

July 7, 2023

The Honorable Cathy McMorris Rodgers
Chair
Committee on Energy and Commerce
United States House of Representatives
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Mike Crapo
Ranking Member
Committee on Finance
United States Senate
219 Dirksen Senate Office Building
Washington, D.C. 20510

Dear Chair McMorris Rodgers and Ranking Member Crapo,

On behalf of the American College of Emergency Physicians (ACEP) and our nearly 40,000 members, thank you for your attention to the ongoing crisis of drug shortages, both emerging and persistent. Shortages of everyday, lifesaving emergency medications are one of the most significant problems that emergency physicians encounter, and unfortunately, they have been dealing with these shortages for years. ACEP appreciates the opportunity to respond to your request for information (RFI) on this critical issue, which adversely affects emergency physicians' ability to provide care and jeopardizes the health of patients in need of lifesaving emergency care.

Drug shortages pose numerous challenges in the practice of emergency medicine, requiring emergency physicians to actively monitor what medications may be available on any given day, constantly find alternatives for drugs that are not available (if alternatives even exist), and train and retrain on what drugs to use and what new protocols may be in place each time a new drug shortage is announced. Exploring the viability of alternative treatments and medications diverts clinicians from the bedside (e.g., using a computer, consulting, or coordinating with other experts, etc.) when that time could otherwise be devoted to direct patient care. This exacerbates already-substantial stresses on emergency departments (EDs) throughout the country that are overwhelmed due to the ongoing "boarding" crisis, where patients continue to occupy an ED bed even after being seen by a physician while they wait to be admitted to an inpatient bed. This has led to significant strain on emergency physicians, emergency nurses, and other staff, draining limited and critical resources and resulting in more delays in care. Particularly in emergency medicine where life or death can be a matter of minutes or even seconds, changes or delays in treatment can be life threatening. Furthermore, medication substitutes often prove less effective or induce different side effects, potentially compromising the quality of care, patient comfort, and satisfaction. Unfortunately, in many cases, there are simply no substitutes that exist.

This been a persistent issue for emergency medicine for years. In 2018, ACEP conducted a [survey](#) of our membership and found that 9 out of 10 emergency physicians had experienced shortages or absence of critical medicines in their EDs within the last month. Additionally, nearly all respondents (93 percent) indicated that their EDs were not fully prepared for patient surge capacity in the event of a natural or man-made disaster or other mass casualty incident, and with fewer than half reporting that they were "somewhat" prepared. Unfortunately, these theoretical disaster scenarios would become all too real just a few short years later as the COVID-19 pandemic pushed our health care system to a breaking point (or beyond, in many cases).

ACEP supported a 2018 bipartisan, bicameral congressional letter, led by Representatives Brett Guthrie (R-KY) and Mike Doyle (D-PA) and Senators Bill Cassidy, MD (R-LA) and Chris

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Murphy (D-CT), urging U.S. Food and Drug Administration (FDA) Commissioner Scott Gottlieb to identify the root causes of drug shortages, develop recommendations for Congress to address them, and take appropriate action to ensure these medications remain available. In response, Commissioner Gottlieb announced the creation of the FDA Drug Shortages Task Force in June 2018. Subsequently, in October 2019, the Task Force issued a report entitled [Drug Shortages: Root Causes and Potential Solutions](#).¹ ACEP was invited to participate in a listening session with the Task Force, attended the public meeting it convened, and submitted [comments](#) to the Task Force.

Again, ACEP deeply appreciates your attention to this important issue and the opportunity to share our experiences and suggestions. We stand ready to assist you and your staff in developing policy solutions to improve the drug supply chain and improve patient access to lifesaving emergency care. Our responses to relevant questions in the RFI are found below:

How would you define the scope and impact of the recent and ongoing U.S. drug shortages?

Drug shortages affect care throughout the entire health care system, though their duration and severity can fluctuate wildly for numerous reasons. The American Society of Health-System Pharmacists (ASHP) tracks drug shortages, discontinued drug shortages, no commercially available preparations shortages, and resolved drug shortages. ASHP also allows practitioners, patients, caregivers, drug manufacturers, and others to submit reports of new drug shortages for inclusion in their tracking mechanisms. ASHP's [shortage tracking efforts](#) represent the most comprehensive publicly available tool, offering a snapshot of shortages throughout the broader health care system and underscoring the vast scope of this problem.

With respect to emergency medicine, drug shortages exist across the spectrum of emergency care, including pre-hospital emergency care and emergency medical services (EMS). Shortages of commonly-used but essential medications remain an acute problem and tend to disproportionately affect emergency medicine due to its reliance upon generic medications for rapid sequence intubation, seizures, antidotes, resuscitation, as well as analgesics, antiemetics, and anticoagulants. EMS systems and hospital systems track and report shortages, adapting protocols in real-time to mitigate the effects of these challenges. Drug shortage reports typically include the drug/preparation in shortage, possible substitutes, and estimates of when the shortage will be resolved or when backorders are expected to clear (as reported by the manufacturer). In tracking shortages, what has become clear over the last decade, is that these shortages are not only severe but also *persistent*.

Drug shortages can often last for several months or longer, constituting a significant risk to patients. While there is a mostly predictable demand for essential emergency medications, the supply is becoming increasingly unpredictable. Not having access to critical life-saving medications and drugs such as local anesthetics, injectable pain management drugs for acute pain and trauma, anti-nausea drugs, and even sterile intravenous (IV) fluids is disastrous and potentially devastating in terms of patient outcomes. There should never be shortages of essential and life-saving, but simple, products such as sterile saline, sodium bicarbonate, or epinephrine.

To highlight the persistence of this problem, consider the following example from just several years ago. In June 2017, there were 69 preparations of 28 emergency care medications in shortage, including most forms of adenosine, atropine, bicarbonate, calcium, dextrose, dopamine, epinephrine, fentanyl, furosemide, labetalol, magnesium, lorazepam, and paralytic agents.¹ The shortages were exacerbated by the devastation wrought by Hurricane Maria on Puerto Rico in late 2017. The damage resulted in the largest drug manufacturing hub in the country grinding to a halt, with nearly all of the more than 50 pharmaceutical manufacturing facilities located on the island knocked offline by the storm. With little to no redundancy in the supply chain, manufacturers were not able to produce many of the essential products need throughout the health care system. By July of 2018, those shortages peaked at 170 emergency medication preparations and 50 intravenous fluid preparations that were not available. By December 2018, more than 110 drugs for emergency care remained in shortage. These conditions have not improved since – as of June 2023, there are 117 essential emergency medications in shortage.

Even before Hurricane Maria, sterile saline solution was already in short supply. Again, this is a simple, inexpensive product used every single day in every hospital in the country for nearly any patient, including countless patients in the

¹ Augustine, James J. (2017). "Emergency Departments Need Plan to Deal with Drug Shortages," ACEPNow <https://www.acepnow.com/article/emergency-departments-need-plan-deal-drug-shortages/?singlepage=1&theme=print-friendly>

ED. Saline typically comes in either small- or large-volume bags, both of which were in shortage prior to Hurricane Maria. The U.S. health care system relies on just three suppliers for saline (Baxter International, B. Braun Medical, and ICU Medical), with Baxter supplying small-volume bags to half of all U.S. hospitals alone.² As any manufacturing problems for just one producer can overwhelm the system, Baxter's Puerto Rico facility going offline was extraordinarily disruptive – there was no redundancy built into their supply chain, other facilities cannot simply convert production lines for one product to another, and other manufacturers were not able to increase production capacity to meet the increased demand.

Another more recent example (Fall and Winter 2022) of how shortages can contribute to complications and worsen outcomes throughout the health care continuum are the severe shortages of commonly-used medications, such as liquid formulations of ibuprofen, acetaminophen, and amoxicillin. Shortages of these drugs have left many parents unable to manage mild symptoms for their children's illnesses, resulting in increased visits to the ED and prolonged stays that could have been avoided with proper access to necessary medications. It also contributed to countless phone calls from pharmacies to EDs, urging emergency physicians to change prescriptions as they could not fill the orders.

What are the impacts of recent and recurring shortages of generics and other critical medicines on patient care?

Shortages of commonly-used but essential medications remain an acute problem throughout the health care system, but these shortages tend to disproportionately affect emergency medicine (both hospital and pre-hospital) due to its reliance upon generic medications for rapid sequence intubation, seizures, antidotes, resuscitation, as well as analgesics, antiemetics, and anticoagulants. One study conducted in 2015 found that half of all reported drug shortages from 2002 to 2014 involved acute care drugs used in ED, and these shortages are increasingly frequent and prolonged.³

The clinical impact of a shortage is highly variable, depending on the drug. For example, amoxicillin is a common antibiotic to treat bacterial infections and is used across the entire age spectrum, but shortages particularly affect pediatric populations. While there is a current nationwide shortage of amoxicillin, fortunately, this appears to be improving somewhat in recent weeks. Shortages of common topical anesthetics, frequently referred to as the “caines” – lidocaine, bupivacaine, etc. – have existed for years, but are worsening throughout the country. These drugs are used every single day in EDs everywhere to numb lacerations and other similar injuries, but their availability is so unpredictable that supply can change daily. And recent, well-documented shortages of albuterol, an inhaled bronchodilator used for treatment of asthma, chronic obstructive pulmonary disease (COPD), and other lung diseases, limit both patients' and clinicians' ability to treat exacerbations of their conditions, which can result in ED visits and longer stays that would otherwise be preventable. Shortages of opioids and sedatives persist in the palliative care space, impacting the ability to relieve acute pain and discomfort.

In many cases, shortages may not be due to a lack of the medication itself, but rather the container. Some emergency physicians are currently reporting shortages of sodium bicarbonate syringes both in the 4.2 percent syringes used for pediatric patients and 8.4 percent syringes. As an alternative, their hospital pharmacy will likely supply vials, rather than syringes, until the shortage resolves. However, this also requires an additional layer of precaution to avoid medication errors, with the facility placing the pediatric vials in a separate location to prevent any possible confusion between the two concentrations. This is the currently the case for many other medications, where the container itself is in shortage and the medication may be available in different volumes or concentrations – but constantly changing protocols and different container sizes and concentrations increase the risk of medication errors and negative patient outcomes.

What market and economic conditions undermine pharmaceutical supply chains or the availability of drugs? Please discuss any specific barriers in public payment programs.

² Mazer-Amirshahi, M. & Fox, E. (2018). Saline Shortages – Many Causes, No Simple Solution. *The New England Journal of Medicine*. 378:1472-1474. <https://www.nejm.org/doi/full/10.1056/NEJMp1800347>

³ Chen, S.I. et al. (2015). National Shortages of Drugs Used in the Emergency Department, 2002-2014, *Annals of Emergency Medicine*, Volume 66, Issue 4, S64

The 2019 FDA Drug Shortages Task Force Report (revised February 2020) found three major, foundational root causes for drug shortages: a lack of incentives to produce less profitable drugs; no recognition or reward for manufacturers for investing in and implementing mature quality management systems; and logistical and regulatory challenges that make it difficult for the market to recover after a disruption. The report further notes that these root causes are driven by a wide variety of economic factors driven both by the public and private sector.

Other reasons for drug shortages cited by the Government Accountability Office (GAO), the FDA, Pew Agency for Charitable Trusts, and others, include greater scrutiny and regulatory oversight on the manufacturing process and quality controls, as well as additional factors such as consolidation of manufacturers (especially for generic injectables), low profit margins, shortages of raw materials, absences of redundancies in the supply chain, increased demand, and product discontinuations. The 2017 Pew report on drug shortages for example found that while quality factors are one of the most significant driving factors, it is not the only issue leading to shortages, and that other key factors are market withdrawals, supply chain design, purchaser-manufacturer incentives, limited market insights into future demands, and managing regulatory expectations.⁴

The 2016 GAO report also found that two factors were strongly associated with shortages of sterile injectable anti-infective and cardiovascular drugs – a decline in the number of suppliers, and failure of at least one establishment making a drug to comply with manufacturing standards resulting in an FDA warning letter.⁵ According to the GAO, this suggests that “...shortages may be triggered by supply disruptions.” The report also indicates that a third factor, drugs with sales of a generic version, is associated with shortages in that low profit margins for generic drugs mean that “manufacturers are less likely to increase production, making the market vulnerable to shortages.”

The ongoing price increases of certain essential medications also present a major challenge to the budgets of emergency care providers, such as EMS organizations. For example, a critically-needed drug for emergency care is naloxone, the rescue medicine for patients suffering respiratory depression due to an opiate overdose. As you well know, this frequently-used medication has been employed as a first-line response for opioid overdose treatment for more than fifty years but has recently become prohibitively expensive or difficult to source, especially at the higher doses or in formulations now needed to treat many patients with opioid use disorder (OUD) or individuals who have overdosed on fentanyl or fentanyl analogues that are significantly more potent. Various factors may contribute to this particular price increase: higher overall rates of opioid overdoses, increased awareness and promotion of naloxone as an overdose reversal agent, or even recent state and federal policies enacted to encourage co-prescribing of naloxone.

What are the regulatory challenges to manufacturing drugs in the United States, as compared to other countries? Please specify which agency issued and enforced such regulations.

In the FDA Drug Shortages Task Force report, logistical and regulatory challenges are identified as one of the three key root causes of drug shortages, as they hinder the market’s ability to recover after disruptions in production or elsewhere in the supply chain. Many of these regulatory considerations fall under the purview of the FDA. However, like nearly any modern supply chain, the drug manufacturing supply chain has grown increasingly complex and is a global enterprise. As a result, manufacturers not only have to seek FDA approvals for things such as alternative manufacturing sites or alternative suppliers of active pharmaceutical ingredients (API), but also “...many post-approval changes to regulatory fillings require prior approval by the regulatory authority of every country individually, and this can be over 100 countries for globally marketed products.” Additional details on the various regulatory considerations are included in the report.

How can federal agencies, such as the Centers for Medicare and Medicaid (CMS), better address the economic forces driving shortages? Are these agencies using their current authorities effectively?

⁴ The Pew Charitable Trusts, “Drug Shortages An exploration of the relationship between U.S. market forces and sterile injectable pharmaceutical products: Interviews with 10 pharmaceutical companies,” January 2017, https://www.pewtrusts.org/-/media/assets/2017/01/drug_shortages.pdf.

⁵ United States Government Accountability Office, “Drug Shortages: Certain Factors Are Strongly Associated with This Persistent Public Health Challenge,” July 2016, <https://www.gao.gov/assets/680/678281.pdf>.

ACEP believes there are four overarching objectives that federal agencies must focus upon. These objectives are:

1. Routine measurement in the way of inventory surveillance
2. Broadly applied transparency as related to manufacturing and distribution practices to ensure adequate competition (including how existing federal laws may affect transparency and competition)
3. Flexibility in terms of granting authority to adjust protocols to fit the needs of real-time circumstances
4. Comprehensive strategies to increase the manufacturing of generic drugs in shortage, especially generic sterile injectables (such as developing regulatory or process incentives to accelerate the development of new manufacturing sites)

How does the current generic drug reimbursement structure in federal programs, including those programs' mandatory discounts and rebates, contribute to drug shortages, and what solutions exist?

Innovative payment models can help encourage the development of new drugs to address future needs, better prepare us against emergencies, disasters, and mass casualty events, or better equip our health care system to resolve drug shortages of essential emergency medications in a timely manner. As Congress considers any such approaches, ACEP believes a key piece of any new solution or payment model should ensure that essential emergency medications are prioritized and made available for emergency departments and EMS that maintain the health care safety net. EMS agencies in particular have still not fully recovered from the effects of the pandemic and struggle to respond to steep price increases or price gouging for everyday medications like naloxone or epinephrine autoinjectors (EpiPens), so Congress should consider policies that ensure EDs and EMS units are protected and not left to absorb severe price increases.

Any solutions should look at both short- and long-term needs – resolving existing shortages and insulating our health care system from future shortage scenarios. As ACEP has noted in responses to Congress regarding the upcoming reauthorization of the Pandemic and All-Hazards Preparedness Act (PAHPA), growing antimicrobial resistance and the reduction of remaining effective antimicrobial armamentarium represent a critical threat to public health and the health of patients in emergency departments throughout the U.S. and the world.

The Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) noted in a 2021 letter to HHS Secretary Xavier Becerra that the U.S. continues to face a "...severe lack of new antimicrobial drugs." This growing deficit is exacerbated by increasing antimicrobial resistance to existing treatment options, leaving health care professionals more limited ability to treat infections. To help address the investment and development pipeline challenges for new antimicrobial drugs, ACEP urges Congress to include the Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (PASTEUR) Act in PAHPA. The PASTEUR Act would establish an innovative, subscription-based payment model for novel antimicrobials, allowing the federal government to enter purchasing contracts with companies that delinks payment from sales volume. This will help reduce risks for companies seeking to develop new antimicrobials, while also ensuring the federal government only pays for successful FDA-approved treatments that are available to patients and meet unmet antimicrobial resistance needs. The PASTEUR approach is similar to Project Bioshield, which helps support the development and procurement of medical countermeasures for other biological and radiological threats.

Similar approaches for essential emergency medications or other drugs frequently in shortage could be employed as well.

Given that supply chain issues can trigger manufacturing delays and disruptions that result in shortages, are further incentives necessary to address manufacturing issues?

Ensuring redundancy and resiliency within the pharmaceutical supply chain is critical for everyday needs as well as emergency preparedness needs, and as we have experienced directly, major natural disasters or disease outbreaks have pushed our health care system to or beyond its breaking point. Further incentives are undoubtedly essential to encourage manufacturers, primarily to ensure a consistent supply of essential medications at all times, particularly for low-cost/low-margin drugs. Additionally, these incentives should promote investment in equipment and technologies to facilitate efficient and rapid scalability of medication production. Moreover, they should incentivize domestic production and

sourcing of active pharmaceutical ingredients (APIs) to reduce dependence on intricate and fragmented global supply chains.

How has consolidation among Group Purchasing Organizations and Prescription Drug Wholesalers led to less redundancy in the drug supply chain? Has this consolidation contributed to drug shortages, especially among generic drugs? Have business practices, such as just-in-time deliveries and limited-source contracts contributed to the drug shortage issue we are seeing?

The 2020 FDA Drug Shortages Task Force report identified several challenges related to these issues. The report noted that consolidation of group purchasing organizations (GPOs) resulted in the four largest GPOs accounting for approximately 90 percent of all medical supplies in the U.S., adding that as a result of this growing consolidation, GPOs are able to exert control over the market and “...have been able to negotiate low prices, especially for multi-source generics.”⁶ With manufacturers unable to raise prices or compete with other manufacturers seeking to gain market share, this often results in a “race to the bottom” where manufacturers sell a drug at or below cost. This is a contributing factor to unfavorable pricing dynamics that discourage manufacturers by limiting their profitability:

“When market conditions limit manufacturers’ profitability, they reduce a firm’s motivation to maintain a presence in, or enter the market for older prescription drugs, and to invest in manufacturing quality and redundant capacity. Manufacturers of older generic drugs, in particular, face intense price competition, uncertain revenue streams, and high investment requirements, all of which limit potential returns. Current contracting practices contribute to a ‘race to the bottom’ in pricing.”

Many GPOs include “failure to supply” clauses in contracts with manufacturers, ostensibly intended to provide an incentive for manufacturers to invest in efforts to ensure a reliable and consistent supply chain for drugs. However, even despite growing GPO consolidation and outsized market presence, the report further notes that these clauses are “generally weak,” and that manufacturers face few or no repercussions beyond minimal revenue losses or reputation impacts.

As the FDA Drug Shortages Task Force, the Government Accountability Office (GAO), and numerous other analyses and studies have found, drug shortages are complex and multifactorial, and the issues described here are only pieces of a larger puzzle. There is only limited understanding and study of the broader, system-wide impacts of GPO contracting practices, including on how they may contribute to drug shortages. Given the already challenging economics of producing generic drugs, especially generic sterile injectables, it is possible that the significant downward pressure exerted by GPOs on already-low margin generic products could force manufacturers out of the market. Additionally, “sole-source” exclusive contracts could prevent some facilities, particularly drug compounders, from mitigating drug shortages.⁷ While not a key driver of drug shortages, it could potentially be an underlying factor. One issue Congress could examine in more detail is any role of GPOs in drug shortages, including whether the safe harbor provisions under federal anti-kickback statutes afforded to GPOs contribute to shortages, and consider repeal of the provisions if so.

With respect to business practices, many stakeholders throughout the health care system – drug manufactures, GPOs, distributors, and health systems alike – have employed “just-in-time” inventory management practices, driven by financial incentives and potential operational efficiencies. While this may provide short-term benefits in normal, day-to-day operations, the Task Force noted that there is “...little redundancy in the supply chain when a disruption occurs,” and that resulting shortages cannot be easily addressed because of difficulties in ramping up production, expanding capacity, or sourcing necessary components including API.

⁶ [Drug Shortages: Root Causes and Potential Solutions](#)

⁷ Barlas S. (2019). Do GPOs Play a Role in Drug Shortages? Long-Standing Allegations Disputed by The GPOs. Mar;44(3):94-121. PMID: 30828227; PMCID: PMC6385730 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6385730/>

Given that drug shortages are complex and multifactorial, and that there are numerous stakeholders involved in manufacturing, distribution, and utilization, we must be strategic and intentional about determining aligned incentives and cooperative initiatives that focus on providing quality patient care.

Again, thank you for the opportunity to share our comments and experiences. ACEP remains hopeful that we can build upon our collective efforts to ensure stable, predictable, and affordable supplies of emergency medications for both everyday operation and disaster preparedness and response. Should you have any questions, please do not hesitate to reach out to Ryan McBride, ACEP Congressional Affairs Director, at rmcbride@acep.org.

Sincerely,

A handwritten signature in black ink, appearing to read "Chris Kang", written in a cursive style.

Christopher S. Kang, MD, FACEP
ACEP President