Subcommittee on Oversight and Investigations

Examining the Root Causes of Drug Shortages: Challenges in Pharmaceutical Drug Supply Chains.

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The economic viability of the generic pharmaceutical industry, which represents over 90% of the medications prescribed in the United States is diminishing, contributing to supply disruptions and drug shortages, with negative implications for U.S. health security.

The offshoring of pharmaceutical manufacturing is not new. It is a phenomenon that has been occurring for the past 30 years as the industry, particularly the generic manufacturers, offshore its production to countries with lower labor and manufacturing costs to gain market share. Economic conditions indicate that this environment will worsen, increasing quality and supply risks to the nation's healthcare security.

COVID-19 created a significant demand shock to the US drug supply chain revealing the country's' over reliance on foreign production of essential drug active pharmaceutical ingredients (API), which is the component of a drug that produces the intended medical benefit. Most of the drugs consumed by Americans, including our antibiotics, antivirals, and the top 100 prescribed generic drugs, have no US-based source of API. Over 85% of the API's and 60% of the finished dose forms for the U.S. market, with a notable reliance on China throughout the value chain, are located outside of the United States. This has created both a public health and a national security risk.

A confluence of factors has led us to this point, and will require a multifaceted, coordinated approach to resolve. To strengthen our health security by keeping our nation's drug supply chain secure, robust, and resilient, we must address the economic instability of the generic pharmaceutical market, expand public-private partnerships, and incentivize domestic drug manufacturing.

The generic pharmaceutical market plays a significant role in the healthcare of the nation. Generic drugs account for 92% of U.S. prescriptions.[1] By rule, generics must be perfectly substitutable to the originator (i.e., branded) product, and to each other. Because they are interchangeable, price becomes the dominant factor in market success and these medicines are, generally, inexpensive.

As medicines, particularly high-volume essential medicines, become generic, market entrants and competition increases, market pricing decreases, profit margins erode, lower cost production options are explored, and a transition occurs to the least-cost locations to gain economy of scale. Over time, price and margin erosion lead to essential medicines becoming low-margin commodities, and eventual production and supply issues create vulnerability to shortages and susceptibility to low reinvestment.

In a study I published April 21, 2023, I show that price erosion, greater than 50% since 2016, is further accelerated by the market consolidation of the number of drug wholesalers and group purchasing organizations. Manufacturers are vying for the business of fewer, more powerful buyers. With no distinguishing product differentiation, cost reduction trends continue year after year, in what has been referred to as the 'race to the bottom', squeezing generic manufacturer's margins further, and further degrading the economic viability of the manufacturing supply base. An average high-volume 30-count bottle of medicine is now less than $1.50, the equivalent of 5 cents per tablet.

Predictably, hyper-competition has had a direct effect on manufacturer's earnings. My analysis of the top twenty-four generic companies by revenue over the past five years revealed a rapid degradation in earnings due to these price pressures. While all top manufacturers saw a drop in earnings since mid-2021, the bottom quartile has notably fallen below a 15% operating profitability ratio. The implications of such economic indicators can be dire: reduced earnings will lead to cost-cutting and a reduced ability to invest in new product development, factory maintenance, overheads, technology innovation and investment in quality systems.

This drop also correlates to a reduction in the ability for manufacturers to address sometime expensive and complex compliance challenges. In my research I show that the trend in addressing FDA manufacturer warning letters has dropped from one-in-four warning letters closed out to one-in-twenty by 2022. It is important to note that warning letters do not necessarily suggest an issue regarding the

safety of the drug product but indicate a non-conformance to FDA manufacturing standards. My research indicated one of the drivers for this decreasing trend of closing out compliance issues is the high cost to address compliance and quality challenges relative to the low profitability. The economic pressures facing generic manufacturers are contributing to increased quality and compliance risks evidenced by greater than 1 in 4 prescriptions in the US filled by companies that have received FDA warning letters in the last 26 months.

Generic drugs also account for most of the essential and critical drugs in shortage.[2] As my research shows however, and other studies have found, the very segment of the pharmaceutical industry most critical to a reliable supply chain is the segment which can least afford to do so. Strengthening our domestic manufacturing capabilities requires a coordinated approach between public entities and private enterprise across the entire supply chain.

The optimal public-private model is the creation of regional nodes across the country that are successful in bringing together a supercluster of innovators, researchers, investors, and commercial manufacturers into project consortiums to actively participate in opportunities to commercialize new technologies that drive U.S. based biomanufacturing. A coordinated approach between federal and state public entities and regional private enterprise has the greatest likelihood of de-risking the challenges of building stronger, and sustainable supply chains.

An example of this is the API Innovation Center in St. Louis, Missouri. A non-profit public benefit corporation, the API Innovation Center has secured $9.45 million dollars in state funding and is currently building a consortium consisting of academic research institutions, advanced manufacturing equipment companies, and FDA-approved cGMP drug manufacturers to begin prioritizing reshoring critical drugs back to the U.S. using continuous flow manufacturing. A public-private partnership such as this can help de-risk industries adoption of advanced manufacturing technologies to enable U.S. based domestic manufacturing of generic drugs to take hold.

To successfully incentivize domestic manufacturing, it is necessary to minimize the inherently risky 'go it alone' approach by either the public or private sector. An example of this is the application of new advanced manufacturing equipment, such as continuous flow, placed in existing FDA-approved cGMP manufacturing sites with idle capacity. In September of last year, I published a study which revealed that of the 37 U.S. generic manufacturing sites surveyed in my research, on an annual basis, these sites were producing at just half of their production capacity.

By retooling or repurposing dormant or low volume manufacturing lines, 57% of the manufacturing sites said they could be operational within one year, and 86% within two years. This equates to an additional 30 billion doses of essential and critical medicines within two years.

The application of new, advanced manufacturing, such as continuous flow, into sites with idle capacity offers a promising path for building resiliency. Advanced manufacturing is estimated to reduce production cost between 30%-50%. Industry 4.0 proponents believe automation of traditional drug manufacturing processes can make these gains even greater, when the right technologies extend across the supply chain. Advanced manufacturing can also accelerate production timeline from months down to days, which will be critical when we need to quickly get product to market, it is more efficient, utilizes a much smaller environmental footprint, and creates new workforce development and job skills.

There are multiple potential options to address supply disruptions and drug shortages, but they each must acknowledge and combat the economic root causes. A driver of price erosion for generic drugs is the inability to differentiate on product quality which is a dimension of market competition in virtually all other industries. Quality-price trade-off can be addressed by creating a transparent quality score that enables competition on dimensions beyond only price and incentivizes quality.

Leveraging the buying power of the federal government, which accounts for 34% of total healthcare spending in the United States, is unique in not having sourcing policies that favor and incentivize domestic manufacturing or manufacturers with stronger compliance records – a practice

already employed in Germany, Brazil, India, and China. Improving provider reimbursements for US-made generic products and realigning preferred drug lists/formularies for Medicaid/Medicare can drive incentive for US based manufacturing.

I would like to thank Chairman Griffith and Ranking Member Castor for convening this oversight hearing on prescription drug shortages. By identifying and addressing the factors that have contributed to our drug shortages, we can build stronger, sustainable drug supply chains and address our health security risks by resolving our over-reliance on foreign sourced API and finished drug product. Thank you.

References

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