How Civica Rx Aims to Solve the US Hospital Drug Shortage Crisis
EXECUTIVE SUMMARY

Over the past two decades, shortages of generic, injectable drugs critical to the lifesaving work of hospitals in the United States have become commonplace. These drug shortages are so ubiquitous that hospitals and health care systems now maintain permanent drug shortage response teams that seek alternatives to unavailable drugs.

As a result, time that hospital pharmacists, technicians, nurses and others would prefer to spend caring for patients is spent ensuring that the patients who most need short-supply drugs get whatever supply is available. They must spend time researching safe and effective alternatives, moving supplies from one department or facility to another, communicating changes to physicians and nurses, and updating the corresponding electronic health records.

This problem can result in delayed surgeries and less-than-optimal therapies for hospitalized patients. A recent survey found that drug shortages cost hospitals just under $360 million annually in labor expenses.1 In addition, hospitals spend some $230 million buying more expensive alternative medications when preferred generics are not available.

Despite efforts by the health care industry and government2 regulators to anticipate shortages, adapt to them as they occur, and provide incentives for manufacturers to produce safe and sufficient supplies of generic drugs, the problem has not only persisted but also increased.

According to a 2018 industry presentation by the U.S. Food and Drug Administration (FDA) Drug Shortages Task Force, drug shortages increased in 2017 and 2018. The shortages are lasting longer, with more than 10 drugs being in short supply for five years or more. Nearly 30 generic medications have been in short supply for two years or more. The five longest shortages have lasted more than eight years.

The FDA also reported that shortages remain consistently intense, meaning that much less product is available than needed. The combined impact of generic drug shortages on public health is high, according to the FDA. The need to find alternative drugs that can serve the same purpose, or make changes to electronic health records to support changes in products, adds millions of dollars in staff time to health care costs.

Worse, it increases the risk of human error in calculating and administering appropriate dosages and can result in patients receiving less-than-optimal therapies. Some reports have even linked shortages to patient deaths.3

The root of the problem is an unsustainable economic model for the manufacture and sale of commonly used generic drugs. Despite their important role in hospital patient care, the fact that they are older generic medicines rather than innovative drugs creates competition to sell them at unrealistically low prices. The resulting low profit margins drive manufacturers to seek the least expensive suppliers, often from manufacturers in China and India, where quality control may not be as stringent as in the United States. This can result in poor-quality products and quality-related recalls. Additionally, many U.S. factories have not been modernized with improved quality systems, resulting in shortages at domestic facilities.

Investigative journalist Katherine Eban reports in her 2019 book, “Bottle of Lies: The Inside Story of the Generic Drug Boom,” that some companies “routinely falsify data, and executives circumvent almost every principle of safe manufacturing to minimize costs and maximize profits.” As a result, Eban writes, some generic drugs are very different from the brand-name versions they are supposed to replicate.

Low margins also provide little incentive for manufacturers to enter or stay in the generics market. For those who do, low profits provide little motivation and few resources to maintain or upgrade manufacturing facilities, buy from suppliers of quality active pharmaceutical ingredients (APIs), or ensure that business continuity plans, redundant manufacturing capacity, and well-stocked inventories to prevent shortages remain in place in the event of a natural disaster.

The Civica model brings together hospital systems and drug manufacturers to work collaboratively, ensuring both stable and fairly priced generic drugs for hospitals and fair profits at predictable volumes for manufacturers.

Civica Rx is a nonprofit, non-stock corporation formed in 2018 by hospitals, health care systems, and philanthropists that uses a new economic model to prevent shortages and provide a reliable supply of quality generic drugs at a fair price.

The Civica model brings together hospital systems and drug manufacturers to work collaboratively, ensuring both stable and fairly priced generic drugs for hospitals and fair profits at predictable volumes for manufacturers.

The system works as follows: 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 that information to 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 promptly improves as hospitals receive a reliable supply of the essential generic medications needed daily.

The Civica business model ensures that member hospitals have a safe,
long-term supply of the drugs they need at the same transparent, fair prices, regardless of the purchase volume committed to by each hospital. This means that small, rural hospitals have the same access to vital drugs at the same prices as large urban hospital systems. Civica will provide transparency in the production and supply origins of its medications and ensure redundant capacity and adequate safety stock to help avert drug shortages.

As a nonprofit business, Civica can sell essential generic drugs at fair and sustainable prices while providing contract manufacturing organizations and Civica manufacturing operations with the long-term volume certainty they need to stay in business, provide quality products at fair and sustainable prices, and invest in their facilities and people as needed.

Further, by maintaining safety stock or reserves of generic drugs, Civica helps ensure a constant supply in the event of manufacturing problems, supply chain disruptions, and crises such as natural disasters or pandemics.

In the future, as more members join Civica, the company plans to develop the Abbreviated New Drug Applications (ANDAs) necessary to manufacture generic drugs in its own facilities as well, ensuring fair pricing and a high-quality and reliable supply for its member organizations.
Civica Rx was founded in 2018 by health systems and philanthropies to address drug shortages and the high costs of vital medicines. More than 50 health systems have joined Civica Rx, representing nearly 1,400 hospitals and more than 225,000 licensed hospital beds – approximately 1/3 of licensed hospital beds in the U.S. To date, over 50 Civica medications are available to hospitals, with many being used to help treat COVID-19 patients.

GOVERNING HEALTH SYSTEMS
- CommonSpirit Health
- HCA Healthcare
- Intermountain Healthcare
- Mayo Clinic
- Providence St. Joseph Health
- SSM Health
- Trinity Health
- Kaiser Permanente

GOVERNING PHILANTHROPIES
- Gary and Mary West Foundation
- Laura and John Arnold Foundation
- Peterson Center on Healthcare
SOLVING THE US DRUG SHORTAGE CRISIS

DRUG SHORTAGES AND THEIR FREQUENCY

Today, the United States is experiencing a national crisis—shortages of generic, sterile injectable drugs that are used within hospitals every day. These medications play an essential role in surgeries, emergency care and patient treatments.

During the past several years, more than 200 drugs have been listed on the FDA and the American Society of Health System Pharmacists’ drug shortage lists. Drugs in short supply include older medications that are commonly prescribed and accessed by everyone.

The typical drug in shortage is a generic, sterile injectable. Many are life-saving products commonly used in surgeries and in emergency rooms at hospitals. Anesthesia medications, antibiotics, pain management medications, nutrition and electrolyte products, and chemotherapy agents have all experienced shortages. Even the sterile saline solution used to administer drugs intravenously has been in short supply.

These drugs are used daily. They can be challenging to manufacture and are sold at very low prices because they are not under patent. These chronic shortages are negatively affecting patient care. They can cause surgeries to be canceled or delayed and treatments to be suboptimal when providers must use a less effective drug.

According to a 2019 report from the American Hospital Association, the Federation of American Hospitals, and the American Society of Health System Pharmacists, about 80% of hospitals are finding it to be extremely or somewhat challenging to obtain the following:

- Pain management injectables
- Saline (widely used for purposes such as intravenous therapy, rehydrating patients and wound cleaning)
- Sodium bicarbonate (an alkalinizing agent used for oral or parenteral [injected] therapy)
- Sterile water (an essential ingredient in preparing many drug products for IV use)
- Epinephrine (used in severe, acute anaphylactic reactions)
- Dextrose (used as a source of calories and water for nutrition and hydration)

Many drugs in shortage are lifesaving products commonly used in surgeries and emergency departments.

The shortage of drugs used daily in U.S. hospitals is well known to hospitals and health care systems, health care professionals, and government regulators. Over time, shortages not only persist but have increased in frequency, intensity and duration.

Note: Each point represents the number of active shortages at the end of each quarter. University of Utah Drug Information Service Erin.Fox@hsc.utah.edu, @foxinr
MULTIPLE FACTORS CAUSE DRUG SHORTAGES

The cost of drug shortages for U.S. health systems is estimated to be $230 million in spending on alternative therapies. In addition, a 2019 survey by Vizient found that these daily, persistent drug shortages force hospitals in the United States to dedicate more than 8.6 million hours of additional labor, at a cost of $359 million annually.\(^5\)

Economics and market dynamics lead to manufacturing challenges, shortages of raw materials, voluntary recalls, supply and demand issues, business and economic issues, regulatory challenges, supply chain issues, lack of inventory, and health care system practices – all contributing to drug shortages.

Life-saving drugs are treated as commodities. Generic manufacturers compete solely on price. When a drug’s patent expires, the initial competition among producers of generics lowers prices and increases supply availability. When more generic manufacturers enter the market, prices are driven unsustainably lower. This leads some manufacturers to exit the market or move some (or all) of their manufacturing to less expensive locations, such as China or India—countries that lack stringent regulatory oversight.

Typically, only one or two suppliers of essential generic medicines operate in the U.S. market. The factories producing those products must run at the highest utilization to make a profit and provide enough product for the market. If a manufacturer has a quality problem and shuts down production, shortages quickly spread across the national health care system. Worse, the one or two producers of generics have monopolistic powers to dominate the market, dictate price and limit supply.

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Poor-quality drugs affect supply. When competition forces prices for generic drugs unrealistically low, manufacturers look to cut their costs to maintain profitability. As a result, the majority of generic drugs and their APIs are manufactured in countries where costs are lower. China and India are the biggest producers of APIs; however, one reason for lower costs is a lack of quality oversight by facility owners and governments. As a result, it has become common to encounter problems with purity and quality in drugs produced in these countries. This leads to drug recalls, which can then trigger shortages.

Supply chains are long, complex and fragile. The danger is compounded by the fact that too few in the supply chain maintain an inventory of essential medicines in case problems arise anywhere. If a supply chain breaks down, shortages appear within 30 days.

For example, lidocaine, a widely used injectable local anesthetic, has been on shortage lists for many months. When the dominant manufacturer failed to supply the drug, it immediately created a surge in demand. Other manufacturers have been unable to fill the void, leading to drug shortages. A single delay at one facility caused an immediate shortage, forcing health systems to devote significant time and money to secure necessary supplies.

THE PROFOUND AND WIDESPREAD IMPACT OF DRUG SHORTAGES

The drug shortages are estimated to cost U.S. health systems hundreds of millions of dollars in expenses, labor costs and increased risks.

When a medication is in short supply, it can cause delays or changes in medical procedures and limit treatment options. Instead of focusing on patient care, health care providers and hospital management must spend time looking for alternative medications. Pharmacists must communicate with manufacturers and wholesalers, provide education to personnel, develop or modify policies or clinical guidelines, and update electronic medical records and medication dispensing systems.

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MORE THAN 90% of hospitals reported having to identify alternative therapies to manage spending.

90% of emergency physicians in an American College of Emergency Physicians survey reported having to take time away from patient care to explore alternative treatments and medications.
There have been numerous studies\(^7\) and surveys\(^8\) that confirm the severity of the drug shortage situation in the U.S. They show how the lack of supply of essential generic medicines used in hospitals negatively impacts patient care. These studies show:

- Almost 80% of hospitals said that drug shortages resulted in increased spending on drugs to a moderate or large extent.\(^9\)
- More than 90% of hospitals reported having to identify alternative therapies to manage spending.
- 90% of emergency physicians in an American College of Emergency Physicians survey reported having to take time away from patient care to explore alternative treatments and medications.\(^10\)
- Pharmacy technicians and pharmacy buyers reported having to determine how much medication is on hand, how long it will last, where it is located in the hospital, and possible sources of alternative medications.\(^11\)
- Drug shortage response teams must evaluate alternative treatments based on safety, efficacy, availability and cost.

- Patient care processes must change in the face of shortages. If an alternative product is available, new procedures must be put in place throughout the hospital for prescribing, preparing, distributing and administering medications.

What is the story behind these issues?

**Hospital expenses rise because of drug shortages.** Drug shortages increase the cost of delivering patient care. In late 2010, it was estimated that drug shortages cost hospitals at least $200 million annually because of the need to purchase more expensive therapeutic substitutes.\(^12, 13\)

**Labor costs increase.** Indirect costs are associated with drug shortages, such as the additional labor required.

A 2019 survey from Vizient found that, on average, hospitals in the United States dedicated more than 8.6 million hours of additional labor annually to manage drug shortages. The financial impact on labor costs totaled $359 million annually.\(^14\)

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Departments across the hospital must dedicate staff and increase hours to source products, review shortage lists, track medications in short supply, and communicate to staff on a daily basis what medications are being substituted and how to administer them.

Hospitals facing shortages must spend time planning and implementing solutions to effectively address new shortages. This involves procurement and management by pharmacists and other professionals, as well as pharmacy technicians and staff, to identify shortages, source alternative products, and determine how best to deliver care.

Technicians on staff must increase the amount of time they spend stocking, unstocking and restocking supplies across the hospital. Smart IV pumps must be reprogrammed, and electronic prescribing and patient records all must be updated if alternate therapies are prescribed.

Safety risks increase. Shortages increase the likelihood of medication errors and safety risks. When one drug is substituted for another, efficacy might be reduced and the likelihood of side effects increases. For example, when cancer therapies are unavailable, physicians may have to delay or alter carefully timed chemotherapy regimens.
DRUG SHORTAGES INCREASE SAFETY RISKS

A 2017 Institute for Safe Medication Practices (ISMP) survey\(^{15}\) found the following:

- **71%** of pharmacists and others involved in providing medications in hospitals were unable to provide patients with the recommended drug or treatment for their condition because of shortages.
- **75%** stated that patient treatments had been delayed because of drug shortages.
- **47%** thought that drug shortages resulted in patients receiving less effective drugs.
- **5%** reported other types of adverse outcomes for patients related to drug shortages, including increased pain or discomfort during a procedure caused by a shortage of a required analgesic or sedation agent.

Quality control risks increase. Although health care personnel can often source and formulate solutions as alternatives in drug shortage situations, these can present quality-control risks.

In its 2017 survey, the ISMP also reported that “nearly a quarter (21%) of all respondents in our 2017 survey were aware of the occurrence of at least one medication error related to a drug shortage in the 6 months prior to the survey. The respondents to the ISMP survey provided descriptions of close to 100 errors; most (67%) were associated with the wrong dose or concentration.”

Hoarding supplies of alternate therapies may be triggered. When hospitals know that a shortage of an essential medication is imminent, they may begin hoarding that medication. They will also begin increasing inventory of alternative products, increasing their demand, accelerating the shortage of the original drug, and potentially starting a run on the alternate therapy.

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A national survey published in JAMA Internal Medicine (and reported in Pharmacy Today) “showed that most pharmacists experienced a drug shortage in the previous year and hoarded available supply as a common mitigation strategy.”

Drug shortages impact patients. For patients, drug shortages have both direct and indirect consequences: The direct consequences of drug shortages on patients include suffering from the need to transfer to facilities that offer suitable health care and appropriate treatments. Patients complain to health care professionals about drug shortages. Not surprisingly, patients feel anxious and distressed.

Health care is about more than just treating illnesses. Humanistic outcomes such as quality of life are important measures of successful health care. In a Public Library of Science (PLOS) study published in 2019, patients faced with drug shortages reported frustration, anger, and feeling like a burden to themselves and caregivers.

Indirectly, patients may not ever know they have encountered a shortage. A 2016 New York Times article examined how shortages placed physicians in the uncomfortable role of rationing medications and deciding whether to inform patients—this despite an editorial in the journal Anaesthesia and Analgesia that encouraged health professionals to disclose shortages and their implications.

STRATEGIES FOR SOLVING DRUG SHORTAGES

For the most part, existing solutions try to deal with shortages after they happen or use regulations to increase incentives or reduce regulatory costs and pressures for manufacturers; however, none of them address the underlying market causes of generic drug shortages.

Solutions to the Drug Shortage Problem

What are the necessary factors to ensure a reliable supply of high-quality generic drugs at a reasonable price?

Long-term Guaranteed Volumes. Because generic drug sales earn a low profit margin, manufacturers and vendors need to know that they will be able to sell enough product to justify their investment in production.

Sustainable Prices. Spikes in prices for generic drugs are preceded by pressure to cut prices so much that manufacturers must either cut corners to make a profit or leave the market. Cutting corners can threaten drug quality, and a manufacturer leaving the market causes an almost immediate shortage.

Transparency. Hospitals need to know where the drugs they order are produced. They also need to know the origin of APIs purchased from other suppliers, so they can be sure that no ingredients in the drug appear in the FDA's list of unsafe products.

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Stockpiles of Critical Drugs. In the event of a shortage, manufacturers need to have a stockpile of drugs that are essential to patient care. Having a sufficient reserve to cover shortages will help prevent hospitals from instituting instinctive hoarding and make it impossible for other providers to overprice their medications.
Civica Rx is a nonprofit, non-stock corporation founded by health care systems and philanthropists to serve the best interests of patients by providing a safe, reliable supply of quality generic drugs at fair and stable prices.

To do this, Civica has developed a new business model, one that is expected to disrupt and transform the business-as-usual situation of the generic drugs market. This is how it works: Civica member hospitals and health systems come together to ensure the quality and quantity of the generic injectable drugs they use every day for surgeries, pain relief, cancer treatment, and heart attacks, among many other types of patient care. Their combined commitment to purchase at volume over the long term allows them to negotiate directly with producers, assuring them of long-term sales volume at a fair and sustainable price.

In the future, as more members join, Civica will develop or purchase the ANDAs necessary to manufacture its own generic drugs for purchase by member hospitals. By working with both health systems and manufacturers, Civica will be able to bring stability to the marketplace for the benefit of hospitals, producers, and, most importantly, patients.
Civica’s model has the following benefits:

It ends price pressures on manufacturers that result in a “race to the bottom,” causing shortages and opportunistic price increases.

It eliminates variations in price for the same product by offering a single, transparent price to all customers, regardless of the volume purchased. This also ensures predictability and stability for hospital budgeting by eliminating unanticipated price spikes and the possibility of predatory pricing by manufacturers with a monopoly on the market for a particular drug.

It can ensure quality. Representing the commitment to purchase for its combined member organizations, Civica includes quality-assurance measures in the long-term contracts it negotiates with trusted manufacturing partners. Those measures include transparency in labeling drugs regarding the location of their manufacture, as well as the origins of the ingredients used.

It benefits manufacturers by providing them with long-term purchasing contracts at reasonable profit margins with Civica. The Civica model allows manufacturers to invest in the quality and capacity of their production facilities, quality suppliers of APIs and other drug components, and process improvements.

“It is fascinating to watch what the private sector hospitals in the United States are doing...they formed a nonprofit called Civica Rx in response to persistent shortages of vital life-saving medicines...and they are doing direct contracting with trustworthy manufacturers...with long-term contracts...I think it’s a game-changer.”

ROSEMARY GIBSON, AWARD WINNING HEALTH CARE AUTHOR
Civica’s ability to negotiate directly with manufacturers, as well as acquire its own manufacturing facilities, will enable the company to ensure that a combination of producers maintains redundant manufacturing capabilities for finished drug products, APIs and critical materials. If a problem occurs at one site, Civica or other producers can increase production at another site while the issue is resolved, preventing a drug shortage. Civica also will maintain reserves of finished drug products, APIs, and the critical materials needed to fulfill orders in case of shortages.

NEAR-TERM PLANS: 2019–2020

Civica is prioritizing the most urgent needs of its member organizations for generic drugs, such as the following:

- Drugs listed by health system members as currently in short supply or of “top concern.” Civica has enlisted the support of a Drug Selection Advisory Committee consisting of hospital pharmacists and supply chain experts to prioritize the medicine it makes based on the most urgent needs.
- Drugs that are critical to patient care on a daily basis.
- Drugs that have increased 50% or more in price during the past three years.
- Drugs sold by only a few vendors, making them vulnerable to shortages and price increases.

By the end of 2020, Civica intends to produce dozens of drugs and associated dosing options that meet these criteria. Civica’s strategies for accomplishing this goal include the following:

- Contract with manufacturers that originally held the ANDA but have stopped manufacturing, enabling them to resume production rapidly.
- Develop ANDAs and contract production with existing manufacturers.
- Purchase or build manufacturing facilities for its own Civica brand, or purchase exclusively by member organizations under long-term contracts.
SOLVING COMPLEX DRUG SHORTAGES REQUIRES MULTIPLE SOLUTIONS

No single company or organization can solve the problem of drug shortages in U.S. hospitals alone.

Because the U.S. government actively regulates drug manufacturing, it can play an important role in ending drug shortages. In 2018, the U.S. Food and Drug Administration formed a Drug Shortages Task Force. This task force included leaders from the FDA, the Centers for Medicare and Medicaid Services, and the Department of Veterans Affairs. Collectively, these organizations provide or pay for prescription medicines for millions of Americans.

The goal of this task force was to investigate the reasons that shortages remain a challenge and to find holistic solutions for the causes of those shortages. This task force is designed to expand upon work created by the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA). FDASIA broadened the requirements that manufacturers notify the FDA of events that might lead to drug shortages, including discontinuations of medications or temporary interruptions in manufacturing.

ADDITIONAL ACTIONS GOVERNMENT CAN TAKE TO PREVENT SHORTAGES

1. Develop a list of essential drugs and assess drug shortages as a national security threat: Civica agrees with the American Hospital Association’s assertion that the FDA should use the World Health Organization’s Model Lists of Essential Medicines and other existing resources to develop a list of critical drugs needed for emergency response and for saving and preserving life. To date, the FDA has not done this, and it could help immensely by working with manufacturers to provide transparency across the supply chain for these most essential medications and create redundant capacity to ensure that we are covered when things go wrong.

2. Offer government incentives to manufacturers: To encourage manufacturers to establish and maintain high-quality domestic manufacturing practices, develop redundancy in operations, expand capacity, and/or create conditions to prevent or mitigate shortages, the FDA could take the following steps:

   • 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.
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• Accelerate and streamline the approval of new technologies, redundant manufacturing facilities, or raw materials suppliers that could have a positive impact on reducing potential and real drug shortages.

• Accelerate and streamline the approval of new products that could reduce the risk of drug shortages.

• Extend the interval between routine GMP inspections for companies with excellent compliance status that have established and implemented a risk management program to protect against potential drug shortages.

• Offer additional incentives in the best interests of patients by collaborating with other government agencies, including the following:
  – Offer financial incentives, such as tax credits and/or federal grants for companies that have a robust risk-management program that includes establishing and maintaining redundant manufacturing capacity or extra manufacturing capacity dedicated to mitigating drug shortages.
  – Waive fees for manufacturers where minimal competition and little incentive to invest in developing or manufacturing a product exist (waiving fees for ANDAs or paper New Drug Applications [NDAs]).

• Invest in building manufacturing facilities and license them to quality companies committed to solving/preventing drug shortages.

3. Create a strategic stockpile program for drugs on the essential medicines list, similar to the programs run by the Biomedical Advanced Research and Development Authority (BARDA).

4. Enhance supply chain transparency requirements: For the pharmaceutical industry, increased transparency could improve the quality, reliability and availability of medications.
Government should consider requiring companies to list the location of production at every step, with the manufacturing city, state, and country on the product label, and list the location of API production on the company’s website. Consumers can easily see where their clothing is made, just by checking the tag; in contrast, no manufacturing information is currently available to them about their medications.

Drug shortages continue to persist and increase. Lasting solutions for the issue require not only government efforts and interventions but also contributions from private industry.

Civica is proud to be part of the solution, creating an innovative new business model to ensure that critically important generic drugs are available to hospitals that need them and the patients they care for at fair, affordable, and sustainable prices.

For more information, contact Civica Rx at 888-304-0120 or visit our website at www.civiarx.org.

ADDITIONAL RESOURCES


