

July 7, 2023

The Honorable Cathy McMorris Rodgers
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Mike Crapo
Senate Finance Committee
219 Dirksen Senate Office Building
Washington, DC 20510

Dear Chair McMorris Rodgers, and Ranking Member Crapo,

We appreciate the opportunity to comment on the House Energy and Commerce Committee and Senate Finance Committee's bicameral request for information (RFI) on drug shortages. We applaud your efforts as Chair of the House Energy and Commerce Committee and Ranking Member of the Senate Finance Committee to better understand drug shortages and identify policy solutions to address them. HDA and its members appreciate the House Energy and Commerce and Senate Finance Committees' dedication to work on issues impacting public health, such as drug shortages.

The Healthcare Distribution Alliance (HDA) is the national organization representing primary pharmaceutical distributors — the vital link between the nation's pharmaceutical manufacturers and pharmacies, hospitals, long-term care facilities, clinics and others nationwide. HDA advocates on behalf of pharmaceutical wholesalers and distributors, leads the sector on relevant policy and fosters relationships across partner organizations. Healthcare distributors ensure the safe, efficient and reliable delivery of medications, vaccines and other critical medical products. HDA's members find the safest and most efficient ways to get medical products to providers and patients at the place and time they are needed.

Drug shortages peaked in 2011 with more than 250 new shortages. Since 2011, the number of drug shortages has declined, while the threats have remained. It is important to note that each drug shortage stems from a different scenario which should be examined independently – driven by a myriad of factors such as demand/supply shortages, quality / plant issues, etc. In the [2022 FDA](#)

[Report to Congress](#)¹ on drug shortages, there were 49 new drug shortages. Drug distributors employ innovative strategies, take proactive actions and invest in solutions to help mitigate the impact that drug shortages have on providers and patients. Our focused efforts and ongoing partnerships with the FDA have contributed to reducing drug shortages. The continued focus on causes of drug shortages should recognize the capabilities used to prevent shortages as well as the myriad of factors which contribute to a drug shortage. The COVID-19 pandemic increased the focus on the supply chain and various elements of supply chain resilience, as there was increased demand for medical products to support the healthcare response to COVID-19 and maintain continuity of care.

In this response, HDA offers the following recommendations and policy solutions to mitigate and prevent drug shortages:

- The FDA should work with the private sector to conduct a focused review of the challenges that affect specific classes of products.
- The FDA should review the relationship between the number of Abbreviated New Drug Applications (ANDAs) and the number of suppliers currently in the market, specifically for products at high risk of shortage.
- Congress and the FDA should examine financial incentives and operational considerations for strategically investing in product development, capacity and working with distributors to build targeted safety stock/buffer inventory.
- The US Government Accountability Office (GAO) should conduct a study to explore additional potential solutions and partnerships, specifically with the FDA, Department of Health and Human Services (HHS) and the Administration for Strategic Preparedness and Response (ASPR), to reduce potential drug shortages or lessen the impacts of current shortages.
- The Centers for Medicare and Medicaid (CMS) should give [preferred formulary position](#)² to new generics and biosimilars.
- Congress should work with the FDA to understand how it plans to address the potential for significant drug shortages and supply chain disruptions resulting from healthcare supply chain stakeholders not being fully ready for the full implementation of the Drug Supply Chain Security Act (DSCSA). Congress should encourage the FDA to adopt HDA's previously submitted recommendation for a phased approach to implementation and enforcement discretion of the DSCSA that enjoys the support of myriad stakeholders.

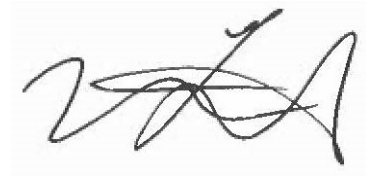
HDA and its members recognize the challenges drug shortages may pose to the healthcare system, and that is why we work to mitigate and manage them when they occur. HDA and its members stand ready to provide our continuing perspective and insight on behalf of the pharmaceutical distribution

¹ US Food and Drug Administration. "Tenth Annual Report on Drug Shortages for Calendar Year 2022." <https://www.fda.gov/media/169302/download>.

² Association for Accessible Medicines. "Drug Shortages: Causes & Solutions." Published 2023. https://accessiblemeds.org/sites/default/files/2023-06/AAM_White_Paper_on_Drug_Shortages-06-22-2023.pdf.

industry, related to the complex dynamics associated with drug shortages. If you have any questions or would like additional information, please contact Dr. Nicolette Louissaint by email at nlouissaint@hda.org.

Sincerely,

A handwritten signature in black ink, appearing to read 'NL', enclosed in a light gray rectangular box.

Nicolette Louissaint, PhD, MBA
Senior Vice President, Policy and Strategic Planning

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

Distributors are the backbone of the pharmaceutical supply chain, handling approximately 94 percent of medicines moved across the United States and finding [the safest and most efficient ways to get products where patients need them the most in a continuous and reliable manner](#).³ Distributors are logistics experts who work daily to connect 1,400 manufacturers to [330,000 sites of care](#).⁴ Distributors work diligently to deliver products to customers daily, sometimes multiple times a day. [83 percent](#)⁵ of distributors' customers receive deliveries [five times or more per week](#).⁶

While drug shortages affect only 1 percent of all prescriptions, and yet even this very limited occurrence can lead to frustration for millions of U.S. patients and their healthcare providers, as upwards of 5.9 billion prescriptions are dispensed each year.

Distributors ensure a streamlined supply chain that can coordinate the delivery of critical medical products across the United States, while maintaining a [0.6 percent net profit margin \(after taxes\)](#).⁷ In the supply chain, distributors create a value of [up to \\$63 billion annually](#)⁸, through logistics expertise that allows for safe storage and delivery of up to approximately 11 million products from nearly 1,400 manufacturers daily. In the last decade, distributors have increased savings by reducing operating expenses by almost 40 percent from [\\$7.5 billion to \\$4.6 billion](#).⁹ [Without distributor services](#)¹⁰, approximately 1,400 manufacturers would still have to connect to over 330,000 sites of care multiple times a week to ensure continued daily access to medical

³ Healthcare Distribution Alliance. "Insights and Recommendations from the National Academies' Report on Building Resilience in the Nation's Medical Product Supply Chain." Published 2023. <https://www.hda.org/getmedia/7290a259-5893-4fbb-9391-d8a91aa3eb85/Insights-and-Recommendations-From-the-National-Academies-Supply-Chain-Report.pdf>.

⁴ Healthcare Distribution Alliance. "Delivering Value Across Healthcare." Published 2023. <https://hda.org/getmedia/807f7717-3a3a-4e8a-9011-2c8a91502dec/hda-factsheet-deliveringvalueacrosshealthcare-2023.pdf>.

⁵ HDA Foundation. "The Role of Distributors in the US Health Care Industry." Published 2019. <https://www.hda.org/publications/the-role-of-distributors-in-the-us-health-care-industry-8210cd8c1b20adf4dd87db4f48b2503d/>.

⁶ Healthcare Distribution Alliance. "Delivering Value Across Healthcare." Published 2023. <https://hda.org/getmedia/807f7717-3a3a-4e8a-9011-2c8a91502dec/hda-factsheet-deliveringvalueacrosshealthcare-2023.pdf>.

⁷ HDA Foundation. "93rd Edition HDA Factbook: The Facts, Figures and Trends in Healthcare." Published 2022. <https://www.hda.org/publications/93rd-edition-hda-factbook-the-facts,-figures-and-trends-in-healthcare/>.

⁸ Healthcare Distribution Alliance. "Delivering Value Across Healthcare." Published 2023. <https://hda.org/getmedia/807f7717-3a3a-4e8a-9011-2c8a91502dec/hda-factsheet-deliveringvalueacrosshealthcare-2023.pdf>.

⁹ HDA Foundation. "The Role of Distributors in the US Health Care Industry." Published 2019. <https://www.hda.org/publications/the-role-of-distributors-in-the-us-health-care-industry-8210cd8c1b20adf4dd87db4f48b2503d/>.

¹⁰ Healthcare Distribution Alliance. "How do Medicines Get to Where They Need to Go?" Published 2023. <https://hda.org/getmedia/ee0c6753-3549-4fd6-a58d-8ffaed19936d/hda-factsheet-howdomedicinesgettowheretheyneedtogo-2023.pdf>.

products. That scenario would place a burden on hospitals and pharmacies, creating a logistical challenge and administrative burden for each facility to set up individual linkages to each manufacturer.

HDA and its members have monitored drug shortages very closely. The availability of medicines impacts distributors' ability to serve their downstream customers. While the definition of a drug shortage may vary based on the vantage point, distributors align with the US Food and Drug Administration (FDA) definition of a [drug shortage](#),¹¹ which states that a shortage is defined by the total commercially-available supply of a medical product not being able to meet the current demand. Other entities use a broader definition of a drug shortage, which may include classifying a product as being in a shortage when there are stockouts of a product (i.e. temporary inability to receive a product) or a product being distributed based on fair-share allocation (i.e. receiving a partial fulfillment of a requested order). Despite the importance of these perspectives, maintaining multiple definitions has created confusion and a lack of context in the drug shortages conversation. The importance of the drug shortages conversation reinforces the need to rely on a single definition for a drug shortage in policy discussions.

To avoid significant disruptions due to challenges in the supply chain, distributors focus on maintaining [operational resilience](#).¹² Distributors maintain communication with manufacturers and customers (including healthcare facilities that depend on medicines for patient care) to understand the dynamic changes in the supply chain and build plans to adjust to ensure that available product is delivered to the facilities that need them most through [fair-share allocation](#).¹³

Due to our unique vantage point in the supply chain, we see that the issue of drug shortages is highly nuanced and dynamic, with multiple drivers and factors at play – categorized by both manufacturer *supply-driven* or consumer *demand-driven shortages*. *Supply-driven shortages* are characterized by the availability of a drug that is affected by upstream disruptions to manufacturing or raw materials supply availability. Supply-driven shortages can be impacted by scenarios such as raw materials and active pharmaceutical ingredient (API) shortages, manufacturer disruptions, quality issues, etc. *Demand-driven shortages* are considered to be sudden medical surges or other increases in demand which would create a sudden uptick in ordering. We consider *supply-driven shortages* as a different category of drug shortages, as the causes and potential solutions are very different than the demand-driven shortage scenarios.

¹¹ US Food and Drug Administration. “Drug Shortages: Root Causes and Potential Solutions.” Published 2019. Updated February 21, 2020.” <https://www.fda.gov/media/131130/download>.

¹² Healthcare Distribution Alliance. “Bolstering Disaster Preparedness and Operational Resilience in the Healthcare Supply Chain.” Published 2023. <https://www.hda.org/getmedia/f13bb354-88eb-494e-81ca-2456ea4d795c/Bolstering-Disaster-Preparedness-and-Operational-Resilience-in-the-Healthcare-Supply-Chain.pdf>.

¹³ Healthcare Distribution Alliance. “Drug and Medical Product Availability: Distributors Promote a Resilient Supply Chain.” <https://www.hda.org/getmedia/45f48c39-69e6-4ff8-8919-af1c4cfb7432/Drug-and-Medical-Supply-Shortages.pdf>.

While reviewing the scope, impact, and root causes of recent drug shortages, we find that they can be varied, depending on manufacturer and type of product. From our perspective, this means that while there is no single solution that will address shortages, finding ways to categorize drug shortages based on key factors may help us think about how to better understand, and hopefully, mitigate them.

HDA and its members support overall [supply chain resilience](#)¹⁴, as enhanced resilience across the entire system creates the ability for the healthcare ecosystem to manage disruptions and shocks, including drug shortages, without significantly impacting patient care and healthcare delivery. To mitigate drug shortages and support as many providers and patients as possible, distributors have long used [fair-share allocation programs](#)¹⁵ and other tools to understand the upstream supply chain, assess available product and equitably distribute. Fair-share allocation programs account for the available supply and customer needs, limiting the amount that a single customer can purchase of medical product to assure products are available to as many customers as possible. This helps avoid practices such as hoarding from distorting the market. Other tools distributors use to combat drug shortages include supporting hospital / government stockpiles, offering product alternatives, and forecasting public health events that may shift demand. Distributors have a national network of distribution centers and in the event of a demand surge due to a disaster, they may coordinate with federal and state stakeholders to direct resources to where they are necessary.

Distributors support stockpile expansion and one of their services is to continuously cycle and manage products to supplement disruptions. To respond to disaster-driven demand surges, distributors manage the commercially available products in the Strategic National Stockpile (SNS) through the use of [Vendor Managed Inventory \(VMI\)](#).¹⁶ Another tool distributors use to combat shortages is to expand product availability by [leveraging their national distribution network](#)¹⁷ to minimize the impacts of disruptions and offering product alternatives when appropriate. Distributors may also mitigate drug shortages by using public health data to forecast demands for surges, like the seasonal flu. This practice is also utilized by manufacturers of the seasonal flu vaccine in order to predict demand.

¹⁴ Healthcare Distribution Alliance. "Healthcare Supply Chain Resilience and Data Illumination." Published Spring 2023. <https://www.hda.org/getmedia/38b4ad3e-1164-4ef5-9516-963f7dbfb048/HDA-Data-Illumination-Report.pdf>.

¹⁵ Healthcare Distribution Alliance. "Drug and Medical Product Availability: Distributors Promote a Resilient Supply Chain." <https://www.hda.org/getmedia/45f48c39-69e6-4ff8-8919-af1c4cfb7432/Drug-and-Medical-Supply-Shortages.pdf>.

¹⁶ Healthcare Distribution Alliance. "Pandemic and All-Hazards Preparedness Act Reauthorization: Background and Opportunities to Enhance Resilience." Published 2023. <https://www.hda.org/getmedia/c77c0197-674d-46cf-a870-8017ac070ae0/PAHPA-Background-and-Opportunities-to-Enhance-Resilience.pdf>.

¹⁷ Healthcare Distribution Alliance. "Drug and Medical Product Availability: Distributors Promote a Resilient Supply Chain." <https://www.hda.org/getmedia/45f48c39-69e6-4ff8-8919-af1c4cfb7432/Drug-and-Medical-Supply-Shortages.pdf>.

Recent supply-driven shortages including albuterol sulfate inhalation solution and cisplatin / carboplatin oncology treatments, were triggered by manufacturing shutdowns. In the case of albuterol, the shortage was triggered by a manufacturer exiting the market due to financial insolvency, partially due to quality issues known to the FDA. The ongoing albuterol shortage has been worsened by an increase in medical surge combined with Akorn Pharmaceuticals' closure. After years of financial insolvency, [Akorn Pharmaceuticals declared chapter 11 bankruptcy](#)¹⁸ before finally declaring bankruptcy again in 2023 and dissolving. In the case of cisplatin / carboplatin, there is an ongoing shortage due to Accord receiving an import ban following an FDA inspection in December 2022. This import ban was triggered by breaches to cGMP and data integrity issues. Accord had a large share of the market volume, and as a result the restriction to supply created a market shortage. Recently, to mitigate the shortage of cisplatin / carboplatin, the [FDA has authorized the importation](#)¹⁹ and distribution of cisplatin from an international company (product intended for sale in another country / market) and were approved temporary importation into the US to help resolve some of the shortage issues.

HDA has discussed medical surge as an [operational resilience priority](#)²⁰ and continues to support policies to improve surveillance (to detect disease outbreaks that would create a surge in demand), [stockpiling partnerships](#)²¹ (such as expansion of the Strategic National Stockpile and the vendor-managed inventory strategy with distributors), and preparedness and response planning. HDA and its members often categorize shortages by the drivers that cause them. For demand-driven shortages, we consider sudden medical surges or other increases in demand which would create a sudden uptick in ordering. Demand may increase due to disaster-related medical surge or non-disaster-related medical surge. Often, the tools to address demand-driven shortages are planned around the disaster context, which includes measures to decipher between legitimate demand and hoarding practices. Without reviewing orders / ordering patterns, discussions with customers, and other steps to prevent hoarding practices from triggering a shortage event, there would be far more shortages. Examples of disaster-related medical surge are the COVID-19 pandemic and the COVID-19 / RSV / flu surge in December 2022. Last year, the nation faced an unprecedented surge of medical products for COVID-19, RSV, and the flu all simultaneously, resulting in a shortage of medical products such as antivirals and pediatric acetaminophen. Emergency department visits with diagnosed RSV and RSV-like illness were higher in November 2022 than 2019 to 2021²² and the flu hospitalization rates were higher in

¹⁸ Fierce Pharma. Becker, Zoey. "Bankrupt Akorn Pharma calls it quits and closes all US sites, laying off entire workforce." Published February 23, 2023. <https://www.fiercepharma.com/manufacturing/akorn-pharma-bankrupt-calls-it-quits-closes-all-us-sites-and-cuts-entire-workforce>.

¹⁹ US Food and Drug Administration. "DHCP Letter: Temporary Importation of Cisplatin Injection with non-US labeling to Address Drug Shortage." Published May 24, 2023. <https://www.fda.gov/media/169001/download>.

²⁰ Healthcare Distribution Alliance. "Bolstering Disaster Preparedness and Operational Resilience in the Healthcare Supply Chain." Published 2023. <https://www.hda.org/getmedia/f13bb354-88eb-494e-81ca-2456ea4d795c/Bolstering-Disaster-Preparedness-and-Operational-Resilience-in-the-Healthcare-Supply-Chain.pdf>.

²¹ Ibid.

²² Centers for Disease Control and Prevention. Centers for Preparedness and Response. Flu, RSV, COVID-19 and other Respiratory Threats this Fall and Winter. Presented November 29, 2022. https://emergency.cdc.gov/epic/pdf/2022/112922_slides.pdf.

November 2022 than every previous flu season since 2010 -11.²³ The healthcare supply chain had to respond to a surge in cases that exceeded even the highest projections for the season. HDA and its members recognize that more disasters and disease outbreaks will increase the demand on the supply chain. We have seen and expect to continue to witness an increase in events and multiple events happening at the same time, commonly referred to as the *polycrisis* phenomenon.

HDA and its members have analyzed recent shortages caused by a surge in demand. Distributors monitor demand for drugs and try to anticipate changes. However, one example of when neither distributors nor supply chain stakeholders can predict an increase in demand occurs in cases where demand is fueled by social media trends which contribute to increased off-label prescribing. A trigger of non-disaster-related medical surge is the significant level of social media activity associated with recommendations of products for weight loss, resulting in unpredictable demand. [Advertisements and viral videos on the Meta and Tik Tok platforms](#)²⁴ turned the weight loss side effect of the type 2 diabetes drug, Ozempic, into a selling point for non-diabetes patients. [Prescriptions for Ozempic](#)²⁵ have more than doubled to 1.2 million since mid-2021, growing at a rate of 76.9 percent, which impacted available supply for diabetic patients.²⁶ Demand-side shortages fueled by social media are unpredictable and may put patients who depend on a drug at risk.

Another healthcare trend that has increased prescribing practices is the use of telehealth, which was spurred during COVID-19 and will likely remain as a viable tool for providers. In 2022, 7 to 9 percent of provider visits were administered via telehealth, which we expect to see sustained in future years.²⁷ As this may increase access to needed drug therapy for patients, this is a laudable trend. And yet, methods to address demand-side shortages must be done on a case-by-case basis and must consider the factors, such as the effect social media or the positive impact of increased telehealth access, can have on demand surge.

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

²³ Centers for Disease Control and Prevention. Centers for Preparedness and Response. Flu, RSV, COVID-19 and other Respiratory Threats this Fall and Winter. Presented November 29, 2022. https://emergency.cdc.gov/epic/pdf/2022/112922_slides.pdf.

²⁴ Forbes. Johnson, Arianna. "What to Know About Ozempic: The Diabetes Drug Becomes a Viral Weight Loss Hit (Elon Musk Boasts Using It) Creating A Shortage." Published December 26, 2022. <https://www.forbes.com/sites/ariannajohnson/2022/12/26/what-to-know-about-ozempic/?sh=1519ccf65adb>.

²⁵ Associated Press. Murphy, Tom. "What's behind shortages of Adderall, Ozempic and other meds?" Published April 30, 2023. <https://apnews.com/article/drug-shortages-adderall-ozempic-855632a04a17c2bf75b6a89e4c08ef79>.

²⁶ IQVIA. Long, Doug. US Pharmaceutical Trends, Issues & Outlook for HDA. Presented March 13, 2023.

²⁷ IQVIA. Long, Doug. US Pharmaceutical Trends, Issues & Outlook for HDA. Presented March 13, 2023.

When considering market and economic conditions, distributors see two categories that challenge the pharmaceutical supply chain – *manufacturing quality issues* and *market access*.

- Manufacturing quality issues
 - Drug shortages in certain product classes (such as generic sterile injectables, some of which are produced in the United States²⁸) have been driven by quality issues.²⁹ Some of these challenges are a function of the complexity of the production (i.e. continuous manufacturing) or sterilization requirements associated with the process. These issues are often related to the need for greater investment in robust manufacturing processes to mitigate the contamination issues that may arise.

- Market access
 - Stable market share for generic manufacturers provides for greater operational continuity and the ability to better forecast needs. Distributors enter partnerships with multiple suppliers that provide them with the opportunity for long-term contracts with generic trading partners, which can ensure their market access. Distributors focus on supplier diversification and reliable supply of product to serve customer needs, which are considerations in their supply chain strategies (see pg. 10).
 - The Abbreviated New Drug Application (ANDA) process allow an unlimited number of new entrants into the market, and while there is a need to have a robust level of suppliers for products, it is important to balance the number of entrants with the current / future market trends.

The passage of the “[Drug Price Competition and Patent Term Restoration Act of 1984](#)”³⁰, otherwise known as the Hatch-Waxman Act³¹, has established a system in the United States for generic medicines to enter the market, predicated on a market-driven interest in providing patients and the healthcare system with lower-cost alternatives to the originator branded medicines upon expiry of their intellectual-property based monopolies. The path for approval of generics medicine has been based on bioequivalence (safety, efficacy) against the reference product, with the assumption / assurance that the cost of the product would be significantly decreased as a generic. This system has set up a structure where the generic market has continually been challenged to reduce their costs as a benefit to patients, which creates a lower operating margin. These lower costs, while a clear and necessary benefit to patients, create challenges in adoption of broader resilience practices or opportunities to add additional

²⁸ Pharmaceutical Technology. “Pfizer’s Sterile Injectable Production Facility, Michigan.” Published August 24, 2018. <https://www.pharmaceutical-technology.com/projects/pfizer-portage-facility-michigan/>.

²⁹ Fierce Pharma. Blankenship, Kyle. “Pfizer looks to right sterile injectable woes with modernized manufacturing.” Published April 30, 2020. <https://www.fiercepharma.com/manufacturing/pfizer-looks-to-right-sterile-injectable-woes-remediation-modernized-manufacturing>.

³⁰ Public Law 98-417. 98th Congress. “Drug Price Competition and Patent Term Restoration Act of 1984.” <https://www.congress.gov/98/statute/STATUTE-98/STATUTE-98-Pg1585.pdf>.

³¹ US Food and Drug Administration. “Hatch-Waxman Letters.” Accessed June 29, 2023. <https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/hatch-waxman-letters>.

production or buffer stock without risk of financial insolvency. While recent shortages have been caused by issues identified above, the root causes are diverse and functions of a system which was established to drive down the costs to a point where investment in robust resilience practices may be difficult or cost prohibitive.

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

Many of the economic forces that cause supply-driven shortages relate to generic manufacturer quality control and operational resilience capabilities, as well as generic product market access (the ability for new manufacturers to obtain approval and gain market share to make production profitable, as appropriate pricing may allow).

HDA recommends that the US Government Accountability Office (GAO) conduct a focused review of challenges that plague specific classes of products (such as sterile injectables), as some products are more likely to be in shortage due to manufacturing disruptions rather than myriad economic forces driving shortages.

The ability for the federal government to impact market forces is limited to regulatory authority and reimbursement. Noting this, there may be an opportunity for the Food and Drug Administration (FDA) to review the relationship between the number of [Abbreviated New Drug Applications](#)³² (ANDAs) and the number of suppliers currently in the market, specifically for products at high risk of shortage. While we continue to see a record number of ANDAs approved for generic medicines, many of these products never come to the market with 16 percent of total ANDAs being unlaunched in 2022.³³

There are three plausible considerations, which are worth exploring through the lens of the manufacturing industry:

1. In recent years there have been a record number of ANDAs approved, consistent with one of the goals of the Generic Drug User Fee Act (GDUFA). However, there is still a backlog of ANDAs awaiting approval and the chronically extended timeframe for an ANDA filing to find its way to approval contributes to the challenge. Despite the advent of GDUFA, [approval timelines](#)³⁴ still report some lags. Due to this, the return on investment

³² US Food and Drug Administration. "Abbreviated New Drug Application (ANDA)." Accessed June 29, 2023. <https://www.fda.gov/drugs/types-applications/abbreviated-new-drug-application-anda>.

³³ IQVIA. Long, Doug. US Pharmaceutical Trends, Issues & Outlook for HDA. Presented March 13, 2023.

³⁴ Pink Sheet. Gingery, Derrick. ANDA Approval Records Will End As US FDA Mops Up Backlog. December 04, 2019 (Accessed on July 6, 2023). <https://pink.pharmaintelligence.informa.com/PS141304/ANDA-Approval-Records-Will-End-As-US-FDA-Mops-Up-Backlog>

for generic companies can be delayed and often entirely eroded as the 36 month “wait” for a submitted ANDA to receive FDA approval. More timely review timelines can effectively encourage product development and ANDA filings of limited competition products is well demonstrated in the FDA’s programs such as:

- a. Publishing lists of brands with no patent protection and no generics;
 - b. Offering accelerated approvals or a period of market exclusivity for the first filer of a generic for one of these products; and
 - c. The voucher program that provides a priority review voucher for a company that successfully develops and files a drug for a rare pediatric disease (RPD).
2. Manufacturers see no viable market to make production worthwhile. This results in unlaunched ANDAs – manufacturers may choose to get an ANDA approval, but not begin to produce the medicine (because there is no market value).
 3. New manufacturers in the market create more competition and drive price down even further, reducing margins and lowering investments in operational resilience.

In addition to the potential revisions to the ANDA approval process, there is a need to address manufacturing and quality issues that are responsible for many drug shortages. The [increase in FDA inspections](#)³⁵ has resulted in enforcement ([Form 483](#)³⁶, etc.) and at times, temporary closure of manufacturing facilities. We believe that the FDA inspection process is critically important and believe that additional investment in enforcement of quality standards is important to the resilience of the generics sector. While we support this focus on pharmaceutical quality and the FDA’s role therein, we caution against any mandates that would increase more examination of quality *without* support or funding to invest in quality control measures. The 2019 FDA shortages report notes that [about half \(47%\) of the 163 drugs](#)³⁷ that went into shortage between 2013 and 2017 were both generics and [sterile injectables](#).³⁸ This is an area where collaborative effort and investment between the private sector and the FDA may be advantageous to address the root causes. We defer to manufacturers to provide more specific insights.

We do see instances of the FDA working with manufacturers to prevent new drug shortages. In the 2022 FDA Report to Congress on Drug Shortages, the FDA reports that they worked with manufacturers to [prevent 222 drug shortages](#).³⁹

It is important to note that the generic medicines industry operates in a commoditized market, which means that standard market forces are the primary driver of price and market stability. In this instance, the pharmaceutical industry has long been tasked with decreasing the cost of

³⁵ US Food and Drug Administration. “Drug Shortages: Root Causes and Potential Solutions.” Published 2019. Updated February 21, 2020.” <https://www.fda.gov/media/131130/download>.

³⁶ US Food and Drug Administration. “FDA Form 483 Frequently Asked Questions.” Accessed June 29, 2023. <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/fda-form-483-frequently-asked-questions>.

³⁷ US Food and Drug Administration. “Drug Shortages: Root Causes and Potential Solutions.” Published 2019. Updated February 21, 2020.” <https://www.fda.gov/media/131130/download>.

³⁸ Ibid.

³⁹ US Food and Drug Administration. “Tenth Annual Report on Drug Shortages for Calendar Year 2022.” <https://www.fda.gov/media/169302/download>.

medicines – an impetus that continues to be centered in the drug pricing debate to this day. The current dynamics of the generics market have focused on a resilient supply of quality, approved, low-cost generic medicines to patients.

HDA notes that there may be potential solutions and partnerships, specifically with the HHS – FDA and ASPR, which might be helpful to reduce potential drug shortages or lessen the impacts of current ones. Voluntary partnerships may create avenues for industry and the FDA to work together on any insights they have about potential supply-side and demand-driven shortages. The [Supply Chain Control Tower \(SCCT\)](#)⁴⁰, a public private partnership (PPP) that relied on data-sharing agreements with individual supply chain stakeholders, sought to increase the government’s visibility on the availability of key medical products during the COVID-19-related public health emergency (PHE). The SCCT, which provided visibility into [90 percent](#)⁴¹ of the US pharmaceutical distribution market, was used as a tool to provide visibility into the supply chain during the COVID-19 pandemic, was also used to track product during the [baby formula shortage](#)⁴² as well as the [2022 cold and flu season](#).⁴³ It is HDA’s position that the SCCT does streamline reporting in the federal government during an event or PHE. HDA is supportive of appropriate use of the SCCT to avoid distributors reporting into multiple entities within the federal government during an event, a burdensome task that can detract from operations staff performing other key functions to respond. However, it is important to note that the SCCT was not designed for prediction or visibility into drug shortages, and it is our recommendation that the SCCT only be activated during a PHE. That said, the SCCT is not a single solution to address shortages, and does not obviate the need for other coordinating mechanisms between the private sector and the federal government. It is also important to note that [the ongoing coordination](#)⁴⁴ between manufacturers and the FDA has enhanced the ability of the FDA to mitigate potential drug shortages.

Another barrier to the broader adoption of generic and biosimilar medicines is prescription drug formularies imposed by commercial and even government-mandated plans. Often times, these plans will feature a higher priced product on a Tier 1 formulary due the fact that plans or PBMs representing the plans are receiving higher rebates for that product. This makes it very difficult for lower cost products to gain traction in the marketplace. This not only impacts a patient’s access

⁴⁰ Healthcare Distribution Alliance. “U.S. Healthcare Supply Chain Monitoring Structure: Issues and Recommendations.” Published 2023. <https://www.hda.org/getmedia/3f1f79ea-5d32-4897-b81b-899d290732ec/HDA-FactSheet-US-HC-Supply-Chain-Monitoring-Structure-FINAL.pdf>.

⁴¹ Ibid.

⁴² US Department of Health and Human Services. “HHS Secretary Becerra Invokes Defense Production Act for Third Time to Further Increase Production of Infant Formula for American Families.” Published May 27, 2022. <https://www.hhs.gov/about/news/2022/05/27/hhs-secretary-becerra-invokes-defense-production-act-for-third-time-to-further-increase-production-of-infant-formula-for-american-families.html>.

⁴³ US Department of Health and Human Services. “HHS Increases Access to Tamiflu through the Strategic National Stockpile.” Published December 21, 2022. <https://www.hhs.gov/about/news/2022/12/21/hhs-increases-access-to-tamiflu-through-the-strategic-national-stockpile.html>.

⁴⁴ US Food and Drug Administration. “Tenth Annual Report on Drug Shortages for Calendar Year 2022.” <https://www.fda.gov/media/169302/download>.

to lower cost products, but it can also stifle investment in additional generic and biosimilar medicines. We support the Association for Accessible Medicines' (AAM) recommendation to give [preferred formulary position](#)⁴⁵ to new generics and biosimilars.

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

Supply-side shortages are often the result of upstream supply chain issues, such as raw material shortages or manufacturing disruptions. Distributors have limited insight and no control over raw material shortages or manufacturing issues. Further investments are needed to prevent manufacturing issues, which would have to be consistent. HDA recommends that the FDA work with CMS to ensure that products that receive investment are included in Medicare / Medicaid prescription drug plan formularies. Also, there should be clear parameters guiding how the products to invest in would be chosen equitably that do not discourage competition.

HDA and its members believe that while it is crucial to address existing drug shortages, it is also important to note the success of the healthcare supply chain, in part due to the competition and resilience maintained. In the US, 90.2 percent of prescriptions dispensed were generic drugs (2022 data).⁴⁶ Factors that drive shortages in the US are consistent with the global trends and drug shortages observed in other countries, which suggests that some factors are driven by the global market. [The European Union \(EU\) issued a report](#)⁴⁷ citing the drivers of shortages to be increased demand, manufacturing and quality problems, factory closures, and supply-chain bottlenecks. Any investments made into the healthcare supply chain should be considered carefully so that competition and continuity of the supply chain are not disrupted, and unintended consequences (such as greater shortages or more rigidity in the supply chain) are minimized.

We defer to manufacturers on what specific investments should be made. However, we want to note that there are currently successes in the efficiency of the healthcare supply chain. When considering investments, we caution against actions that may disrupt the continuity of the supply chain. Any investments made into the healthcare supply chain should be considered carefully so that competition and continuity of the supply chain are not disrupted. HDA and our members advocate for increased supply chain resilience, which includes addressing drug shortages.

How has consolidation among Group Purchasing Organizations and Prescription Drug Wholesalers led to less redundancy in the drug supply chain? Has this consolidation

⁴⁵ Association for Accessible Medicines. "Drug Shortages: Causes & Solutions." Published 2023. https://accessiblemeds.org/sites/default/files/2023-06/AAM_White_Paper_on_Drug_Shortages-06-22-2023.pdf.

⁴⁶ IQVIA. Long, Doug. US Pharmaceutical Trends, Issues & Outlook for HDA. Presented March 13, 2023.

⁴⁷ Politico. "Non-Paper – Improving the security of medicines supply in Europe – (BE, AT, NL, LU, HU, CZ, ES, FR, DE, EE, SI, RO, LV, LT, EL, MT, PL, IT, PT)." Published May 2, 2023. <https://www.politico.eu/wp-content/uploads/2023/05/02/Non-paper-security-of-medicines-supply-02.05.23.pdf>.

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?

Primary pharmaceutical distributors are the vital link between the nation's pharmaceutical manufacturers and pharmacies, hospitals, long-term care facilities, clinics and other healthcare facilities across the nation. Consolidation among distributors has allowed them to be able to create redundancies to handle approximately 94 percent of medicines moved across the United States. Distributors provide necessary services to the healthcare supply chain; without distributors manufacturers and pharmacies would face logistical challenges connecting approximately 1,400 manufacturers to [330,000 sites of care daily](#).⁴⁸

The net profit margin after taxes for distributors was [0.6 percent](#)⁴⁹ in 2022; distributors operate with the smallest profit margins compared to other healthcare supply chain stakeholders. Business practices of prescription drug wholesalers have ensured resilience in the supply chain, by maintaining consistent partnerships with suppliers for product and providing a buffer to the manufacturer against the variability of ordering patterns of customers.

HDA and its members have been long-standing advocates of [enhancing supply chain resilience](#)⁵⁰ and understand the role they and their trading partners have within the healthcare supply chain. Supply chain resilience is a core component of responding to public health threats, which includes drug shortages. The core competencies of the healthcare supply chain have allowed distributors and their trading partners to utilize strategies to increase supply chain resilience and reduce drug shortages. As part of business operations, distributors create redundancies within the supply chain to bolster resilience and ensure adaptability. Those redundancies allow distributors to leverage their logistical expertise and coordination capabilities to create efficiencies, saving the healthcare ecosystem up to [\\$63 billion annually](#).⁵¹ Every day, distributors go above and beyond to provide value and efficiency within the healthcare supply chain.

While some supply chain stakeholders have sought to claim that pharmaceutical wholesalers conduct sole-source procurement for generic medicines, this is simply not a standard business practice for the distribution industry. Based on the dynamics of the pharmaceutical supply chain,

⁴⁸ Healthcare Distribution Alliance. "Delivering Value Across Healthcare." Published 2023. <https://hda.org/getmedia/807f7717-3a3a-4e8a-9011-2c8a91502dec/hda-factsheet-deliveringvalueacrosshealthcare-2023.pdf>.

⁴⁹ HDA Foundation. "93rd Edition HDA Factbook: The Facts, Figures and Trends in Healthcare." Published 2022. <https://www.hda.org/publications/93rd-edition-hda-factbook-the-facts,-figures-and-trends-in-healthcare/>.

⁵⁰ Healthcare Distribution Alliance. "HDA Guiding Principles for Increasing Supply Chain Resilience." Published 2022. <https://www.hda.org/getmedia/2d816602-0c28-46c6-a52f-d1d36c094cd9/Resilience-Report.pdf>.

⁵¹ Healthcare Distribution Alliance. "Delivering Value Across Healthcare." Published 2023. <https://hda.org/getmedia/807f7717-3a3a-4e8a-9011-2c8a91502dec/hda-factsheet-deliveringvalueacrosshealthcare-2023.pdf>.

multiple factors are considered – including reliability, cost, quality, supply, and sound business practices. Distributors maintain a strategy to ensure that their customer bases are supported by multiple manufacturers, and this supplier diversification strategy has redundancy at its core. Supplier diversification and stable contracting relationships with manufacturers are a part of the business strategy that ensures a constant supply of generic medicines. The current composition of the pharmaceutical wholesaler market has not impacted the redundancy in the pharmaceutical supply chain, because the number of customers (healthcare facilities) has not diminished. The number of customers ordering pharmaceutical product is the primary basis for the number of orders and demand for pharmaceutical product. Distributors build in redundancy for every type of product sourced.

From the distributor perspective, there are a number of factors to balance, most importantly the customer perspective. Ultimately, distributors procure the products that customers want to buy at the price customers are willing to pay. By maintaining a diversified supplier set in the supply chain strategy, distributors are maintaining both competition and redundancy in the market, while also working to provide generic manufacturers with the assurance of meaningful market share for awarded products. Additionally, the ordering patterns of customers can be highly variable. As a result, inventory held by distributors can act as a buffer thereby minimizing variability in ordering patterns to the manufacturer, which in turn assists their production planning.

Just-in-time inventory management⁵² systems have been used to ensure efficiency, reduce costs, and streamline delivery of pharmaceuticals in the pharmaceutical supply chain, a tool that can be used to build supply chain resilience and expand supply chain capacity. This strategy is important for healthcare facilities that have little capacity to hold large product volume, it also maximizes efficiencies and cost savings. For healthcare facilities, pharmacies and providers this strategy helps to reduce the need for large volume storage space, as well as reduces security risks of holding expensive (high risk of diversion) product on hand. However, distributors generally do not operate with solely a just-in-time inventory management system, as the distributor supply chain strategy ensures that there is some buffer available to ensure resilience, especially during times of likely surge (hurricane season, flu season, etc.). Increasing product inventory levels, specifically for products that would be at high risk of shortage (especially during a demand surge), is one strategy that could be considered and would require every part of the supply chain to hold more product. A key component of the value pharmaceutical distributors provide is the ability to track the market and manage supply in a manner that prevents or minimizes shortages. It is difficult to predict what product might be in shortage, so distributor capabilities help to anticipate disruptions and manage available supply without disrupting patient care.

⁵² Healthcare Distribution Alliance. “Insights and Recommendations From the National Academies’ Report on Building Resilience in the Nation’s Medical Product Supply Chain.” Published 2023. <https://www.hda.org/getmedia/7290a259-5893-4fbb-9391-d8a91aa3eb85/Insights-and-Recommendations-From-the-National-Academies-Supply-Chain-Report.pdf>.

Are there any other issues leading to drug shortages that we have not considered in this RFI?

Full implementation of the Drug Supply Chain Security Act

An issue that may lead to drug shortages is the full implementation of the Drug Supply Chain Security Act (DSCSA). This law was enacted in 2013 and will be fully implemented on November 27, 2023. As of November 27, 2023, supply chain trading partners will be required to provide and maintain serialized transaction data and serialized products upon a change of ownership. An example of a change of ownership is a manufacturer selling product to a distributor or a distributor to a pharmacy. This will allow the FDA to, at any point in the supply chain, trace a product's chain of custody at the unit level from the time it left a manufacturer's loading dock until it arrives at a pharmacy. Product traceability does not extend to the individual patient.

As of November 27, 2023, products that are not DSCSA compliant cannot be distributed. Those non-compliant products will include legitimate prescription drugs from drug manufacturers whose products do not have conforming serial numbers and/or corresponding electronic data records.

Distributors are preparing to comply with DSCSA's full implementation requirements, but are dependent on trading partners to also be ready for full implementation. [Manufacturers are reporting](#)⁵³ that they are facing difficulties meeting DSCSA's full implementation requirements. Unless all healthcare supply chain stakeholders are fully ready to comply with DSCSA requirements on November 27, 2023, or there is government intervention, there will likely be disruptions in the healthcare supply chain.

[HDA and its members have recommended](#)⁵⁴ that the FDA issue guidance, as quickly as possible, address the genuine potential of drug shortages and supply chain disruptions resulting from the healthcare supply chain stakeholders not being fully ready for the full implementation of DSCSA. HDA has also submitted a plan to FDA for a phased approach to implementing this important law. This phased implementation strategy would allow the law to go into effect on November 27, 2023, but provide flexibility to allow manufacturers to ensure that the products and data they are sharing with downstream trading partners are accurate and able to be forwarded to subsequent supply chain provider organizations.

⁵³ Healthcare Distribution Alliance. "HDA Survey Results Indicate More Preparation Necessary for Connecting EPCIS-Enabled Systems Before DSCSA Deadline." Published May 22, 2023. <https://www.hda.org/newsroom/2023/hda-survey-results-indicate-more-preparation-necessary-for-connecting-epcis-enabled-systems-before-d/>.

⁵⁴ Healthcare Distribution Alliance. "HDA Comments to the FDA on the State of DSCSA Readiness." Published February 6, 2023. <https://www.hda.org/getmedia/c1deccbd-3dfd-4765-bbe6-126deaccfaaa/HDACommentsonFDAMeetingFollowUp262023.pdf>.