

Testimony to the United States Senate Committee on Finance

“COVID-19 & Beyond: Oversight of the FDA’s Foreign Drug Manufacturing Inspection Process”

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Chairman Grassley, Ranking Member Wyden, and Members of the Committee,

My name is Martin VanTrieste. I am the President and CEO of Civica, Inc. I am also a 35-year veteran of the pharmaceutical industry.

It is an honor to appear before you today, and an honor to follow a group of dedicated public servants. My dealings with the FDA and BARDA over the past few months have reminded me how tirelessly these officials work to serve the American people.

In my testimony today, I will:

- Introduce you to Civica and our non-profit model
- Discuss several policy options to help the United States ensure a robust supply of drugs, and
- Share some background on a recently announced agreement with the federal government to enhance U.S. manufacturing capacity for essential medicines.

About Civica

Civica is a non-profit 501(c)(4) social welfare organization established by U.S. health systems and philanthropies to reduce chronic drug shortages and ensure a safe and stable supply of essential medicines to U.S. patients.

That is our mission: to serve patients by making quality medications available and affordable.

Today, more than 50 health systems have joined Civica (Figure I). They represent approximately 1,200 hospitals and over 30 percent of all U.S. hospital beds. Civica also supplies the Veteran’s Administration, the Department of Defense and “340B” hospitals, which care for vulnerable patients in some of the most underserved areas of the country.

FIGURE I.



The Supply Chain

Civica was primarily created to improve the resiliency of the supply of essential medicines used in hospitals daily, often for critical care. The drugs we make are not those with the highest return on investment. Rather, they are the ones that are identified and prioritized by our health systems – by doctors and pharmacists on the front lines – as the medications most important for high-quality patient care. Civica’s members have also identified generic medications that are excessively priced, such as daptomycin, where Civica lowered significantly the market price.

Civica is implementing, simultaneously, a three-pronged product supply strategy to reduce chronic drug shortages and secure the supply of essential generic medicines for patients:

- Working with multiple generic drug manufacturers that have the U.S. Food and Drug Administration (FDA) approved manufacturing facilities and capacity to produce generic drugs under Civica’s National Drug Code,¹ allowing manufacturers to re-enter the market or increase existing capacity. Civica is currently working with five supplier partners and is in negotiations with several more.
- Developing Abbreviated New Drug Applications² (ANDAs) to produce Civica medications using contract manufacturers
- Building Civica manufacturing capability using Civica’s ANDAs

Civica is fully committed to stabilizing the supply of antibiotics, anesthetics, cardiac medications, pain management medications and other essential sterile injectable medicines. To date, and in just over a year, Civica has launched 24 sterile injectable medications for use in

¹ A unique numerical identifier indicating the labeler (manufacturer, repackager or distributor), strength and dosage form of each drug

² The approval pathway for generic drugs

hospitals across the country (see Table I). Civica is on track to deliver approximately 20 more medications in 2020, building toward 100 medications (in hundreds of dosage forms) by 2023.

Many of our drugs are used in the management of patients with COVID-19 (see Table I). And during this pandemic, Civica has contributed 1.6 million containers of medicine to the Strategic National Stockpile.

TABLE I. CURRENT CIVICA MEDICATIONS

DRUG	Source of finished drug	API Source	COVID-19	Surge	SNS
AMINOCAPROIC ACID	USA	Japan			
CALCIUM CHLORIDE	USA	Germany			
CEFTRIAXONE	Portugal	Italy*			
DAPTOMYCIN	India	Hungary			
DEXAMETHASONE	USA	France			
DIAZEPAM	Italy	Italy			
FENTANYL	USA	USA	Y	5mL - 224%	
GLYCOPYRROLATE	USA	Finland	Y		
HEPARIN	USA	USA	Y		
HYDRALAZINE	USA	Japan			
KETAMINE	Portugal	Germany	Y	5mL – 367% 10mL - 265%	Y
LABETALOL	Portugal	Italy	Y		Y
LIDOCAINE	Portugal	Spain	Y		Y
METOPROLOL	Portugal	Spain/India			
MIDAZOLAM	USA	Israel/India	Y	5mL - 324%	Y
MORPHINE	USA	USA	Y		
NALOXONE	USA	USA			
NEOSTIGMINE	USA/India	Austria	Y		
NICARDIPINE	USA	Italy			
ONDANSETRON	USA	Spain/India			
PROCHLORPERAZINE	USA	Italy			
SODIUM BICARBONATE	USA	USA	Y		
TRANEXAMIC ACID	USA	Italy			
VANCOMYCIN	Denmark/USA	Denmark*	Y		Y

Source of finished drug refers to the country of manufacture of the sterile vial or prefilled syringe

API Source refers to the country of origin of the active pharmaceutical ingredient.

COVID-19 identifies those drugs used in the management of patients with COVID-19, including management of patients on ventilators and treatment of secondary pneumonia.

Surge represents the increase in demand over anticipated volume for select drugs during the initial weeks of the COVID-19 pandemic. Note that some health systems had no increased demand; others ranged as high as 800 percent for select drugs. These data illustrate the ability of the “Civica model” to cope with a demand surge, but can’t be used to extrapolate to national increase in demand or predict future demand.

SNS indicates that the initial set of identified drugs contributed to the Strategic National Stockpile

* China is backup API source.

The Civica model brings together hospital systems and drug manufacturers to work collaboratively, ensuring both stable and fairly priced generic drugs for hospitals and predictable volumes for manufacturers. Key elements of the model include:

- Hospital systems join Civica, allowing them to purchase drugs in predetermined volumes at transparent and stable prices. Member health systems prioritize the medications needed to reduce shortages for patients and identify the volume requirements for their hospitals.
- Civica conveys this information to its manufacturing team or trusted manufacturing partners – those with a history of producing high-quality products. Manufacturers commit their production capacity based on long-term projected volumes of medications identified by the health systems.
- As a result, patient care improves as hospitals receive a reliable supply of the essential generic medications.

Because its specific mission is to create a robust, high-quality supply of essential medicines, several features of the Civica supply chain model may have lessons for the larger U.S. system, including:

- Long-term purchase take-or-pay commitments allow Civica, and our suppliers, to invest in quality systems
- Use of backup suppliers and maintenance of a reserve stock averaging at least six months' supply
- A preference to purchase medicines made in the U.S. where possible, followed by other highly regulated markets, followed by India and avoiding Chinese ingredients where possible in our drugs due to quality concerns
- Entrusting those on the front lines – hospital physicians and pharmacists – to prioritize the medications Civica makes, based on their experiences day-to-day or in times of crisis like the pandemic

The importance of a robust supply chain

The global coronavirus pandemic has highlighted weaknesses in the U.S. supply chain for essential medicines and other medical supplies. Key products required to manage the epidemic have been unavailable or in short supply. Increased demand, both within the United States and among our trading partners, are important factors but have largely served to exacerbate supply chain shortcomings that are pre-existing and longstanding.

It is important to note that many of the medicines used to manage COVID-19, including the sedatives and neuromuscular blocking agents essential for patients on ventilators, were already in short supply prior to the pandemic. They represent a longstanding weakness in our supply chain that is explained, in part, by the relentless pursuit of ever-lower costs.

The desire for low-cost drugs – the race to the bottom in manufacturer pricing in order to get market share – is understandable, but it creates unintended consequences. Facing low margins and uncertain sales, companies are discouraged from investing in quality and incentivized to move production out of the U.S. to economies with lower labor costs, lower regulatory compliance costs and where they may receive direct or indirect support from foreign governments for to build new facilities.

Reliance on a sole source of supply, whether that is a single manufacturer or a supply from a single country, increases the risk of supply disruption. No purchaser should source essential drugs or other products from a single supplier.

Indeed, Civica’s policy is not to supply all of any health system’s needs for a given drug. If we were the sole supplier, we would be increasing rather than reducing vulnerabilities in the supply chain.

Longer supply chains and just-in-time inventory systems are especially vulnerable to disruption, whether due to quality problems or, as we’ve recently witnessed, export restrictions by foreign governments who understandably put their domestic needs ahead of those of their trading partners.

No single policy caused the exodus of pharmaceutical companies from the U.S., and it will take a multi-faceted approach – and a sustained commitment – to further diversify the supply chain and rebuild our domestic manufacturing capacity.

Policy tools

Nevertheless, the U.S. government has a range of tools that can help rebuild capacity as well as protect against supply interruptions and keep the cost of medications in check. These include:

- Creating an essential medicines list to set priorities for investments, policy and regulatory reviews
- Improving transparency in sourcing, pricing and drug quality
- Utilizing incentives to encourage U.S. investment
- Committing government programs to prioritize purchase of U.S.-made goods
- Enhancing the Strategic National Stockpile
- Directly supporting U.S. manufacturing, and
- Focusing on advanced manufacturing

Target essential medicines

Civica selects medicines to manufacture based on the needs of patients, as prioritized by those on the front lines of the health care system. The U.S. government could benefit from a similar priority list to guide policy.

For these essential drugs, policymakers should incentivize contingency planning or redundant production lines for manufacturers to use in the event of a shortage, particularly for medicines that already have too few manufacturers.

To encourage investments in critical drugs, policymakers should consider waiving FDA user fees for drugs on the drug shortage list and when there is minimal competition.

Congress may also want to reconsider policies that turn generic drugs into sole-source products without competition. Specifically, the Drug Efficacy Study Implementation (DESI) program provides market exclusivity to companies in exchange for filing a New Drug Application on very old products. While intended to create an incentive for companies to submit efficacy and safety data to the FDA, this can result in unintended consequences, including reduced supply chain resiliency and dramatic price hikes.³

Transparency in sourcing and quality

Civica provides not only complete transparency on the source of its finished drugs, but also on the source of the active pharmaceutical ingredients (APIs) [Table I]. But such transparency is not required by law. Any purchaser wishing to avoid active ingredients from high-risk countries is currently constrained by a lack of information. Congress could require country of origin labeling for both finished drug and API.

Similarly, Congress should consider steps to increase publicly available manufacturer quality information. It is a well-known quality principle that quality cannot be tested or inspected into a product. For example, if five tablets are tested from a batch of one million and they all pass, then all that is known is that those five tablets passed. In contrast, a mature quality system requires protocols, standard operating procedures, appropriate oversight and a culture of compliance. These are the ingredients of a quality system that are essential to producing quality pharmaceuticals. The supply chain itself must be considered a part of a quality assessment: A drug that does not reach patients cannot be considered high quality, whatever its other attributes.

There are tools that can be used to measure the maturity of a pharmaceutical quality system, such as those used for the Malcomb Baldrige National Quality Award and Parenteral Drug Association Quality System Maturity Model.

Making robust quality data available to health systems would help purchaser to take quality into account when buying medications. Congress could consider requiring the FDA to validate its quality metrics program⁴ with a limited number of manufacturers within one year.

³ Civica letter to Congress, February 6, 2020. <https://civicarx.org/letter-closing-loopholes-that-lead-to-unreasonable-price-increases-for-decades-old-drugs/> Accessed May 24, 2020.

⁴ Geok Yan Loo, U.S. Food and Drug Administration. https://static1.squarespace.com/static/58d0113a3e00bef537b02b70/t/5e726c5316537f1aa5309d79/1584557142149/2P0410_Loo_CDERSApproach.pdf. Accessed May 24, 2020.

Manufacturers could be incentivized to participate. When the metrics have been sufficiently validated, manufacturer participation should be required.

We also commend Congress and the FDA for recently adding requirements for manufacturers to notify the FDA of discontinuance or interruption in active pharmaceutical ingredient supply and in the event of a demand surge or other factors that could interrupt supply.⁵

Tax incentives

As a non-profit organization, Civica does not benefit directly from tax incentives to encourage U.S. manufacturing, but other manufacturers may, including some of our suppliers. For example, one recent proposal would allow 100 percent expensing for any new U.S. pharmaceutical manufacturing facility placed in service before 2026.⁶

Priority purchase of U.S.-made goods

One change Congress could make, as proposed in recent legislation,⁷ would be to amend the Trade Agreements Act of 1979 to clarify that pharmaceutical products would not be considered to have originated in a country if the API originated in a different country. Updating this definition would reverse a recent court decision, *Acetris Health, LLC v. United States*, that precludes U.S. government purchasers from giving preference, under the Buy American Act, to pharmaceutical products that originated entirely within the United States or our preferred trading partners.

Congress could also consider recognizing the real cost differences between U.S. drug production and manufacturing in low-wage countries, by increasing the incremental additional cost the government will pay in order to purchase U.S.-made goods from the current level of 6 percent.

Given that it will take time to rebuild U.S. manufacturing, it may be inadvisable to set a firm short-term deadline to exclude Chinese suppliers completely, but the government should have a goal of having at least one U.S. supplier for every U.S. essential drug, with annual targets and progress tracking.

Enhanced Strategic National Stockpile

The U.S. essential medicines list identified above can be used to guide an enhanced national stockpile. The federal government currently maintains an emergency stockpile of drugs and medical equipment in warehouses around the country. While some supplies are inexpensive

⁵ Food and Drug Administration Guidance for Industry: Notifying FDA of a Permanent Discontinuance or Interruption in Manufacturing Under Section 506C of the FD&C Act (March 2020).

<https://www.fda.gov/media/136486/download>

⁶ For example, S.3537, the “Protecting Our Pharmaceutical Supply Chain from China Act of 2020,” introduced by Senators Cotton, Blackburn and Cruz.

⁷ For example, S.3538, “The Strengthening America’s Supply Chain and National Security Act,” introduced by Senators Rubio and Warren.

and/or can effectively be warehoused for long periods, the cost of stockpiling more expensive products with limited shelf lives, such as drugs, could be reduced with a commercially managed “flow through” inventory so that drugs are distributed and used prior to expiry, with the stockpile being continually replenished with newer product.

Direct government support of U.S. manufacturing

Recently, the Biomedical Advanced Research and Development Authority (BARDA) announced a new partnership that will help build more U.S. advanced manufacturing capacity for essential drugs.⁸

The BARDA Partnership

Under this agreement, BARDA will fund Phlow Corporation, a newly formed public-benefit pharmaceutical manufacturing company in Richmond, Virginia, to build a new state-of-the-art continuous manufacturing facility to produce API.

On the same site, Civica will build a facility capable of producing finished sterile injectable medicines for U.S. patients on an ongoing basis and to meet the needs of the national stockpile. Civica will use API from Phlow and from Ampac Fine Chemicals, an API maker on the same site.

This partnership will create a 100 percent U.S.-owned and -operated end-to-end domestic drug manufacturing infrastructure to secure essential medicines and prevent shortages of these vital medicines in the future.

Advanced manufacturing

Advanced manufacturing is a term for newer technologies that will help improve the speed and flexibility of drug manufacturing. In the case of the BARDA agreement, Phlow will commercialize continuous manufacturing technology developed at Virginia Commonwealth University's College of Engineering. In contrast with traditional batch manufacturing, this approach offers several advantages, including:⁹

- Precise control of product quality
- Ability to rapidly respond to changes in demand
- Lower cost of production
- Reduced environmental impact

⁸ Health and Human Services, May 19, 2020. <https://www.hhs.gov/about/news/2020/05/19/hhs-industry-partners-expand-us-based-pharmaceutical-manufacturing-covid-19-response.html> Accessed May 24, 2020.

⁹ Statement of Janet Woodcock, MD, U.S. Food and Drug Administration, October 30, 2019. https://energycommerce.house.gov/sites/democrats.energycommerce.house.gov/files/documents/Testimony-Woodcock-API_103019.pdf. Accessed May 20, 2020.

As set forth in recent proposed legislation,¹⁰ Congress could further support the development of advanced manufacturing by supporting the creation of Centers of Excellence and providing expedited review if a technology is likely to prevent or resolve a drug shortage, maintaining an adequate supply of critical medications for national emergencies, or promote the adoption of innovative approaches to drug product design and manufacturing.

Thank you again for your attention to this important topic. Civica looks forward to working with this Committee as it considers how best to protect the interest of American patients.

¹⁰ For example, S.3532, the “Securing America’s Medicine Cabinet Act of 2020,” introduced by Senators Blackburn and Menendez, and S.3780, the “Help Onshore Manufacturing Efficiencies for Drugs and Devices Act,” introduced by Senator Peters.