 60 years old and those with compromised immune systems. In fact, people who are younger and otherwise healthy may present as asymptomatic, thus increasing the chances of spreading the contagious disease without even realizing it. Could telemedicine be the answer in addressing the challenges of unnecessarily exposing susceptible populations by requiring them to visit their physician or a hospital emergency room during a public health emergency?

While no telemedicine program can be created overnight, U.S. health systems have already implemented telemedical innovations that can be leveraged for responses to such healthcare emergencies. The central strategy begins with a surge control called "forward triage" which functions as a method of sorting patients before they arrive at the typical emergency room within an urgent care or hospital. Through this same triage strategy, patients can be screened by clinicians to determine the severity of their illness while keeping them out of the general population risking exposure. Patients can access healthcare providers 24/7 via smartphone or webcam-enabled computer on something as widely acceptable as Skype, or by some other proprietary system. In the case of Covid-19, a patient can be screened for respiratory symptoms (common among those who contract the virus) and evaluated for other symptoms such as fever. Healthcare professionals can also determine if the patient has traveled to an area that is a high risk for exposure. Automated screening algorithms can be built into the intake process and local epidemiologic information can be used to standardize screening and practice patterns across providers.

Telemedicine health programs are already widely-used across health systems including Jefferson Health, Mount Sinai, Kaiser Permanente, Cleveland Clinic and the U.S. Medicare system for seniors.

In a presidential news conference on March 17th, officials discussed increasing the use of telemedicine with Medicare patients in order to keep them safe in their homes and without risk of exposure, while still offering medical advice and assistance as needed. As availability for Covid-19 expands, local telemedicine systems can determine which patients should be tested in facilities that are focused on minimal exposure, such as dedicated office space, tents, or in-car testing. These options will require further development and integration into telemedicine workflows. Once a patient presents with an infection, they can be further isolated to prevent exposure to others. Before the Covid-19 outbreak, common practice of face-to-face intake had been modified to

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Covid-19 Vaccine (cont.)...

to market sometime during the first half of 2021, but doctors are setting expectations low for how likely it will be. Developing, testing and reviewing any potential vaccine is a long, complex and expensive endeavor that could take months or longer according to global health experts. Before researchers can begin human trials, they must have a firm understanding of the pathogen, run safety tests and find enough human volunteers.

The early stage trial will be led by Dr. Lisa Jackson, a senior investigator at Kaiser. Study participants will receive two doses of the trial vaccine via intramuscular injection in the upper arm approximately 28 days apart. Each participant will be assigned to receive a 25 mcg, 100 mcg or 250 mcg dose at both vaccinations, with 15 people in each dose group, the agency said.

"This work is critical to national efforts to respond to the threat of this emerging virus," Jackson said. "We are prepared to conduct this important trial because of our experience as an NIH clinical trials center since 2007."

Dr. Fauci told reporters that the potential vaccine by Moderna contains genetic material called messenger RNA, or mRNA, that was produced in a lab. The mRNA is a genetic code that tells cells how to make a protein and was found in the outer coating of the new coronavirus, according to Kaiser researchers involved in the project. The mRNA instructs the body's own cellular mechanisms for making proteins to make those that mimic the virus proteins, thereby producing an immune response.

Fauci also told reporters last month a vaccine may not solve problems in the next couple of months but it certainly would be an important tool in the fight against the virus. He noted that it's possible the virus will prove to be seasonal, thus likely to subside in the warmer months much like the flu.

Some health authorities have resorted to using Gilead Sciences' antiviral drug, *remdesivir*, which, although not proven to be effective, may be the best shot for treating the coronavirus, said an official from the World Health Organization (WHO). According to sources, Gilead collaborated with Chinese health authorities on two trials of the drug in Covid-19 patients.

Remdesivir, an experimental drug developed to fight Ebola virus, is currently undergoing clinical trials in coronavirus patients in China. Trials began in February and the WHO expects the trial data to be available within weeks.

At a press briefing in Beijing, WHO assistant director-general Bruce Aylward said: "There is only one drug right now that we think may have real efficacy and that's remdesivir."

Telemedicine (cont.)...

allow for remote provider evaluation. Healthcare providers would partner with a telemedicine vendor. As the process evolved, many developed their own software for this purpose. Web conferencing software with a secure open line were implemented with relative ease. A single clinician can cover multiple sites, addressing workforce challenges. This does, however, require a "queuing" function.

Medical decision-making is cognitive in nature, and telemedicine can provide rapid access to subspecialists who would otherwise not be available in person. For example, this approach has been explored and implemented most fully with patients suffering from a possible stroke, allowing for virtual emergency neurological care. The Mount Sinai system leverages specialists at eight hospitals and more than 300 sites to provide such emergency consultations. The biggest barriers to implementation of these programs are related to payment, credentialing and staffing of specialists.

In the case of a pandemic situation, telemedicine allows for clinicians who are otherwise quarantined to still continue to care for non-exposed patients by converting scheduled office visits to telemedicine visits. Both patient and clinician can interact via teleconference from their own home, greatly limiting risks involved with travel and exposure to other patients who are infected.

It has become very apparent, with the onset of the Covid-19 pandemic, that these situations pose unique healthcare delivery challenges. Though telemedicine cannot solve all these challenges, it is well-suited for scenarios where infrastructure is intact and clinicians are available to see patients. Payment and regulatory structures, state licensing, credentialing and program implementation all take time to work through. Health systems have already begun to invest in telemedicine and are well-positioned to ensure that patients with Covid-19 receive the care they need.

In Brief (cont.)...

U.S. living with HER2-positive breast and gastric cancers, and their providers," *Brendan O'Grady*, Teva executive vice president of North America commercial, said. "The launch of *Herzuma* continues our commitment to help lower healthcare costs and increase price competition through the availability of biosimilars."

- The three leading generic makers in Japan will see their average product prices cut by 12.2% next month as compared to FY2018 revision prices, according to a JIHO survey. With two smaller players included, **Nipro** and **Nihon Generic**, the average reduction rate drops to 10.9%. Among the three major companies, **Nichi-Iko Pharmaceutical** will face a 10.7% reduction in the FY2020 revision versus the FY2018 prices (3.1% versus October 2019 revision prices given the consumption tax hike), **Sawai Pharmaceutical** 13% (no response versus tax hike) and **Towa Pharmaceutical** 13%. Nichi-Iko softened its reduction rate by nearly 2 basis points thanks to collaborative efforts with wholesalers to ensure appropriate delivery prices.
- U.S. biosimilar manufacturer **Amgen** points to building momentum in the U.S. biosimilars market. *Chad Pettit*, executive director of global value, access and policy for Amgen's biosimilars business unit pointed to the number of approvals and launches underway, and the market share biosimilars are overtaking from branded biologics, including key Amgen brands. "We've invested about US$200 million per molecule and with the 10 molecules that we've got we've invested about US$2 billion now," Pettit said during an interview at the *World Biosimilar Congress* in Coronado, California. "We're committed to the marketplace and we're excited about it. We think it's a great opportunity. All indications are really positive."

(Sources: Company Press Releases, Drug Store News, Pharma Japan, and Scrip Pharma Intelligence)