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JUNE 23, 2021

Biden Administration Issues 100-Day Supply Chain Review Report

Industry-Specific Primer — Pharmaceuticals and Active Pharmaceutical Ingredients

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On June 8, 2021, four Executive Branch Departments issued reports mandated by President Biden's February 24, 2021 Executive Order on America's Supply Chains (the "America's Supply Chains E.O." or the "E.O."). The E.O. directed the federal government to assess the supply chains of four critical products: (1) semiconductor manufacturing and advanced packaging; (2) large capacity batteries; (3) critical minerals and materials; and (4) pharmaceuticals and active pharmaceutical ingredients ("APIs"). The four reports have been consolidated into a report to the President (the "100-Day Report"), and on June 8, the Biden Administration issued a Fact Sheet and held a press briefing about the reports. As we wrote in February, the 100-Day Report will be followed by six additional sector-specific supply chain assessments that are due by February 24, 2022.

This Industry-Specific Primer focuses on the "Review of Pharmaceuticals and Active Pharmaceutical Ingredients" section of the 100-Day Report that was coordinated by the U.S. Department of Health and Human Services ("HHS") (the "Pharmaceuticals and API Report"). The Pharmaceuticals and API Report identifies both immediate and long-term actions needed to strengthen the domestic manufacture of critical drug products and APIs, reduce dependence on foreign nations for supply chain needs, create jobs, and address unfair trade practices. The policy objectives and related funding opportunities described in the report present a wide range of opportunities for life sciences manufacturers and other industry stakeholders to engage with the Biden Administration to help shape mutually beneficial policies.

GENERAL FINDINGS OF THE 100-DAY REPORT

The combined 100-Day Report contains an Executive Summary that identifies common vulnerabilities and policy recommendations across each of the four critical supply chains. The Report highlights:

- **Insufficient U.S. manufacturing capacity:** The United States lacks sufficient manufacturing capabilities in each of the identified key sectors for a variety of reasons, including competition from low-wage nations and stagnating productivity that impacts opportunities for continued innovation.
- **Misaligned incentives and "short-termism" in private markets:** Short-term profit concerns, such as low-wage workforces and stock buybacks, negatively impacted productivity and reduced long-term investments, such as research and development ("R&D") and new facilities.
- **Industrial policies adopted by allies and competitor nations:** Industrial policies adopted by the EU, Taiwan, South Korea, Singapore, and, China (especially), have hurt U.S. competitiveness. As to geopolitical competitors, the 100-Day Report notes that China "stands out for its aggressive use of measures—many of which are well outside globally accepted fair trading practices—to stimulate domestic production and capture global market share in critical supply chains."
- **Geographic concentration in global sourcing:** The search for low-cost production and intensive efforts to attract investment by other nations "has led to geographic concentrations of key supply chains in a few nations, increasing vulnerabilities for United States and global producers." As one example, the 100-Day Report notes that "China dominates the processing of strategic and critical materials, giving it de facto control over the flow of material through the supply chain."
- **Limited international coordination:** That the "United States cannot manufacture all needed products at home" and states that the United States "has not systematically focused on building international cooperative mechanisms to support supply chain resilience."

The Report's Executive Summary includes the following recommendations.

- **Rebuilding domestic production and innovation capabilities:** Public funding should be increased for investments in manufacturing and R&D related to the four critical products, including at least $50 billion to expand domestic manufacturing of semiconductors and other investments under the Biden Administration's American Jobs Plan. The Biden Administration also recommends: (1) the establishment of a Supply Chain Resilience Program at the Department of Commerce to "monitor, analyze, and forecast supply chain vulnerabilities and partner with industry, labor, and other stakeholders to strengthen resilience"; (2) the establishment of an interagency Defense Production Act ("DPA") Action Group "to recommend ways to leverage the authorities of the DPA to strengthen supply chain resilience"; and (3) development of an Export-Import Bank Domestic Financing Program "to support the establishment and/or expansion of U.S. manufacturing facilities and infrastructure projects in the United States that would support U.S. exports."
- **Leverage Buy American requirements and government investment in critical goods:** The Biden Administration recommends identifying critical products that would receive additional preference for government purchases under the Buy American Act and Federal Acquisition Regulatory Council regulations. The Biden Administration also recommends "updat[ing] manufacturing requirements in federal grants, cooperative agreements and R&D contracts to ensure that taxpayer funded R&D leads to products made in the United States."

- **Create a new "trade strike force" to strengthen international trade rules, including trade enforcement mechanisms:** The U.S. Trade Representative should establish and lead a "trade strike force" to "identify unfair foreign trade practices that have eroded U.S. critical supply chains and to recommend trade actions to address such practices." The Biden Administration also recommends the initiation of an investigation under Section 232 of the Trade Expansion Act of 1962 on imports of neodymium magnets.
- **Monitor near-term supply chain disruptions as the economy reopens from the COVID-19 pandemic:** A new Supply Chain Disruptions Task Force led by the Department of Commerce is recommended, which should "provide an all-of-government response to address near-term supply chain challenges to the economic recovery" and focus on key industries that have faced pervasive supply issues during the pandemic, such as "homebuilding and construction, semiconductors, transportation, and agriculture and food." In addition, the Biden Administration recommends that the Department of Commerce leverage data from across the federal government "to improve the federal government's ability to track supply and demand disruptions and improve information sharing between federal agencies and the private sector to more effectively identify near term risks and vulnerabilities."

THE PHARMACEUTICALS AND API SUPPLY CHAIN

The Pharmaceuticals and API section of the report highlights the government's concerns for the sector, putting a spotlight on issues that companies should monitor and address as the Administration develops new policies in this area. The report identifies three critical pillars for establishing a robust pharmaceutical supply chain to support the United States' drug supply:

- The ability to manufacture high-quality products for the U.S. market;
- Diversification of the drug supply chain, such as relying on a geographically diverse set of manufacturers; and
- Redundancy of the supply chain, such as the existence of multiple manufacturers for each product and its precursors.

The report focuses primarily on the supply chain for drugs, particularly small-molecule drugs, sterile injectables, and therapeutic biological products, including APIs. The report does not address vaccines, cell therapies, blood products, and their APIs. The report highlights that generic drugs make up 90 percent of the small molecule and therapeutic biologic drugs that are prescribed in the United States, which are "most critical across populations," and have been subjected to consolidations causing firms to shift manufacturing to low-cost, largely foreign sites creating vulnerabilities in the supply chain. In addition, HHS identifies tax incentives, lower labor, energy, and transportation costs, and differences in environmental standards resulted in pharmaceutical manufacturers in the 1970s to relocate their facilities overseas to Europe and developing countries. As a result of these current dynamics, more than half of all U.S. Food and Drug Administration ("FDA")-registered Finished Dosage Forms ("FDFs") manufacturing facilities and nearly three quarters of all FDA-registered API facilities making FDF relocated outside the United States. Importantly, however, the report acknowledges the reported data may not capture the true reliance on foreign countries, such as China, which may produce large quantities of fine chemicals for registered facilities, but the quantities are not reported through registration requirements.

DRUG SHORTAGES ARE THE PRIMARY CONCERN

The report highlights drug shortages as the primary cause for concern. Shortages can "worsen patients' health outcomes," increase "the risk of medical errors with substitutions," hamper federal procurement, and lead to unexpected price increases for federal agencies under price or vendor restrictions. The report further underscores the risk from the lack of a mechanism to appropriately allocate essential drugs during periods of acute shortage.

The report noted specifically that the sterile injectable market is susceptible to a high risk for shortage. Contributing factors range from recalls from a limited number of suppliers, quality-related failures of manufacturing FDFs, manufacturing disruptions that can lead to contamination, and the concentration of market share due to the need for highly specialized facilities. Concerning quality-related production disruptions, the report identifies that the FDA has determined that the primary reason for such shortages "is the inability of the market to reward quality; instead, generics compete primarily on price."

PRICE COMPETITION IS A MAJOR DRIVER FOR OFFSHORING DRUG MANUFACTURING

Price competition is one of the primary drivers of moving manufacturing overseas, which leads to greater supply chain vulnerability and exacerbates the potential for shortages. As more drugs enter the market, the price of generics goes down, which leads manufacturers to offset lost profitability by reducing costs. Short-term contracting and "low-price clauses" that allow the buyer to walk away if a competing manufacturer is willing to supply the products for a lower price also damage the ability of domestic manufacturers to compete with foreign suppliers.

LACK OF RESILIENCY AND GEOPOLITICAL CONCERNS CONTRIBUTE TO DRUG SHORTAGE RISK

The report also concludes that drug shortages are caused by insufficient ability of domestic manufacturers to address supply disruptions. When disruptions occur the easiest way for a manufacturer to respond is to increase production in an existing production line. However, shifting to an unreliable third-party source or bringing a new facility online requires significant time and investment as well as validation from the appropriate regulatory body. The COVID-19 pandemic revealed an inability to respond quickly to disruptions.

Dependence on manufacturing in foreign countries presents geopolitical risk to the pharmaceutical supply chain. The report explains that foreign governments can leverage this dependency by interrupting the United States' access to such supply chains. For example, the report singles out China and India, which represent the second and eighth highest sources of API supply and the fifth and sixteenth largest exporters of FDFs to the United States. This risk is compounded because India, which supplies roughly 40 percent of generic pharmaceuticals used in the United States, imports nearly 70 percent of its APIs from China. Further, the report observed that Europe imports 90 percent of generic APIs from China. The categories of generic drugs affected by this dependency include antibiotics, anti-depressants, oral contraceptives, chemotherapy for cancer treatments, and medicines for Alzheimer's disease, HIV/AIDS, diabetes, Parkinson's disease, and epilepsy.

THE NEED FOR ADDITIONAL OVERSIGHT OF THE DRUG SUPPLY CHAIN

Although the FDA currently maintains reporting requirements for domestic drug manufacturers and foreign entities that manufacture drugs imported into the United States, the report found that these data do not allow the FDA to monitor adequately and identify vulnerabilities. Examples of information gaps include:

- Foreign API manufacturers shipping drugs to another foreign country to be incorporated into a finished product before the product is imported into the United States;
- API manufacturers not registering third-country manufacturing facilities with the FDA; and
- A lack of volume data that would illustrate whether there is true redundancy in manufacturing by indicating which drugs are actually being produced in each facility.

The FDA continues to rely primarily on notifications from manufacturers about discontinuances of and interruptions in manufacturing certain products. Despite Congress' effort to enhance transparency through the Coronavirus Aid, Relief, and Economic Security ("CARES") Act, which requires manufacturers to report annually the amount of each drug produced for commercial distribution, the FDA still lacks information, such as which drug product manufacturers may be

relying on a given API supplier or the extent of that reliance. As a result, manufacturers should expect to see an increased push to provide production and supply information to the government.

INCENTIVIZING QUALITY MANAGEMENT MATURITY

An opportunity to reduce risks that lead to shortages is to promote manufacturers' efforts to enhance the quality of their products and manufacturing processes. The report discusses, for example, that the prescription drug market does not provide incentives for manufacturers to reach what the report refers to as "quality management maturity." As facilities age and technology evolves, failing to keep up can lead to quality problems. The pharmaceutical industry could benefit from adopting similar approaches to the automotive and aerospace industries, which have reduced quality issues by vigilantly monitoring performance and product quality data, and adjusting operations as needed. For example, supporting the pharmaceutical industry's adoption of advanced manufacturing, such as "continuous manufacturing," wherein the finished drug product is produced as a continuous stream, as opposed to traditional batch manufacturing, can improve pharmaceutical manufacturing by reducing steps, processing times, and equipment, and scaling operations appropriately to accommodate changes in demand.

KEY RECOMMENDATIONS

As noted above, the report finds the pharmaceutical supply chain to be complex, global, and vulnerable, and concludes that the United States must undertake a "comprehensive, multifactorial approach to induce sustained enhancements that drive resilience throughout the many interconnected elements of the supply chain." Active participation of private sector players such as purchasers, intermediaries, and manufacturers will be critical. The Pharmaceuticals and API Report provides key recommendations and next steps:

- **Boosting local production and fostering international cooperation:** The Administration intends to establish a new consortium of stakeholders to promote domestic production, which range from addressing the regulation of novel technologies to mitigating risks from climate change. HHS and the White House will host a high-level summit on drug supply chain resilience to kick off the new initiative and will pull experts from within the government, non-profit, and private sector. The consortium will review the Essential Medicines List[1] and recommend 50 to 100 critical drugs and projected volumes needed for health emergencies, using COVID-19 surges as a benchmark. HHS will also leverage the DPA process to assess the financial incentives needed to onshore or nearshore production capacity. Further, HHS will map the supply chains for the Critical Drug List and determine if there is a need to increase production or stockpile API.
- **Review reimbursement models for key medicines:** The U.S. Government will determine whether changes to reimbursement models could improve the resilience of essential medicines without unduly impacting costs.
- **Increasing resiliency in the sterile injectables market:** The Administration will consider creating financial incentives to spur investment in advanced manufacturing processes and to reduce barriers to entry for new manufacturers or costs to existing manufacturers to upgrade facilities, as well as providing procurement guarantees consistent with agency needs and U.S. procurement laws and obligations.
- **Promote R&D initiatives for innovative manufacturing processes and production technologies:** The Department of Commerce-sponsored National Institute for Innovation in Manufacturing Biopharmaceuticals ("NIIMBL") will launch a "whole-of-industry" effort to develop fully integrated and smaller footprint platforms that will reduce supply chain demands for raw materials, increase domestic biomanufacturing surge capacity, and improve technological capabilities that can lead to the biomanufacturing of APIs. HHS will create an internal

task force to support the development, evaluation, and, if possible, implementation of novel manufacturing technologies and processes.

- **Develop a manufacturer rating system to spur quality management maturity:** HHS and the FDA propose to create a program with a rating system aimed at recognizing and rewarding manufacturers for mature quality management systems that achieve sustainable compliance and focus on continuous improvement, business continuity plans, and early detection of supply chain issues. According to the report, the rating system could be used to inform purchasers and Group Purchasing Organizations, either through voluntary or mandatory disclosure. FDA will begin this program through consultations with stakeholders to develop a framework for rating quality management maturity, and FDA will consider establishing a new Public-Private Partnership ("PPP") with industry to develop and support such a rating system.
- **Make greater use of commercial data sources to identify supply chain risks:** The report recommends that in the short term, the U.S. Government should encourage stakeholders to make greater use of commercial data sources to identify supply chain risks while establishing a robust surveillance system over the long term. Separately, the report notes that the U.S. Government should collect additional supply chain data to improve oversight and supply chain resilience. The additional data may include drug manufacturing volume information, complete registration and listing requirements, and distribution data on prescription drugs and certain biological products. The report recommends requiring manufacturers to notify FDA of an increase in demand and that API and finished product labeling include original manufacturers. To implement this enhanced data collection, HHS intends to consult with industry stakeholders and recommend to Congress statutory changes that will authorize such data collection.
- **Building emergency capacity:** The United States should create a virtual stockpile of APIs and other critical materials necessary to produce the identified Essential Medicines, prioritizing those on the Critical Drug List and relying, to the extent possible, on domestic suppliers. The report recommends that HHS determine specific APIs and finished drugs to be stockpiled along with the amounts needed.
- **Promoting international cooperation and partnering with allies:** Working through established international regulatory collaboration and harmonization organizations, the report recommends focusing on understanding the risks to the global supply chain and collectively developing solutions. For example, the report contemplates that a specific targeted action could be to develop a centralized API supplier database. The United States, using the Critical Drug List, should engage with international partners to map a global supply chain where redundancy and diversity includes sufficient onshoring, production in geographically accessible locations, and production by allies.

KEY TAKEAWAYS

The Pharmaceutical and API Report sends a clear message to industry stakeholders that they must be ready to engage with government regarding their supply chains and expect to face additional scrutiny and requests for information and data. At the same time, the report suggests that there are opportunities for manufacturers with operations in the United States and allied countries to seek government support and get an edge over competitors. Affected companies and other stakeholders should be taking steps now to shape the legal and policy landscape in their favor as this process continues to unfold, and King & Spalding's experienced, multi-disciplinary teams are ready and able to assist with such efforts.

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[1] List of Essential Medicines, Medical Countermeasures, and Critical Inputs, U.S. Food and Drug Administration (October 2020).