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WHEN TO ONSHORE? A FRAMEWORK FOR THE MANUFACTURING OF ACTIVE PHARMACEUTICAL INGREDIENTS

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ABSTRACT

On February 24, 2021, President Joseph Biden issued Executive Order 14017 stating that he intends to strengthen "America's Supply Chains." This involves an in-depth look at risks within the supply chain, specifically related to the production of active pharmaceutical ingredients (APIs). The goal of this research is to analyze API production, understand why certain drugs are in shortage, and develop a framework for when the US Government should onshore critical APIs. This framework will also offer alternative solutions to onshoring, such as stockpiles, subsidies, and advanced manufacturing practices. It is a commonly accepted statistic that seventy to eighty percent of APIs are produced overseas, and copious research has been done to analyze the impact of disasters abroad on the United States' ability to provide critical medication to its citizens. This thesis will build on prior research through interviews and case studies to develop a final framework that the government may use to determine the feasibility of onshoring API production. The utilization of this framework in manufacturing decisions will lower the risk of API shortages along the supply chain in times of future disaster.

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Chapter 1

Introduction

On February 24, 2021, President Joseph Biden issued Executive Order 14017 stating that he intends to strengthen "America's Supply Chains" to better protect the country. A major pillar of this Executive Order is investing in Active Pharmaceutical Ingredient (API) production. President Biden intends to focus on onshoring APIs to reduce the likelihood that the APIs are in shortage due to overseas manufacturing constraints. The task force he assembled to address this problem will review fifty to one hundred critical drugs and attempt to move their production onshore (Executive Order 14017, 2021). The goal of this thesis is to investigate the current state of the problem, including why so many APIs are in shortage. This research will gather information about alterative options for preventing API shortages. This thesis will end with an explanation of whether it is feasible for critical drugs to be moved onshore, or if alternative options should be explored.

The research for this thesis will be conducted through interviews and the review of public resources related to the topic. Primarily, the information used for this research is public knowledge. Due to the subject matter of this thesis, most of the information will be collected from government databases such as FEMA and WHO. The tracking of Active Pharmaceutical Ingredients (APIs) that are currently in shortage will be done primarily through the website PharmaCompass. Much of the initial research to determine market demand and importance of the APIs in shortage will be conducted by searching for key terms and articles in major news reporting websites. Additionally, interviews will be conducted to understand the nature of the

problem, collect information about ongoing solutions, and determine potential next steps. The interviews will begin with an expert in the field of crisis management to gather information about building the framework. Brandon Greenberg, the interviewee, will provide resources related to operational and supply chain resilience, and will explain the SCRAM method created by The Ohio State University. All other interviewees will have experience working in COVID-19 response for the government. This will help determine the feasibility of the alternatives being explored for this thesis.

The remainder of the thesis will include a background section explaining the state of the problem and why the shortages occurred. It will highlight information pulled from government websites regarding API manufacturing and distribution. It will also include information about the COVID-19 pandemic in relation to supply chain shortages. Next, the thesis will include a methodology section explaining how and why the specific research was conducted. The next chapter will include summarizations of interviews and key information collected from online documents. The information will be analyzed and presented in a format that gives context to the framework being built. It will explore the overarching questions of "What is the problem?" and "How can it be resolved?". After detailing and analyzing the information collected, this thesis will describe key findings and results. The final section, the conclusion chapter, will provide an explanation of how to use the alternative options available when determining if a product should be moved onshore.

Chapter 2

Background and Terminology

An Active Pharmaceutical Ingredient (API) is the part of a drug that causes it to have the intended effect on the user. Every other part of the drug is considered an excipient, which is what makes the drug palatable to humans or animals (International Union, 2014). Originally, most APIs were produced domestically by United States companies. However, in recent years these companies moved production overseas, or offshore, in an effort to reduce their production costs. Dr. Janet Woodcock, Acting Commissioner at the FDA, testified before Congress that seventy-two percent of APIs for the U.S. market are being produced overseas (Akin, 2021). While this has many financial benefits, it also caused unintended effects.

Offshoring, the practice of moving production from within a country's borders to overseas, always posed an obvious risk as it lengthened the supply chain. However, the magnitude of this risk was not truly realized until the COVID-19 pandemic. As borders began to close, it became more and more difficult for the U.S. to receive the critical medications its population relies on. When production in China began to slow, there was nothing the United States could do, as the country no longer had the production infrastructure to supply the products domestically. One in three generic pills consumed in the United States is made in India, with seventy percent of the raw materials coming from China (Madhok, 2021). As soon as there is a border closure or stall in production in one of these countries, the effects are felt worldwide. In an effort to protect its population, the United States began to stretch and ration medication and personal protective equipment (PPE) in hospitals around the country.

One way that the United States attempts to protect itself from shortages and emergency situations is through stockpiling critical medications. This federal stockpile is known as the

Strategic National Stockpile, and it includes versatile medications and medical equipment that would allow a local government to respond very quickly to a medical emergency or national disaster. This is a useful stockpile but is not intended to support the entire population for a great length of time (Office of the Assistant Secretary for Preparedness and Response, 2021). Additionally, this stockpile received inconsistent investments during the Trump administration, leaving the U.S. population at a disadvantage when the pandemic hit (Timm, 2020).

Under the Biden administration, the U.S. federal government began to investigate ways to prevent future shortages in times of crisis. The government and supply chain community have begun to agree that if U.S. based companies had kept production of APIs in the U.S., the country may not have experienced the shortages that it did. The government has begun to look at the strong reliance on foreign countries and view it as a weakness along U.S. supply chains. With this in mind, on February 24, 2021, President Biden issued Executive Order 14017 stating that he intends to strengthen America's supply chains. This executive order specifically references onshoring, which is the practice of moving production from a foreign production site back into the country of origin. In this case, companies that used to produce in the U.S. but moved production to India or China should move their manufacturing sites back into the United States (Executive Order 14017, 2021).

While onshoring might seem like the obvious solution to overreliance on foreign countries, it is easier said than done. Companies go through extensive cost-benefit analyses before making the decision to produce overseas, and it involves a lot of capital to build overseas manufacturing sites. It is a decision not made lightly, and one that is not easy to quickly reverse. Additionally, offshoring is utilized because it is a better financial option than producing domestically. In order to onshore, companies would need a financial reason for giving up their

overseas manufacturing sites and investing in a new facility and labor force within the United States. While it may be better for the strength of the United States' supply chains, it is unlikely to be a better financial investment for individual firms.

Offshoring might currently be the most inexpensive option, but it is not without hope for the U.S. government to say that the country should expect firms to begin producing domestically once again. The cost of offshoring, once incredibly inexpensive, is rising. As the complexity of a supply chain increases, so does the cost. Global supply chains involve increased investment in transportation, warehousing, and logistics strategy. In recent years, events such as the Suez Canal blockage and the west coast port congestion have steeply driven up the cost of global supply chains for companies attempting to ship from overseas. Containers may be stuck in the ports or in open water for multiple extra weeks at a time, increasing both the cost of fuel and labor associated with shipping the product (SupplyChainBrain, 2021).

Additionally, there is a cost associated with stocking out of the product. Companies producing generic drugs found on supermarket shelves feel significant impacts when those medications are not able to be sold to customers due to shortages and stock-outs. Customers arriving to stores and seeing empty shelves leaves both a negative impact on the brand image and increases the risk that the customer would switch to a competing product. In many cases, this is a lose-lose situation for both the API producer and the customer, as neither receives a positive benefit from the loss of a transaction.

As the cost of offshoring rises, onshoring becomes a more attractive option once again. Producing domestically would reduce U.S. reliance on foreign governments and would increase oversight into production processes and product quality. United States companies have had to invest heavily in quality control practices when producing overseas in order to ensure that

foreign facilities are upholding U.S. legal standards for medical products (Blankenship, 2020). Onshoring would allow companies to decrease some of these investments, as it would be much cheaper and easier to oversee the production process.

While onshoring might make sense for some firms, others will likely be resistant. If the financial benefits do not lean towards onshoring, companies are unlikely to choose to move their production sites unless specifically required by the government. For this reason, it is important to explore alternatives to onshoring. While onshoring might be the simplest way to strengthen America's supply chains, there are plenty of options to explore if companies are unwilling to move production. This thesis will investigate alternatives to onshoring and synthesize the options to offer choices that can be used in combination with each other in an effort to prevent further shortage situations and strengthen America's API supply chains.

Chapter 3

Methodology

The methodology behind this research primarily involves first-person accounts from experts in the field of supply chain, pharmaceuticals, and government practices. Additionally, the information and direction of the research was shaped by online research of publicly available sources, guided by project supervisors at LMI. The interviewees were selected at the direction of the thesis sponsors at LMI, Megan Biek and Kristine Gouveia. Brandon Greenberg was the first interviewee selected due to his expertise in emergency management and contingency planning. Questions related to this interview can be found in Appendix A. The benefit of this interview was gaining information about operational resiliency. Greenberg suggested research into leadership readiness, looking at risk through three lenses: supply chains, organizations, and communities. Additionally, Greenberg provided guidance on framework building and shared research on The Ohio State University's SCRAM method for supply chain assessment.

The next interview conducted was with George Karpin, an employee of LMI working in COVID-19 response and specifically supporting the Department of Health and Human Services. The interview guide for this interview can be found in Appendix B. Karpin is a chemist with pharmaceutical experience who has also worked to support the Joint Rapid Acquisition Cell (JRAC). The purpose of Karpin's interview was to learn more about APIs specifically causing HHS trouble, and the manufacturing process of APIs. Additionally, his experience supporting JRAC was intended to support the research on leadership readiness. Through this interview, information was gained about the Defense Production Act and the American Rescue Plan Act. Additionally, this interview supplemented the research on generic drugs that can be produced

overseas without adding significant risk. Karpin also provided information about the risk-impact scale and how to accurately analyze situational risk.

The final interview was conducted with Aaron Amick, a chemist who also supported JRAC and worked in emergency government acquisition processes. The goal of Amick's interview was similar to Karpin's due to the similarities in their work experience. The questions from this interview can be found in Appendix C. Amick's interview was instrumental in shaping both the leadership readiness portion of this research, and the chemistry information included in the API background. Amick explained the reagent process in chemical formulation utilizing examples of diabetes medication. He also provided information on Industrial Based Expansion, the foundational idea behind the leadership readiness sub-chapter.

Beyond the interviews, this research was primarily guided by Megan Biek and Kristine Gouveia. Biek is a supply chain consultant at LMI. Gouveia is a project manager at LMI with experience in the pharmaceutical sector. Biweekly meetings were conducted to guide the research process and provide direction on research material. Utilizing their networks at LMI, both Biek and Gouveia were able to find interviewees with experience specific to the alternatives offered in this research.

Besides first-person accounts and meetings with the LMI thesis sponsors, a primary portion of this research was conducted through online research of public sources. After learning about specific topics from the interviews, in-depth research was conducted through government sources such as the FDA and FEMA websites. Additionally, the list of drugs in shortage was found on the PharmaCompass website which provides information about APIs and their sources of supply. The 100 Day Supply Chain Review Report published by the White House was also

instrumental in shaping the foundations of this research and providing background on the source of the problem.

After conducting interviews and online research, it was determined that the direction of this research would follow four key alternatives to onshoring. As onshoring is not always a feasible option for many firms, it was important to determine ways to strengthen America's supply chains without producing domestically. The four alternatives can be found in Chapter Four – Analysis. These alternatives may be used individually, or in combination with each other.

Chapter 4

Analysis

This chapter will offer options available to the United States government and U.S. based firms when investing in API supply chains. It will investigate the feasibility of four main practices: nearshoring, expansion of the Strategic National Stockpile, investment in advanced manufacturing practices, and increased leadership readiness and government oversight. Each sub-chapter will provide an overview of the topic, including an explanation for how it could be utilized to strengthen America's supply chains. The goal is not to use one alternative as a blanket choice, but to instead tailor a combination of the alternatives to the specific needs of the firm or critical medication production. These alternatives could be made in combination with onshoring and would likely serve to increase the strength of America's API supply chains even greater when doing so. However, these alternatives are given under the assumption that firms are resistant to onshoring, and the U.S. government is instead looking to make up for the risk posed by overseas production. It is important to note that these are not the only options available to the U.S. government but serve as four main categories of options available. Additionally, this research does not explore the option of simply requiring companies to produce domestically. These alternatives were chosen with the idea of either incentivizing domestic production or stockpiling in an effort to not specifically rely on U.S. pharmaceutical firms instead of enforcing strict requirements on them. The option to require domestic production is available to the federal government but would require a more in-depth legal analysis that is outside the scope of this research.

Sub-Chapter 4: Nearshoring

While onshoring might be the preferred option, nearshoring is a close alternative. Nearshoring is the practice of moving production closer to the point of use. In the case of United States API production, this would mean moving production from overseas to countries such as Mexico, Canada, and Latin America. The benefit of this alternative production location is increased customer responsiveness and a decreased turnaround time between order and receipt (*Definition* – What, n.d.). By moving production from Asia to North America or Latin America, the supply chain is significantly shortened. This plays the largest influencing role on increased responsiveness, as it is easier to decrease lead times when the total transportation time is significantly shorter. Additionally, the United States already has strong relationships with these countries and would benefit from agreements such as the United States Mexico Canada Agreement (USMCA) which replaced the North American Free Trade Agreement (NAFTA). While labor overseas may be cheaper than labor in Canada or Mexico, the U.S. would still benefit from lower labor costs than if they were to onshore API production. United States companies would also still receive the benefit of skilled workers, along with increased oversight into the production process. The closer proximity to the point of production would allow for greater visibility into quality control during production, leading to a product that is less likely to be recalled due to production defects (Artecona & Jorge, 2021).

Mexico and Canada are both viable options. However, Mexico appears to be more prepared to ramp up production. According to recent government reports, Mexico is currently just as dependent on China and India as the United States is, but the government recognizes the benefit of producing domestically. However, the likelihood of onshoring is stalled by a lack of demand incentive (Bello, 2021). Mexico does not currently have the same level of demand for

API production that the United States faces. If the United States government or private US companies were able to create stable demand, it is likely that the Mexican government would be willing to invest in infrastructure to create APIs domestically. Additionally, World Bank International Finance Corp (IFC) is offering loans for the manufacturing of APIs. If Mexico was able to utilize these loans, it could significantly decrease the cost of creating the infrastructure, and the United States would benefit from closer proximity to their demand source (Bello, 2021).

While slightly less viable, production of APIs in Canada is another alternative to completely onshoring production in the United States. Less information is available about Canada's willingness to move production, which gives the impression that the government is not overly concerned with producing domestically. Currently, Canada only accounts for two percent of global pharmaceutical consumption, as compared to the United States which makes up forty-four percent of total consumption (Daley, 2020). In the past, the Canadian government has struggled with handling their medical supplies. Canada, like the United States, has a stockpile of medication and medical supplies. However, when the COVID-19 pandemic hit the country, the Canadian government realized that many of the masks in their stockpile had passed their expiration date (Daley, 2020). Canadian workers would be highly skilled, and the United States would benefit from increased quality and oversight. However, it appears that Canada is less prepared for a major shift to domestic production of active pharmaceutical ingredients.

Sub-Chapter 4: Strategic National Stockpile

While onshoring might be the preferred option by the government, it is not always feasible. For reasons related to cost or availability, sometimes APIs need to be produced overseas. However, there are actions the government can take to prevent shortages in times of crisis. One way to strengthen America's pharmaceutical supply chain without onshoring the production of APIs is through increased investment in the Strategic National Stockpile (SNS). The SNS was originally created in 1999 under the name of National Pharmaceutical Stockpile. Over time, it expanded beyond just medication, and was renamed to its more accurate title in 2003 (Office of Public Health Preparedness and Response, 2014). The SNS is currently managed by the Office of the Assistant Secretary for Preparedness and Response (ASPR) after transitioning in 2018 out from under the management of the Center for Disease Control (CDC). The stockpile is used as a back-up system when states run out of critical medication in times of crisis or terrorist events (Office of the Assistant Secretary for Preparedness and Response, 2021). The stockpile can be deployed at any time, sending states "Push Packs" within twelve hours of their request for help. These Push Packs weigh fifty tons and are full of medications and pharmaceutical supplies that can be generally useful in times of crisis. For more specific needs, the government will tap into the managed inventory (MI) supply in the SNS, and states will receive the specialized supplies within twenty-four to thirty-six hours of request. These supplies will be sent to one predetermined location in the state, and the state government will then take over distribution to local jurisdictions (Office of Public Health Preparedness and Response, 2014).

It is important to recognize that while the SNS is helpful in the short term, it is not meant to supply the entire population indefinitely This stockpile is to be used after exhausting

alternative options. Because the inventory is not utilized at a highly predictable rate, it is important to consistently quality check and rotate the medications and supplies. The Push Packs are required to undergo quarterly quality assurance checks to ensure that they are in good condition and have not expired. Additionally, one hundred percent of the inventory in the SNS is inspected on an annual basis. One of the checks that the federal government utilizes is participation in the Shelf-Life Extension Program (SLEP). This is a program run by the Department of Defense and the Food and Drug Administration that allows manufacturers to run tests on their medical inventory to see if the shelf life can be extended and the expiration date pushed further into the future. It was noted that testing typically adds twelve to twenty-four months of shelf life to a product, and that number only increases with increased testing (Office of the Assistant Secretary for Preparedness and Response, 2021). If the government were to invest more heavily in this program, it could create a cost-effective way to extend the use of the inventory and reduce the waste. This would require less cost all along the supply chain in production, transportation, and storage of a more consistently expiring inventory.

While considering increased investment in the SNS and SLEP, it is important to note that states currently cannot participate in SLEP when testing their own state stockpiles. This means that states are not able to individually extend the shelf life of their inventory and will have to destroy the products when they reach their expiration date, although many are likely still safe to distribute (Office of the Assistant Secretary for Preparedness and Response, 2021). In times of medical shortage, having to destroy valuable product that could save lives will only exacerbate the problem and add increased cost unnecessarily. As an alternative to onshoring, investment in both the Strategic National Stockpile and the Shelf-Life Extension Program will increase the

likelihood that the federal government can reduce the damage done by a pharmaceutical shortage.

Sub-Chapter 4: Strategic National Stockpile and BARDA

Storing medication as a finished good allows the government to respond immediately. Recently, however, the federal government has investigated the idea of stockpiling APIs in order to increase the versatility and usefulness of the SNS. The Biomedical Advanced Research and Development Authority (BARDA) recently agreed to a contract with Phlow Corporation to build a stockpile of Active Pharmaceutical Ingredients to supplement the Strategic National Stockpile. The contract agreed to a $354 million investment over four years, with the possibility of a ten-year investment totaling $812 million (Keown, 2020). The goal of the API stockpile, known as the Strategic Active Pharmaceutical Reserve (SAPIR), is to create a large amount of key ingredients that can be transformed into generic drugs experiencing shortage. Phlow Corporation is partnering with Civica Rx to transform the APIs into finished goods and distribute them to the SNS and states in need. In accordance with President Biden's intent to move production onshore, all of the APIs will be produced within the United States (Keown, 2020). According to Phlow's founder, Eric Edwards, storage of APIs both reduce cost and increase shelf life. He stated that the average finished good shelf life is two years, compared to five years in API form. It is also significantly cheaper to store the product as an ingredient instead of a finished good, and it is easier to transform that ingredient into multiple different products quickly (Edwards, 2021).

Sub-Chapter 4: Advanced Manufacturing Practices

One alternative that has recently gained attention is investment in advanced manufacturing practices. Depending on the source of information, advanced manufacturing may have different definitions. According to the FDA, advanced manufacturing can mean anything involved in manufacturing that will improve quality, address shortages, and shorten lead time. The idea is to either come up with new techniques, use them in different ways, or apply the current methods to a new area. Some new types of advanced manufacturing practices include continuous manufacturing and additive manufacturing (U.S. Food, 2022).

Continuous manufacturing is different from the traditional pharmaceutical manufacturing practices in that it does not use the batch method. Traditionally, pharmaceutical companies will produce their products in batches. Each batch involves multiple steps with breaks in between. Sometimes each step is conducted in a different facility along the supply chain. In between each step, there are quality tests of the materials (Lee, 2017). All of this adds time, which makes the lead time between when the demand occurs and when the customer receives the product very long. The benefit of continuous manufacturing is that it removes all the breaks along the supply chain. All the testing occurs throughout the process, without having to stop the line to conduct reviews on the materials. Because it is not using the batch method, continuous manufacturing can be used to scale very quickly when volume needs change. This speeds up reaction time, which makes it easier for companies to respond to emergencies such as the COVID-19 pandemic. The scalability of this process is also important because it addresses a critical issue in pharmaceutical production (Lee, 2017). There are some critical medications that have such a small amount of annual demand that they only require one production line per year. Many companies are unwilling to invest in the production of these medications because the return on cost is so low,

and it is difficult to run a production line only once per year. Therefore, some of the APIs found on PharmaCompass listed as being in shortage are critical APIs that are not used very broadly. Continuous manufacturing addresses this issue, as it is easy to scale very quickly. This means that companies could scale up their production once a year without too much of an extra effort, and then rapidly scale down once they have met the demand.

Because batch manufacturing is the industry standard, Vertex Pharmaceuticals was required to get approval from the FDA before they switched to continuous manufacturing in 2015. Since that time, many large firms have begun to invest in continuous lines (Lee, 2017). GlaxoSmithKline has invested in continuous flow chemistry and has found that it requires significantly less space to make the same products, going from nine hundred meters squared to one hundred meters squared. This decrease in facility space requirement could offset the cost of investing in the infrastructure to begin continuous manufacturing. Continuity Pharma was recently given a DARPA grant of $1.5 million to develop a process to continually manufacture multiple APIs (U.S. Food, 2022). It may be a new process, but it is gaining traction in the pharmaceutical and manufacturing communities, which the federal government is beginning to recognize.

While the benefits of continuous manufacturing are clear, it is important for companies to recognize the costs associated before making the switch. In a traditional batch process, changeovers are relatively easy because there are breaks built into the process. In a continuous environment, changeovers can take a very long time and is a heavily manual task. Along with the manual nature of changeovers, it can be difficult to train employees on the new equipment because the process is so complex. Early investment in this process involves a lot of capital for the business up front to change their entire line (Lee, 2017). However, if companies are willing

to make the switch, continuous manufacturing can be an effective way to decrease lead times, increase scalability, and reduce costs in the long run.

While investment in continuous manufacturing and advanced manufacturing practices does not directly relate to onshoring, it is an important alternative for the federal government and U.S. based firms to consider. Many companies produce overseas purely for cost savings. However, these firms are only doing cost-benefit analysis on manufacturing lines in the U.S. versus overseas running batch manufacturing lines. If these companies were to consider running continuous manufacturing lines in the U.S. versus batch manufacturing lines overseas, they might find that in the long run it is more financially reasonable to produce domestically.

When incentivizing companies to onshore, investment in advanced manufacturing lines seems like a natural time to transition. It would be difficult to convince a company with manufacturing already based in the United States to tear down its facilities and rebuild continuous manufacturing facilities. However, companies with manufacturing overseas would already have to build new facilities in the United States. It would not be as much of a hardship to switch from traditional manufacturing to continuous manufacturing when building entirely new facilities. The benefit of investment in advanced manufacturing practices is that this alternative can be used in combination with any of the other alternatives. Whether it is being done overseas or domestically, increased scalability and decreased response time will greatly serve the United States when strengthening pharmaceutical supply chains.

Sub-Chapter 4: Leadership Readiness

In some cases, it is simply not feasible to relocate production, increase the Strategic National Stockpile, or invest in innovative manufacturing practices. However, this does not mean that the United States is out of options when attempting to strengthen America's pharmaceutical supply chains. One alternative to investing in any type of changed production is investment in leadership readiness. If the government and heads of major pharmaceutical companies are not prepared to react when unexpected shortages occur, the supply chain cannot grow stronger. Investment in emergency planning training would increase the likelihood that leaders are able to successfully navigate the pressure of the shortage situation. Additionally, it would mean that plans are in place for quickly ramping up production or switching to alternative sources of supply.

Along with preparing companies for shortage situations, there are many ways that the government can prepare to react to unexpected events that may influence the pharmaceutical supply chain. Three major alternatives to onshoring are investment in Industrial Based Expansion, extension of the American Rescue Plan Act, and use of the Defense Production Act.

The idea of Industrial Based Expansion as an alternative to onshoring stems from an interview conducted with Aaron Amick, a chemist working for the Department of Health and Human Development, who previously supported the Joint Rapid Acquisition Team. Amick explained that the theory behind Industrial Based Expansion (IBX) is to not force companies to do what the government tells them to do, but to instead incentivize them to make the choice themselves. The concept behind IBX is that the government will pay for a company to build the infrastructure to create a widget, or designated product. Once the infrastructure is in place, the company does not have to always produce the widget. As long as the company can prove that it

can transition quickly back into production of the designated widget, it can use the infrastructure to produce anything it wants (Amick, 2022). This is largely beneficial to companies because it allows the company to invest in manufacturing infrastructure without having to fund it themselves. The benefit to the government is that while they do incur an upfront cost, they now have a system of production constantly at the ready. Companies are happy because they can continue producing their own products, and the government is happy because it has a reliable source for the product.

The concept behind Industrial Based Expansion is like that of the Jones Act and flags of convenience in the United States. Ships in the United States that are made in the U.S. and have an American crew benefit from being able to fly the U.S. flag. The benefit of being a U.S. flagged ship is that domestic transport becomes possible. However, by accepting the benefit of continuous domestic transport, owners of these ships also assume risk. At any time, the government can demand access to the flagged ship and use it for its own purposes (Kenton, 2021). This was seen in Operation Desert Storm when the US government took over flagged commercial aircrafts for its own use. Commercial companies benefit from working with the government. However, they also run the risk of having to halt their own commercial use for that of the public good. Industrial Based Expansion follows a similar concept; companies will benefit but will also assume risk.

While some companies may be apprehensive about the risk of having to halt production, IBX might be the nudge other companies need to bring production back onshore. Cost is generally the driving factor behind the decision to onshore or offshore. For companies that are leaning towards moving production back into the United States but are unwilling to make the jump, receiving financial support from the U.S. government might be the deciding factor. If the

government were to target specific companies which produce critical APIs or other medical products, they might have more success in moving production onshore. Not all companies will buy into the investment, but IBX serves as just one more option for strengthening America's supply chains through increased investment in domestic production.

Another alternative that the government could consider would be expanding and continuing the American Rescue Plan Act. During the COVID-19 pandemic, the 117th Congress passed the American Rescue Plan Act of 2021. Section 2303 specifically allocates funds to improving supply chains for medical supplies (H.R., 2021). If the government were to continue with this focus, they could use the allocated funds to incentivize businesses to move production back onshore. Instead of forcing companies to onshore through regulation, the government could utilize tax break incentives to convince companies to make the switch. Utilizing subsidies or tax breaks as an incentive to move production echo's Amick's idea of "using a carrot, not a stick." Some companies may not move API production onshore without strict regulation, but those on the verge of making the move could use any small incentive as a reason to make the switch. As companies begin to run cost calculations in determining whether it is more financially responsible to produce overseas or domestically, the benefit of a tax break could be the tipping factor.

The final option our government could take when focusing on our leadership capabilities is to utilize the Defense Production Act (DPA). While the first two options, Industrial Based Expansion and the allocation of funds towards subsidies or tax breaks are more preemptive, utilization of the DPA is more reactionary. The DPA gives the government emergency authority to control our domestic industries. This is utilized in times of crisis, such as the COVID-19 pandemic. It allows orders from the federal government to be prioritized, such as face masks or

ventilators, so they can be distributed throughout the country. The idea behind the DPA is that the government can better control the flow of product and ensure that what needs to be produced is being produced. Additionally, the DPA allows for the federal government to provide loan guarantees to companies throughout the United States (Siripurapu, 2021). While utilization of this Act does not inherently strengthen America's supply chains preemptively, it is an important tool for the government to be aware of. In the case of a future disaster or shortage situation, quickly utilizing the DPA could allow the government to manage the situation before it grows increasingly worse.

Understanding the government's capabilities when it comes to influencing business decisions is an important way to strengthen America's pharmaceutical supply chains. While regulation requiring businesses to move API production onshore is a reasonable option in some cases, incentivizing businesses to make the choice for themselves could be much less difficult. Both parties are able to benefit when the government uses its resources to find creative ways to incentivize production onshoring. Going forward, focusing on Industrial Based Expansion and supplementing with tax breaks and use of the Defense Production Act could significantly decrease the cost of a shortage situation. The United States will already have invested time and resources into API production and will be significantly less reliant on foreign governments. Additionally, the businesses will benefit because they will be significantly more prepared to ramp up production or pivot to US based production when the situation necessitates.

One final aspect of leadership readiness that could be expanded on is investment in the Cities Readiness Initiative. This initiative currently looks at population centers where nearly sixty percent of the United States population lives and focuses on creating plans for if there was ever an emergency in the specific city. This is a federally funded program, and it is used to

respond to public health emergencies (Center for Preparedness and Response, 2020). This mission already falls in line with the goal of strengthening America's pharmaceutical supply chains, because one key aspect of the supply chain is distribution. Increased investment in the education aspect of this initiative could help states respond more efficiently in times of emergency. While having a plan in place is important, being preemptively educated on that plan is even more useful. Investment in education on how to better respond to emergency medical shortages, and how to quickly distribute lifesaving products will better protect our most densely populated cities during future emergencies.

Chapter 5

Conclusion

While alternatives to onshoring are useful when attempting to strengthen America's supply chains, nothing can replace the diminished risk that onshoring brings. At the beginning of this research, it seemed unrealistic to expect companies to move production back onshore. The expected result was that onshoring was an unreasonable expectation and that there would be reasonable alternatives. While there are alternatives to address the issue of risk, through interviews and research it has been determined that there is no complete replacement for onshoring.

It was noted throughout the interview process that while alternatives such as increasing the Strategic National Stockpile are useful, no amount of preparedness matters if you run out of product and cannot produce it domestically. While increasing the stockpile would mitigate risk in the short term, it could not support the population forever. Unless the U.S. has a sustainable way to produce domestically in the case of a border closure, the supply chain is not truly strengthened.

In the interview with Aaron Amick, a chemist at LMI, it was also noted that defining what constitutes as an API is a crucial part of incentivizing onshoring. Using the example of Sitagliptin, a Type 2 diabetes medication, Amick highlighted how a company would be unable to distribute Sitagliptin if the company didn't also own the reagent and solvent process along with the API process. While the company would benefit from domestic API production, the chemical process would not occur without the reagents. If the reagent was produced overseas and the company was unable to access it in an emergency or shortage situation, the API would no longer have a use as it would be incapable of being transformed into a finished good (Amick, 2022).

For this reason, it is important that as the government works to strengthen America's pharmaceutical supply chains by investing in API onshoring they also define what processes are necessary to produce a finished good. Storage of APIs that can be quickly transformed to multiple different medications is crucial but owning the entire supply chain will mitigate the greatest amount of risk.

Working towards the goal of mitigating risk in the pharmaceutical supply chain, the United States government has many options available. If companies are unwilling to invest in onshoring on their own, the government can incentivize the move. Industrial Based Expansion, tax breaks, and subsidies could be used to strengthen the financial benefits of onshoring. Nearshoring is another feasible option for companies that would mitigate some risk and still provide financial incentives. On the side of the federal government, investment in the Strategic National Stockpile in both finished goods and API form would create a larger buffer in the case of future shortage situations and national emergencies. Transitioning from traditional manufacturing to continuous flow manufacturing or other advanced manufacturing practices is another option available to both the federal government and private companies. Decreasing the time and labor associated with production will save companies money, potentially offsetting the cost of moving production back into the United States.

While these alternatives may be used as stand-alone options, they could also be combined to increase the strength of the pharmaceutical supply chain. If companies are unwilling to onshore, the government could invest in the SNS, expand the Shelf-Life Extension Program, and begin investments in Industrial Based Expansion to start the process of convincing companies to make the move onshore.

Research has been done to highlight four key options available to the federal government. However, there are a significant number of options available that have not been explored as they were outside the scope of this thesis. The concept of requiring companies to produce domestically through legal action and sanctions was not explored. Further research in this area would be useful in determining whether it would be worthwhile from a cost-benefit perspective to mandate domestic production.

Additionally, an analysis of APIs in shortage on an individual API level by a researcher with experience in chemistry and pharmaceuticals would supplement this research and help to explain which products are more susceptible to shortage. That further research could be used in combination with this research when determining a framework for what products should be onshored, and which products would benefit from alternative options.

Appendix A

Brandon Greenberg Interview Guide

1. Can you tell me a little bit more about your role at LMI?
2. Do you have any suggestions for how I should structure my research?
3. How do you measure risks in your job?
4. How do you think I should weigh the risks of onshoring vs offshoring?

Appendix B

George Karpin Interview Guide

1. Could you tell me more about your experience working in covid response in the department of Health and Human Services?
2. What do you think the government could have done better?
3. What areas are causing you the most trouble? Are there specific APIs you haven't had access to?
4. Do you think the solution is to just onshore?
5. Can you speak to the manufacturing process of APIs? How storing them might be different than storing as finished goods?
6. Part of what I'm working on is leadership readiness to respond to crisis. When you worked to support JRAC, did you pick up any specific frameworks or tactics you think could be useful to prepare leaders to jump into action when there is a problem, and they need to ramp up production quickly?

Appendix C

Aaron Amick Interview Guide

1. What are problems you've experienced with Mexico/Canada production?
2. Do you see onshoring as the only feasible option to improve?
3. What do you think about increasing the national stockpile?
4. How do you feel about the BARDA Phlow deal? Do you think it makes more sense to invest in APIs?
5. Are there any APIs that you know of that aren't capable of being onshored?
6. Why, besides cost, would we need to produce overseas?

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EDUCATION

The Pennsylvania State University | Schreyer Honors College — **University Park, PA**
Smeal College of Business | Bachelor of Science in Supply Chain and Information Systems — *May 2022*
Smeal College of Business | Information Systems Management minor

RELEVANT EXPERIENCE

Dell Technologies — **Austin, Texas (Remote)**
Internal Use Software Procurement Intern — *May 2021 – Present*
- Catalogue top 100 suppliers by spend; analyze MRAs and create knowledge library to reduce inefficient negotiation preparation
- Coordinate with key stakeholders; execute on critical deliverable dates for negotiation preparation and present solution to Dell SVP

L Brands – Mast Global Logistics — **Columbus, OH**
Supply Chain Planning and Analytics Co-Op — *January 2020 – June 2020*
- Led 35 employees in weekly meetings to provide insights on product movement and scheduled production dates
- Created visuals using Tableau for daily distribution to Ops Planners; tracked late articles and identified risk status of late floorsets
- Facilitated transition of data visualization software from Tableau to MicroStrategy Inc. through research and presentations
- Increased efficiency of late PO tracking process; decreased number of late articles by up to 83%

Unilever — **University Park, PA**
Student Project Consultant — *September 2019 – December 2019*
- Researched sustainable cold packing alternatives for polyethylene linings; gained knowledge in polylactic acid production (PLA)
- Created a feasible plan for transition from polyethylene lining to PLA to reduce plastic waste
- Delivered 45-minute project findings presentation to 25 peers and Unilever Supply Chain representative

Council of Supply Chain Management Professionals — **University Park, PA**
Premium Member — *September 2018 – Present*
- Foster academic and professional advancement through exchange of knowledge with peers and supply chain professionals
- Tour distribution centers such as REI and Aldi to gain a deeper understanding of DC operations and full supply chain process

Wegmans — **State College, PA**
Student Project Consultant — *September 2017 – January 2018*
- Researched 12 companies that use real time data logging to monitor internal temperatures of in-transit motor carriers
- Provided opportunities for increased visibility and recall cost reduction; presented recommendations to Wegmans executives

LEADERSHIP & INVOLVEMENT

The Sapphire Leadership Academic Program — **University Park, PA**
Vice President/ Member — *June 2020 – January 2021/August 2018 – Present*
- Represent top 5% of Smeal students in an academic program with specialized curricula to develop outstanding leadership skills
- Lead 13 team captains in 3 meetings per week; develop agendas and provide supervision over event planning
- Coordinate scheduling 50+ events per semester for 200 members; attend every event and provide assistance to team captains
- Studied 24 hours of military leadership styles and decision-making tactics in high stress environments at overnight Quantico trip

Smeal Student Mentors — **University Park, PA**
Mentor — *August 2019 – Present*
- Mentor 8 Smeal freshmen; advise on course scheduling, extracurricular involvement and resume preparation
- Assist in success of Fall College Day; facilitate introduction of 2,000 freshman to Smeal College of Business

Wegmans — **State College, PA**
New Employee Trainer/Cashier — *May 2015 - January 2020*
- Led new employees in 40 hours of cash register technology, job requirements, and customer service trainings

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TECHNOLOGICAL EXPERIENCE

Access | Tableau | LLamasoft Data Guru | Excel | MicroStrategy | SAP | Power BI | VBA | SQL