

The Vital Role of Group Purchasing Organizations in Alleviating Drug Shortages in the United States



A publication of the Healthcare Supply Chain Association (HSCA) with research and compilation of findings

The Role of Group Purchasing Organizations in Mitigating the Effects of Drug Shortages

Executive Summary

Shortages in drugs and biologics are of critical and current national policy concern in the United States, Canada, and abroad.¹ Despite some successes in the fight against shortages of critical prescription drugs, reports indicate that drug shortages continue to be a significant public health threat.² The Healthcare Supply Chain Association (HSCA) and its group purchasing organization (GPO) members remain committed to being a part of the solution. GPOs have made significant efforts to ensure that hospitals and patients have access to the life-saving drugs they need. This report includes a discussion on:

- 1) The ongoing drug shortages;
- 2) The causes of these shortages;
- 3) Case studies regarding what the GPO industry is actively doing to combat this important problem; and
- 4) Policy recommendations to further address the drug shortage problem.

The U.S. Food and Drug Administration (FDA) defines a drug shortage as “a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug.”³

The number of drug shortages remains high. Nearly half involve generic sterile injectables. While cancer drugs are among the products most vulnerable to shortages, a variety of other products are also susceptible to shortages, including heart drugs, pain medications, intravenous (IV) electrolytes, and many others.⁴

The U.S. Government Accountability Office (GAO) recently published a report that reviewed the most recent drug shortage trends using “data from the University of Utah Drug Information Service (UUDIS) on drugs that were in short supply from January 1, 2007, through June 30, 2013, which were the most recent data available at the time” when UUDIS conducted its research.⁵ According to UUDIS, “[t]hese data are generally regarded as the most comprehensive and reliable source of drug shortage information for the time period” UUDIS

¹ See for example, “Cancer Drug Shortages Hit 83 Percent of U. S. Oncologists.” June 3, 2013. ScienceDaily. <http://www.sciencedaily.com/releases/2013/06/130603090547.htm> See also “Voluntary drug-shortage reporting adopted despite concerns” CBC News Online. December 28, 2012. <http://www.cbc.ca/news/health/story/2012/12/27/health-minister-drug-shortage-plan-approval.html> Kermani, Faraz. “Germany’s New Drug Register To Help Tackle Supply Shortages, But Larger EU Problem Looms.” The Pink Sheet. May 13, 2013. <http://www.elsevierbi.com/publications/the-pink-sheet/75/19/germanys-new-drug-register-to-help-tackle-supply-shortages-but-larger-eu-problem-looms>.

² GAO, Drug Shortages, Public Health Threat Continues, Despite Efforts to Help Ensure Product Availability, GAO-14-194 (Washington, D.C.: February 10, 2014).

³ Department of Health and Human Services Food and Drug Administration, Report to Congress, First Annual Report on Drug Shortages for Calendar Year 2013 Required by Section 1002 of the Food and Drug Administration Safety and Innovation Act Public Law 112-144, February 5, 2014.

⁴ Ventola, C Lee. “The Drug Shortage Crisis in the United States.” P T. 2011 November; 36(11): 740-742, 749-757. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278171/>

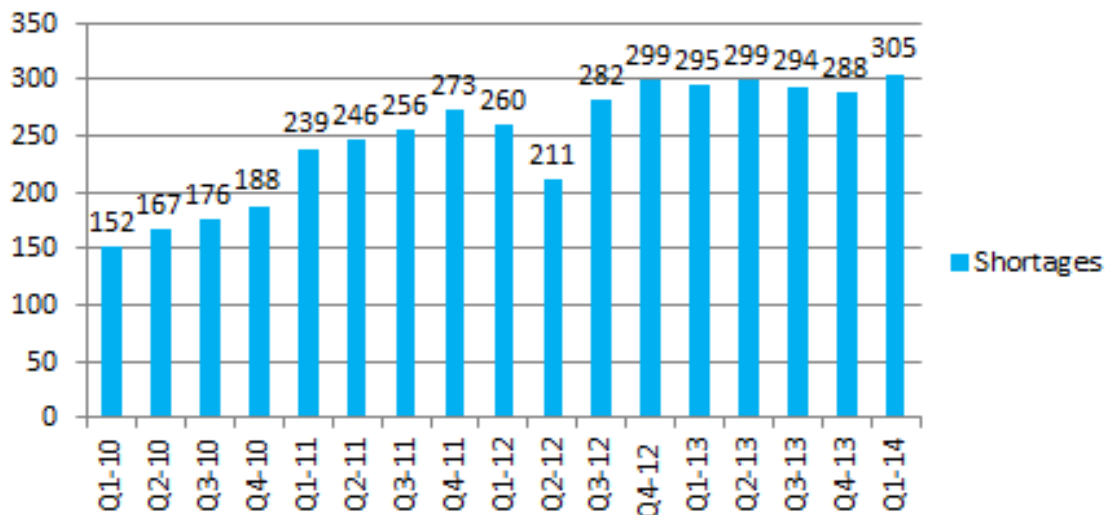
⁵ GAO, Drug Shortages, Public Health Threat Continues, Despite Efforts to Help Ensure Product Availability, GAO-14-194 (Washington, D.C.: February 10, 2014) p. 2.

reviewed and are what the program used in preparing its 2011 report.”⁶ It is worth noting that one HSCA member GPO has for years provided essential funding and support for the UUDIS program.⁷ During the same month that GAO issued its report, a HSCA member released a report detailing the results of its Drug Shortage Survey.⁸ It surveyed pharmacy experts representing its alliance member hospitals to obtain information about their experiences with drug shortages.⁹

The average duration of a drug shortage is 18 months or longer. As of the first quarter of 2014, there were over 300 active shortages in the U.S. (see table immediately below).¹⁰ The effects of these shortages, which include delays and compromised quality of patient care as well as substantial cost burdens on care in specialties such as oncology, have been widely reported in a number of national surveys.¹¹

National Drug Shortages – Active Shortages by Quarter

Active Shortages



Note: Each column represents the number of active shortages at the end of each quarter.
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⁶ GAO, Drug Shortages, Public Health Threat Continues, Despite Efforts to Help Ensure Product Availability, GAO-14-194 (Washington, D.C.: February 10, 2014) p. 2.

⁷ Novation, based in Irving, Texas, is owned by VHA and UHC as well as providing services to the Children’s Hospital Association and Provista members.

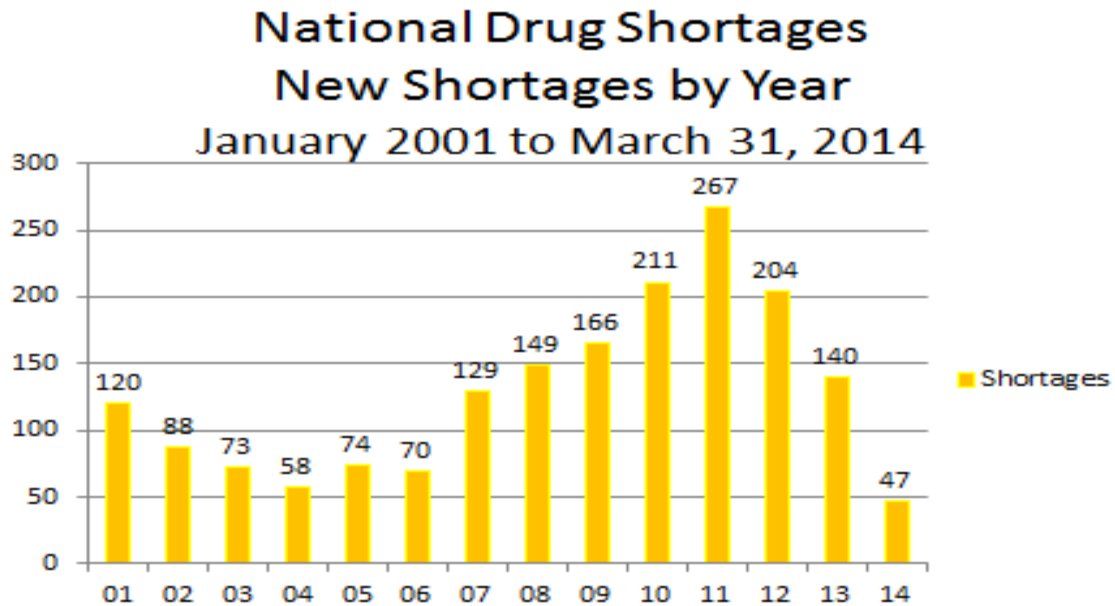
⁸ Premier Inc., Drug shortages 2014: A Premier healthcare alliance update (February 2014).

⁹ Premier Inc., Drug shortages 2014: A Premier healthcare alliance update (February 2014).

¹⁰ <http://www.ashp.org/menu/DrugShortages/CurrentShortages#>; <http://www.ashp.org/DocLibrary/Policy/DrugShortages/Drug-Shortages-Statistics.pdf>

¹¹ “Cancer Drug Shortages Hit 83 Percent of U.S. Oncologists.” Penn Medicine News Release, June 3, 2013.

http://www.uphs.upenn.edu/news/News_Releases/2013/06/gogineni/?utm_source=feedburner&utm_medium=feed&utm_campaign=



Note: Each column represents the number of new shortages identified during that year.

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What are the Causes of Drug Shortages?

The causes of shortages are multifactorial and consequently, their resolution requires integration and collaboration among a wide range of stakeholders beyond federal agencies. The FDA Commissioner has stated that the majority of drug shortages, an estimated 70 percent, are the result of a breakdown in quality and manufacturing.¹² While recent Congressional actions and activities by FDA have bolstered the supply of certain drugs¹³, patient, provider, and other stakeholder concerns continue given the belief that these efforts are not sufficient to fully address the causes of current shortages, or to prevent future shortages.

In this paper, the Healthcare Supply Chain Association (HSCA), the leading trade association for the nation’s GPOs, contributes to ongoing policy dialogues on drug shortages by demonstrating the vital role of GPOs in alleviating pressure on the drug supply chain in the U.S. It is intended to highlight the role of GPOs as key stakeholders in mitigating the impact of the drug shortage crisis. GPOs are entities that help healthcare providers — such as hospitals, nursing homes and home health agencies — realize savings and efficiencies by aggregating purchasing volume and using that leverage to negotiate discounts with manufacturers,

Feed%3A+penn-medicine-news+%28Penn+Medicine+News%29 A Shortage of Everything Except Errors: Harm Associated with Drug Shortages. April 19, 2012. Institute for Safe Medication Practices.

<http://www.ismp.org/Newsletters/acutecare/showarticle.asp?id=20> Kaakeh R, Sweet BV, Reilly C, Bush C, DeLoach S, Higgins B, Clark AM, Stevenson J. Impact of drug shortages on U.S. health systems. American Journal of Health-System Pharmacy. 2011; 68:e13-e21. http://www.aihp.org/site/DrugShortages.pdf?fm_preview=1

¹² Dr. Peggy Hamburg, *FDA Creates Plan To Combat Drug Shortages*, Gastroenterology & Endoscopy News (April 2014).

¹³ Six Month Check Up: FDA’s Work on Drug Shortages. <http://blogs.fda.gov/fdavoices/index.php/2012/05/six-month-check-up-fdas-work-on-drug-shortages/>

distributors, and other vendors.¹⁴ In fulfilling their functions, GPOs (1) track data on drug shortages, (2) strategize with members when there is a potential for a supply disruption, and (3) communicate with manufacturers and distributors when they anticipate a supply problem.

The GPO industry fully supports recent regulatory and legislative activities aimed at solving the drug shortage problem, and remains dedicated to exploring and identifying multi-stakeholder solutions. As an industry, GPOs are committed to alleviating the harmful impacts of scarcity in the U.S. drug market. Collectively, the GPO industry has been committed to:

- 1) Working with manufacturers to ensure timely and appropriate supply of products.
- 2) Working with its supplier partners to communicate and forecast the product demands of provider members. Manufacturers that receive this information from GPOs in a timely fashion are better positioned to have more advance notice about demand and better able to plan their production capacity.
- 3) Supporting entities that facilitate reporting on shortages and alert members of potential access issues. GPOs use various modes of communication to provide this information, including webinars, conferences, newsletters, and electronic alerts as issues warrant.

In addition to these efforts, the HSCA continues to call on all relevant stakeholders to address the drug shortage crisis. The GPO industry has identified specific recommendations that aim to mitigate drug shortages through the following means:

Improving FDA's approval and regulatory processes

- Supporting necessary FDA resources to ensure timely responses to market entry and production issues
- Encouraging the FDA to institute an accelerated approval process for new sources of supply or manufacturing for items listed as in short supply

Adopting early notification systems and public communication

- Having manufacturers provide GPOs with early, advanced warning of potential drug shortages and/or notable increases in product demand
- Strengthening current FDA six-month notification rule
- Developing a broader definition of how FDA defines "medically-necessary" drugs
- Improving FDA website to enhance communication
- Evaluating, and where appropriate, applying, best practices from other countries experiencing shortages
- Requiring immediate allocation of products in shortage by the manufacturer and its authorized distributors to minimize speculative purchasing and hoarding (while recognizing previously existing contractual relationships needing to be respected)

Implementing market and operational efficiencies

- Improving FDA regulatory violation process
- Advocating for FDA to ensure quality in the sterile pharmacy compounding space through regular inspections of compounding outsourcing facilities

¹⁴ Healthcare Supply Chain Association Website. <http://www.supplychainassociation.org/>

- Create “scorecard” information converted from quality indications currently residing within FDA to an easy to access website that provides transparency regarding this data to purchasers in a concise format that trends manufacturer performance in a “quality performance report”

HSCA members are also committed to partnering with all participants in the distribution chain to find proactive, novel, and flexible means to ensure patient access to critical medications.

I. Shortages Are a Multifactorial Problem

Multiple government reports, empirical studies, and academic articles regarding drug shortages, which began increasing in the U.S. in 2005¹⁵, indicate there is no single factor driving the shortages phenomenon but rather a combination of economic and non-economic forces combine to create gaps in the drug supply chain. Some of the most often discussed factors include:

- The availability of pharmaceutical ingredients
- The quality of active pharmaceutical ingredients
- Drug recalls
- “Gray markets”
- Industry consolidation
- Quality control at manufacturing plants
- Regulatory enforcement
- Reduced manufacturing line capacity
- Just-in-time inventories, etc.

Below, we address just a few of these issues.

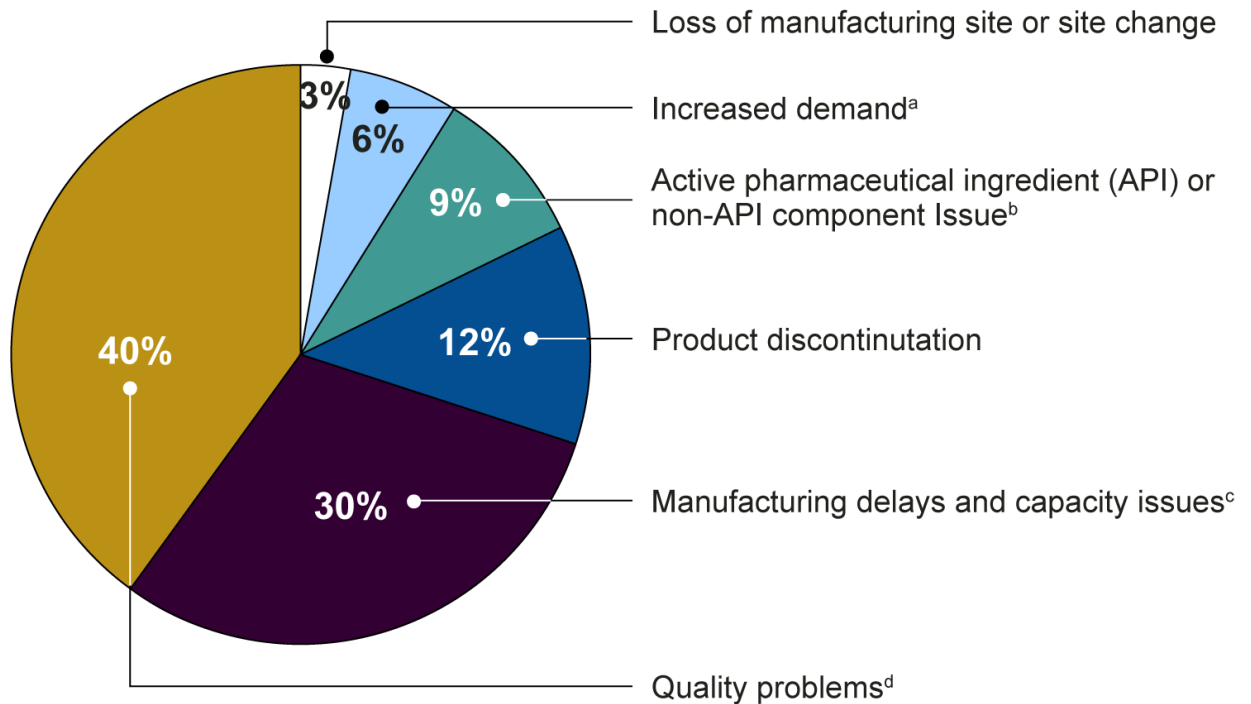
Economic Causes

The expansion of the generic products industry is often cited as a driving economic force behind existing shortages. An October 2011 report by the Assistant Secretary for Planning and Evaluation (ASPE) attributed the cause of drug shortages primarily to the “substantial expansion of the scope and volume of products” produced by the generic drug industry in a short period of time, “without a corresponding expansion in manufacturing capacity.”¹⁶ This expansion in production was prompted by an overall increase in the volume of chemotherapy drugs used and a high rate of patent expirations on the originator reference products that began in 2008. The chart below summarizes information reported by manufacturers to FDA about the causes of drug shortages that the Agency then analyzes and categorizes.¹⁷

¹⁵ Hanninger, Jessup and Amber Koehler, “ASPE Issue Brief: Economic Analysis of the Causes of Drug Shortages.” October 2011. <http://aspe.hhs.gov/sp/reports/2011/drugshortages/ib.shtml>

¹⁶ Hanninger, Jessup and Amber Koehler, “ASPE Issue Brief: Economic Analysis of the Causes of Drug Shortages.” October 2011. <http://aspe.hhs.gov/sp/reports/2011/drugshortages/ib.shtml>

¹⁷ GAO, Drug Shortages, Public Health Threat Continues, Despite Efforts to Help Ensure Product Availability, GAO-14-194 (Washington, D.C.: February 10, 2014) p. 27.



Source: GAO analysis of FDA data.

Vulnerabilities in the structure of the drug market, in particular the lack of incentives for generic drug manufacturers to ensure that manufacturing capacity can always match demand (essentially over-accommodating existing demand), are also contributing to the worsening of shortages. Medicare’s Part B drug reimbursement formula, as altered by the Medicare Modernization Act of 2003, seems to have reduced the incentive for suppliers to invest in increased manufacturing capacity in response to shortages.¹⁸ The 2003 law changed the original reimbursement formula based on "average wholesale price" of the drugs to a formula based on "actual average sales price" (ASP) recorded in the marketplace; this was ASP plus a markup of 6 percent. The modification resulted in lower reimbursement levels for many drugs, especially for sterile injectables.¹⁹ While many have hypothesized that the ASP-based reimbursement system used by Medicare Part B has exacerbated the drug shortage crisis, the data on this subject is inconclusive. What this does show, however, is that a plethora of potential contributing factors exist, emphasizing why one single, unilateral fix is unlikely to exist.

Causes Related to Manufacturing Quality and FDA Enforcement

Manufacturing quality and sterility problems can combine with economic and technological factors to result in shortages. In an article published in *Clinical Pharmacology & Therapeutics*,

¹⁸ Michael P. Link, Karen Hagerty, Hagop M. Kantarjian. "Chemotherapy Drug Shortages in the United States: Genesis and Potential Solutions." *Journal of Clinical Oncology*. January 2012. <http://jco.ascopubs.org/content/30/7/692.full>. See also Rye Brian, "Medicare Price Controls Worsen Drugs Shortages, Boost Grey Markets." Bloomberg Government Study. October 2012. [http://glacialblog.com/userfiles/76/BGov_Drug_Shortage_Report\(2\).pdf](http://glacialblog.com/userfiles/76/BGov_Drug_Shortage_Report(2).pdf)

¹⁹ Rye Brian, "Medicare Price Controls Worsen Drugs Shortages, Boost Grey Markets." Bloomberg Government Study. October 2012. [http://glacialblog.com/userfiles/76/BGov_Drug_Shortage_Report\(2\).pdf](http://glacialblog.com/userfiles/76/BGov_Drug_Shortage_Report(2).pdf)

FDA's Dr. Janet Woodcock and Marta Wosinska, PhD, noted that an important but largely unrecognized aspect of quality in the area of sterile injectables is the ability to reliably meet customer demand. They note that "the inability of the market to observe and reward quality" is a fundamental problem because it reinforces price competition and encourages manufacturers to keep costs down by minimizing quality investments.²⁰ A lack of sustained investment in infrastructure and vigilant quality focus can result in problems in manufacturing reliability. While not every production disruption results in a drug shortage, virtually all shortages are preceded by disruptions in production. Too few supply disruptions are anticipated by manufacturers ahead of time, and with multi-use facilities (i.e., facilities that make several different products) the shortage of one product can have a domino effect on others produced at the same facility.

FDA enforcement actions against manufacturers have also triggered shortages. A House Committee on Oversight and Government Reform report found that of the 219 drugs listed on a shortage list provided by the American Society of Health-System Pharmacists (ASHP) in February 2012, at least 128 products (58 percent) were produced by at least one facility undergoing FDA remediation. The report also observed: "Instead of calling for targeted fixes of troubled plants, the Agency has often required manufacturers to undertake costly, general upgrade[s] to facilities."²¹ According to the report, this "simultaneous remediation" in the past four years has reduced available capacity at facilities by 30 percent relative to capacity in 2009.²² An estimated 30 percent of U.S. drug-manufacturing capacity is currently offline as a result of FDA actions.²³

Global Causes

Despite the widespread tendency to analyze drug shortages through a domestic lens, it is important to recognize that the causes of shortages extend beyond the U.S.'s borders. A number of countries, including Canada and Germany, are similarly facing shortages in supply of critical medications.²⁴ The instability in the supply chain of foreign markets is important to consider because at least 40 percent of drugs on U.S. shelves come from overseas.²⁵ Importantly, U.S. manufacturers rely on foreign manufacturers to produce active pharmaceutical ingredients (API) (i.e., the active component of a drug) for their drugs. Eighty percent of manufacturers of active pharmaceutical ingredients are currently located outside of the U.S.²⁶ This dependence on external sources makes the U.S. drug supply chain vulnerable. Supply

²⁰ J Woodcock and M Wosinska Economic and Technological Drivers of Generic Sterile Injectable Drug Shortages *Clinical Pharmacology & Therapeutics* (2013); 93 2, 170–176.

<http://www.nature.com/clpt/journal/v93/n2/full/clpt2012220a.html>

²¹ Committee on Oversight and Government Reform. FDA's Contribution to the Drug Shortage Crisis. Staff report. June 15, 2012. <http://oversight.house.gov/wp-content/uploads/2012/06/6-15-2012-Report-FDAs-Contribution-to-the-Drug-Shortage-Crisis.pdf>

²² Committee on Oversight and Government Reform. FDA's Contribution to the Drug Shortage Crisis. Staff report. June 15, 2012 at 18. <http://oversight.house.gov/wp-content/uploads/2012/06/6-15-2012-Report-FDAs-Contribution-to-the-Drug-Shortage-Crisis.pdf>

²³ Dr. Erin Fox, *Gastroenterology & Endoscopy News*, April 2014.

²⁴ See for example, "Voluntary drug-shortage reporting adopted despite concerns" CBC News Online. December 28, 2012.

<http://www.cbc.ca/news/health/story/2012/12/27/health-minister-drug-shortage-plan-approval.html> Kermani, Faraz. "Germany's New Drug Register To Help Tackle Supply Shortages, But Larger EU Problem Looms." *The Pink Sheet*. May 13, 2013.

<http://www.elsevierbi.com/publications/the-pink-sheet/75/19/germanys-new-drug-register-to-help-tackle-supply-shortages-but-larger-eu-problem-looms>

²⁵ Presentation by Deborah Autor, (Deputy Commissioner for Global Regulatory Operations and Policy, FDA) at Petrie-Flom Conference, May 3, 2013. Video available here: <http://vimeo.com/66657276>

²⁶ Presentation by Deborah Autor, (Deputy Commissioner for Global Regulatory Operations and Policy, FDA) at Petrie-Flom Conference, May 3, 2013. Video available here: <http://vimeo.com/66657276>

disruptions that occur abroad and concerns about the safety and quality of foreign facilities are contributing to existing shortages. Therefore, while imports are often viewed as a means of mitigating the shortage problem, they are not a true solution because of the instability in other regulated markets.

II. Effects of Drug Shortages

Drug Shortages Impact Patient Access and Quality of Care

While the precise clinical impacts of each drug shortage are not always known and are often difficult to measure, shortages have a widespread effect on patients' access to and quality of care. This effect has been documented in several studies, most recently in a survey study of 250 board-certified U.S. oncologists presented by the Abramson Cancer Center and the Perelman School of Medicine at the University of Pennsylvania at the annual meeting of the American Society of Clinical Oncology in June 2013.²⁷ The survey revealed that 83 percent of U.S. oncologists are experiencing drug shortages.²⁸ In particular, it found that 43 percent of oncologists delayed their patients' treatments and 78 percent of oncologists reported treating patients with a different drug or drug regimen than the one they would have selected originally, which sometimes involved unknown risks to patient safety.²⁹ In addition, the study revealed the frequency with which healthcare providers are forced to make difficult ethical decisions about distributing scarce drugs among different but equally vulnerable patients, with little guidance. Seventy percent of the oncologists surveyed reported that they made their decisions in the absence of formal policies.³⁰

Drug Shortages Drive up the Costs of Care

Shortages are resulting in substantial burdens on the costs of healthcare that vary for different therapeutic areas. The cost of both scarce drugs and their substitutes have risen in recent years, but shortages are contributing to excessive price increases in previously low-cost generic drugs. Providers have difficulty accessing generic drugs. Manufacturing problems also contribute to shortages given amelioration requires a substantial up-front investment on which the return can only be achieved over multiple years. According to the University of Pennsylvania study, physicians had to use branded drugs in place of generic drugs in 60

²⁷ "Cancer Drug Shortages Hit 83 Percent of U.S. Oncologists." Penn Medicine News Release, June 3, 2013.
http://www.uphs.upenn.edu/news/News_Releases/2013/06/gogineni/?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+penn-medicine-news+%28Penn+Medicine+News%29

²⁸ "Cancer Drug Shortages Hit 83 Percent of U.S. Oncologists." Penn Medicine News Release, June 3, 2013.
http://www.uphs.upenn.edu/news/News_Releases/2013/06/gogineni/?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+penn-medicine-news+%28Penn+Medicine+News%29

²⁹ "Cancer Drug Shortages Hit 83 Percent of U.S. Oncologists." Penn Medicine News Release, June 3, 2013.
http://www.uphs.upenn.edu/news/News_Releases/2013/06/gogineni/?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+penn-medicine-news+%28Penn+Medicine+News%29

³⁰ "Cancer Drug Shortages Hit 83 Percent of U.S. Oncologists." Penn Medicine News Release, June 3, 2013.
http://www.uphs.upenn.edu/news/News_Releases/2013/06/gogineni/?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+penn-medicine-news+%28Penn+Medicine+News%29

percent of cases, which can be exponentially more expensive – at times as much as 140 times more.³¹

III. The Evolving Policy Framework

Efforts to ameliorate shortages have focused on improving FDA's capacities to respond to the drug shortage crisis and, more generally, creating a more effective advance warning system for impending shortages such that additional steps can be taken in a more timely manner. In November 2011, President Obama issued Executive Order 13588 that broadened drug shortage reporting requirements by clarifying FDA's authority under Section 506C of the Federal Food, Drug, and Cosmetic Act (FDCA).³² This section requires manufacturers to notify the Agency at least six months prior to discontinuing the manufacture of drug products used for treatment or prevention of serious medical conditions or diseases (recognizing that this is particularly difficult for manufacturers if it is an FDA inspection that precipitates the manufacturing hiatus). Although the Executive Order prompted a six fold increase in reporting in 2011 by encouraging FDA to broadly use the administrative tools at its disposal, but under the FDCA, the Agency does not have authority to impose penalties for non-compliance.³³

In recent years, the Agency has also encouraged manufacturers to voluntarily report anticipated shortages of any prescription drugs. With this comprehensive tracking system in place, the Agency has taken specific actions to resolve shortages, which include expediting review of manufacturer submissions and identifying alternate sources for the drug.³⁴

In addition, the Drug Supply Chain Security Act (DSCSA) was signed by President Obama on November 27, 2013.³⁵ The Act addresses two concerns related to the drug supply. Title I of the Act addresses issues surrounding the safety of pharmaceuticals that are created in the process of compounding – which is the mixing of two or more ingredients to tailor a drug to a specific patient's needs – and Title II of the Act implements a "lot-based pedigree" system that preempts state law.

In the past, compounded sterile products often were overlooked by state and federal regulators. That was until 2012 when the New England Compounding Center was found to have manufactured and sold contaminated steroid injections in 20 states that caused a fungal meningitis outbreak that affected 750 people and was linked to 64 deaths. Although this was not the first time problems were identified with compounded sterile products, the case exposed the flaws in government surveillance and led to Congress giving the FDA more authority over compounders. The law attempts to provide more clarity over state-regulated compounding in

³¹ "Cancer Drug Shortages Hit 83 Percent of U.S. Oncologists." Penn Medicine News Release, June 3, 2013. http://www.uphs.upenn.edu/news/News_Releases/2013/06/gogineni/?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+penn-medicine-news+%28Penn+Medicine+News%29

³² Executive Order 13588 -- Reducing Prescription Drug Shortages, The White House, Office of the Press Secretary. <http://www.whitehouse.gov/the-press-office/2011/10/31/executive-order-reducing-prescription-drug-shortages>

³³ However, FDA is required to issue a non-compliance letter to manufacturers who fail to comply with the drug shortage notification requirements and to make the letter and the company's response to the letter available to the public.

³⁴ Guidance for Industry: Notification to FDA of Issues that May Result in a Prescription or Biological Product Shortage; Draft Guidance (FDA, HHS Feb. 2012), available at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM292426.pdf>

³⁵ Public Law No: 113-54.

hospitals and federal oversight of manufacturers. More recently, FDA in January 2014 urged hospitals to buy drugs only from compounding outsourcing facilities that voluntarily register with the Agency and abide by “good manufacturing practices. GPOs support efforts to have compounders register with FDA.³⁶ The scrutiny of sterile compounding will not stop there. For example, the Office of Inspector General (OIG) for the U.S. Department of Health and Human Services (HHS) will put Medicare oversight of pharmaceutical compounding in hospitals under the microscope. The OIG’s 2014 Work Plan, notes that “most hospitals compound at least some pharmaceuticals on-site.” OIG will look at the quality and safety of sterile compounding practices and examine how the Centers for Medicare & Medicaid Services (CMS) oversee compounding through accreditation and certification.

Title II of the law is often referred to as the “Drug Quality and Security Act.” The law contains a number of requirements including instructions for FDA; manufacturer requirements; wholesale distributor requirements; dispenser requirements; and repackager requirements. For the first 10 years, the DSCSA implements a lot-based pedigree system. That is, for each drug in a shipment, most sellers of drugs in the supply chain will be legally obligated to provide buyers with specific:

- “Transaction Information”;
- “Transaction History”; and
- “Transaction Statements”.

The data does NOT include serial numbers but is at the lot level. This data may be provided in either paper or electronic format and must be retained and retrievable within 48 hours for 6 years after the transaction. Manufacturers must provide this data electronically in 4 years, except when selling directly to a practitioner. This new law may positively affect the drug supply because it will make the process of tracking and tracing of pharmaceuticals more secure and less vulnerable to “gray market” activities. Gray market companies offer to sell shortage drugs for prices that are often hundreds of times higher than the prices they normally pay.³⁷

While these activities have enhanced the supply of certain drugs, there is clearly a need for greater multi-stakeholder involvement to fully address the causes of current shortages and prevent their reoccurrences – GPOs have a vital role to perform in these multi-stakeholder efforts, as will be illustrated in the remainder of this briefing paper.

IV. Background on the Role of GPOs in the Prescription Drug Supply Chain

Group purchasing organizations are buying cooperatives that leverage the collective purchasing power of healthcare providers to negotiate discounts with manufacturers, distributors and other vendors for an array of medical products, capital equipment, and service contracts.

³⁶HSCA Applauds FDA for Leadership on Improving Safety of Drug Compounding, Supports FDA Registry of Compounding Facilities, January 21, 2014
http://c.ymcdn.com/sites/www.supplychainassociation.org/resource/resmgr/press_releases_2014/hzca_statement_on_compoundin.pdf

³⁷<http://www.rockefeller.senate.gov/public/index.cfm/2012/7/rockefeller-says-gray-market-drug-companies-are-profiting-while-hurting-wv-hospitals-and-patients>

Manufacturers receive economies of scale when collaborating with GPOs. By representing the purchasing needs of their clients, GPOs are situated on the demand side of the drug supply chain. Nearly every U.S. hospital uses a GPO to realize savings and supply chain efficiencies and many belong to multiple GPOs.³⁸ In most cases, hospitals purchase drugs through wholesalers at prices negotiated by the GPO.

The mission of a GPO is to contract for products and services, including drugs, that are essential to the operation of hospitals and other healthcare facilities. Through these contract negotiations, GPOs work to obtain the best value for their members and clients, including the lowest possible price for a reliable and safe supply of goods and services. Hospitals use GPO-contracted prices voluntarily – each drug purchase is ultimately made by the hospital or healthcare provider. As a result, hospitals have the ability to pick and choose among multiple options when purchasing these drugs.

GPOs Offer Providers Supply Chain Efficiencies and Cost Savings

GPOs serve as a partner to hospitals and other healthcare providers by negotiating contracts that the latter can use when purchasing essential supplies. GPOs and manufacturers engage in sophisticated contract negotiations. The negotiation process is highly dynamic in that manufacturers are able to adjust pricing based on normal market conditions, such as manufacturing capacity, raw material availability, and competitive suppliers. GPOs manage thousands of price adjustments annually.³⁹ While GPOs are concerned about the need to control healthcare costs and strive to negotiate the best price possible for hospitals and other healthcare providers, a GPO's first and foremost priority is to find and contract for the supplies needed by their own customers and to obtain a reasonable price.

When providers opt to purchase through GPO contracts, they can achieve savings of 10 to 15 percent.⁴⁰ It should be noted that GPOs do not purchase or take ownership of products – rather they develop and negotiate competitive contract pricing. Importantly, it is a wholesaler/distributor that maintains the pedigree of a product, takes ownership of medical products, and then sells the drugs to the GPO members at the GPO-negotiated price. GPOs often have multi-year contracts with manufacturers to secure the best prices and safeguard product availability for hospitals. The manufacturers use the volume projections to forecast manufacturing quantities. GPOs include “failure to supply” clauses in their contracts with suppliers but only when manufacturers will agree to these terms. The purpose of this clause is to discourage generic manufacturers from bidding too low and subsequently not delivering on a contracted supply. When manufacturers underbid on a particular drug, they can potentially drive other manufacturers out of the market for that drug. When a manufacturer is unable to supply the drug under a GPO contract price, the hospital has to purchase a drug from another manufacturer at a higher price than for the GPO-contracted rate. By agreeing to the

³⁸Healthcare Supply Chain Association. A Primer on Group Purchasing Organizations, http://www.supplychainassociation.org/resource/resmgr/research/gpo_primer.pdf (accessed November 2, 2011).

³⁹The Impact of Group Purchasing Organizations on Healthcare-Product Supply Chains by Joice Hu, Leroy B. Schwarz, and Nelson A. Uhan, Krannert School of Management, Purdue University (May 2011).

⁴⁰Healthcare Supply Chain Association. A Primer on Group Purchasing Organizations, http://www.supplychainassociation.org/resource/resmgr/research/gpo_primer.pdf (accessed November 2, 2011).

“failure to supply” clause, the manufacturer commits to pay the difference between the two prices.

GPOs Offer Value-Added Services

In addition to offering discounted prices for medical supplies to their members, GPOs provide them with strategic advice. For example, many GPOs offer e-commerce solutions to help providers manage the complex system of purchasing. These platforms help providers streamline purchasing and reduce administrative overhead by using a web-based product ordering system. Moreover, some GPOs assist providers in reducing medical errors by helping hospitals standardize product use and by educating clinicians on best practices.⁴¹ GPOs often offer benchmarking data services for staffing, inventory controls and other programs, by working directly with their provider members to identify opportunities for cost savings and processes for measuring outcomes.⁴² In turn, this helps hospitals improve patient capacity and health outcomes. Finally, GPOs offer additional services like continuing medical and pharmacy education, materials management outsourcing, and market research.⁴³

V. Case Studies: How GPOs Help Mitigate the Drug Shortage Crisis

GPOs have various tools in their arsenal for mitigating drug shortages. The following GPO case studies include the ways in which several GPOs successfully employed strategies to expand production capacity for drugs in short supply and to ensure shortages are reported in a timely manner.

Case Study 1: GPO Provides Financial and Technical Support for Alerting the Public about Drug Shortages

Strategy

GPO provides funds to University hospital. University hospital publishes a critical drug list (i.e., a list of drugs that are vulnerable to shortage) based on data it compiles, and publishes these on the website of a national professional association. GPO also seeks to educate its members and the broader public about the causes, effects, and solutions to drug shortages through various communication strategies.

Implementation

Under its contract with GPO, University hospital develops the content that professional association then publishes on its website. While FDA only reports on those drugs that are

⁴¹Healthcare Supply Chain Association. A Primer on Group Purchasing Organizations, http://www.supplychainassociation.org/resource/resmgr/research/gpo_primer.pdf (accessed November 2, 2011).

⁴² Group Purchasing Organizations (GPOs) Work to Maintain Access to Product Supply for America's Health Care Providers (2011). Available at: http://c.ymcdn.com/sites/www.supplychainassociation.org/resource/resmgr/research/gpo_drug_shortage_paper.pdf

⁴³ Group Purchasing Organizations (GPOs) Work to Maintain Access to Product Supply for America's Health Care Providers (2011). Available at: http://c.ymcdn.com/sites/www.supplychainassociation.org/resource/resmgr/research/gpo_drug_shortage_paper.pdf

defined by the Agency as being “medically necessary,”⁴⁴ the professional association’s critical drug list is more comprehensive as it includes information about drug shortages that may impact a variety of areas in clinical practice such as oncology and anesthesiology. In contrast, the professional association’s website also provides information on how to access drugs in short supply and where to find alternative sources, if possible. In addition to funding the University’s program, GPO also regularly publishes its own drug shortage alerts on the Internet, sends weekly digest newsletters about developments impacting its healthcare members, and hosts web conferences on the causes and patient care implications of shortages and gray markets.

Impact

Hospital pharmacies highly value the information alerts provided by University hospital and the professional association. The professional association website and GPO’s other public outreach projects aim to detect shortages early, enabling providers time to create effective solutions, such as negotiating increases in manufacturing capacity where possible and locating alternative sources of supply.

Case study 2: GPO Encourages Production of Critical Drugs through Innovative Agreements that Provide Certainty to Manufacturers

Strategy

GPO incentivizes drug manufacturers to produce agreed-upon quantities of certain critical drugs and drugs in short supply (identified with help from member clinicians and the University) by reducing the financial risk manufacturers incur with such production. To accomplish this, GPO now provides manufacturers with the estimated purchasing needs of its members, and then agrees to compensate manufacturers if GPO members’ demand for these drugs falls below the estimated amount. GPO’s willingness to provide these assurances on behalf of healthcare providers encourages drug manufacturers to increase overall production of drugs that might not otherwise have been manufactured. Therefore, it is likely there are more products available for the entire healthcare industry. GPO’s strategy is premised on creating capacity and providing certainty thereby reducing risk for all stakeholders. The manufacturers have certainty around hospitals’ demands for products, while hospitals have certainty as to access to an adequate supply.

Implementation

In 2013, GPO worked with the University and member clinicians to identify a core set of acute-care critical and injectable drugs in short supply. GPO then launched a competitive bid for these drugs. GPO is now negotiating with the manufacturers of these critical drugs to reach agreement as to the production quantities, based on the estimated needs of GPO’s member hospitals. In return for these commitments, GPO agreed to compensate drug manufacturers if actual member purchases fell below the estimated volume of drugs. By providing demand

⁴⁴ Manual of Policies and Procedures MAPP 6003.1, Drug Shortage Management at 19.
<http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM079936.pdf>

certainty to manufacturers and assuming their financial risk, GPO's program offers one way to alleviate some of the pressures in the drug shortage crisis.

Impact

GPO's negotiations now cover 82 percent of the identified critical access drugs and 63 percent of the identified drugs in short supply. As agreements are finalized, drug manufacturers are increasing production in these product lines, and further increases are expected in the coming months. By predicting the demand curve and setting up contracting terms on it, GPO strives to improve the drug inventory situation for hospitals and patients. In other words, by encouraging production and creating capacity, all providers, regardless of GPO affiliation, should benefit through increased production of critical and short drugs.

Case Study 3: GPO Works to Raise Suppliers' Performance Quality Metrics

Strategy

Another GPO has taken a comprehensive approach to the drug shortage crisis. The GPO seeks to continuously raise the performance level and quality of products that suppliers produce by performing due diligence before contracting with a particular supplier and exchanging information with suppliers to better forecast the demand for vital generic products.

Implementation

The GPO requires its contracted suppliers to provide a history of their compliance with FDA, including any regulatory action taken such as FDA 483s, warning letters, and consent decrees. The GPO asks suppliers to reveal the source of the active pharmaceutical ingredients (API) they use and any backup suppliers of API in case of problems with the primary API supplier. The GPO also requires suppliers to provide information about their ability to produce adequate quantities to meet market demand. At the same time, the GPO provides manufacturers with usage data, so that they can improve their production forecasts. The GPO works closely with manufacturers regarding production forecasting of key generic products.

Case Study 4: GPO Launches Initiatives to Expand Supply

Strategy

GPOs have encouraged manufacturers to enter the market in the face of supplier challenges and to meet the market demand for key products, notably by contracting with new manufacturers of generic products. For example, a GPO contracted with Heritage Pharmaceuticals Inc., a subsidiary of Emcure Pharma Ltd., to offer hospitals safer and more reliable access to drugs on the FDA shortages list, including Cidofovir, which is used to treat viruses in AIDS patients. Heritage received the 2013 Healthcare Distribution Management Association best new generic product introduction of the year award for its launch of Cidofovir.⁴⁵

⁴⁵ Premier. All Stakeholders Must Play a Role in Reducing Drug Shortages. Premier Communications. August 22, 2013. <https://www.premierinc.com/about/newsletters/nexus/8-21-13-Nexus.jsp>

Another GPO agreement with Heritage ensured the supply of Ondansetron, which prevents nausea and vomiting caused by surgery or cancer therapy. Becton Dickinson and Company is another example of a company entering the generic injectables market in a time of need.⁴⁶ In addition to contracting with new suppliers, GPOs have also added products to the contracts of existing suppliers such as West-Ward Pharmaceuticals and Pfizer Pharmaceuticals, which had previously not manufactured generic injectables.

Case Study 5: GPO Provides FDA with Data on Generic Injectable Drugs

Strategy

A GPO communicated with FDA regarding manufacturer decisions to stop production of key generic injectable drugs and has supplied FDA with utilization data of certain injectable drugs to enable the Agency to see who the major suppliers in the market are, and to assist in the determination of alternative suppliers. In addition, the GPO has worked closely with FDA and the Generic Pharmaceutical Association (GPhA) and supported the establishment of the Accelerated Recovery Initiative (ARI), to facilitate communication among manufacturers to reduce the impact of production/manufacturing problems with generic injectable drugs.

Case Study 6: GPO Offers Healthcare Providers Critical Information and Best Practices to Avoid the Purchase of Unsafe Products from the Gray Market

Strategy

A GPO has diligently worked to identify problems associated with gray market distributors (e.g., unauthorized distributors) both in alleged price gouging practices and in the availability of critical drugs to hospitals and non-acute sites of care. These efforts benefit hospitals and health systems by enabling them to maintain patient access and provide appropriate treatments in times of shortage.

Impact

The GPO's best practices are helping hospital pharmacies avoid the gray market and conduct business only with legitimate, licensed suppliers. In turn, these purchasing guidelines are also helping protect patients from unintended harm. More generally, the GPO's efforts related to this issue created greater awareness among providers and the public about the widespread nature of price gouging during drug shortages.

Case Study 7: GPO Ensures Access to Key Drugs

Strategy

A GPO has worked with key generic manufacturers and wholesalers/distributors to ensure availability and access to key generic injectable products for its healthcare members. Recent

⁴⁶ For more about this expansion into the generics market, see: "Becton, Dickinson enters generic injectables market, with big plans for expansion." March 28, 2013. http://pharmaceuticalcommerce.com/latest_news?articleid=26818

examples include potassium chloride and calcium gluconate. The GPO coordinated distribution of these urgently needed products through one distribution channel to control their availability.

Case Study 8: Guaranteed Supply Program

Strategy

A GPO proactively guarantees a 4-month supply of drugs that are critical to hospital program members. The supply will be available and allocated to program members if/when any of the items included become shortage drugs. If no shortage occurs during the program, the members do not have to purchase the extra 4-month supply. This is similar to an insurance policy in that the GPO members pay a premium to participate but continue to buy a normal amount of supply, but are guaranteed a supply in a shortage situation.

The projected market data is helpful for planning purposes for manufacturers anticipating product runs. In this program the supplier produces and holds 120 days of inventory at its warehouse that has a minimum of 12-months dating throughout the program. If a shortage occurs, the supplier and GPO release and sell this supply to program members via direct purchase or through controlled distribution (defined at the time of sign-up). If a shortage does not occur and the program is ending, no one has to buy any extra inventory above their normal product use. If a hospital ends its program involvement, it loses its access to the 120-days' supply. If supplier defaults on having the 120-day supply or if that supply is recalled, financial penalties are invoked.

Case Study 9: GPO Adopts Member-Driven Strategy to Contract with More Than One Supplier for Supply Challenged Generic Injectables

Strategy

In an effort to provide contract award opportunities to more than one supplier, GPO is following a member-driven approach to dual (and in some cases, triple) award many key generic injectable medications that have had a history of supply challenges.

Impact

This approach has benefitted GPO's members by providing access to more than one manufacturer's product on contract. This approach also supports the generic injectable industry by enabling more than one supplier to secure a contract position with GPO for a particular product.

Case Study 10: GPO Contributes to Key Stakeholder Understanding Regarding the Impact Drug Shortages Are Having on Patient Care

Strategy

GPO partnered with an Academic Medical Center member to co-develop, conduct, and publish the results of a survey exploring the impact drug shortages have had on patient care. Survey was sent out to GPO's members and following detailed analysis and peer review, the results highlighting several key areas with negative impact were recently published.

Case Study 11: GPO Facilitates Sharing of Best Practices

Strategy

GPO facilitates multiple forums throughout the year to enable GPO's members to share best practices regarding their management of specific drug shortages. GPO's Drug Information Center also works to provide GPO's members with information on alternative products/therapies to assist in drug shortage management.

Implications of Case Studies

The preceding case studies demonstrate the ways in which GPOs are striving to address the problem of drug shortages. However, a comprehensive solution would require a multi-stakeholder approach. To this end, the next section provides policy recommendations that reflect HSCA's support for a broader collaborative approach to mitigating drug shortages.

VI. Recommendations

The GPO industry fully supports recent regulatory and legislative activities aimed at solving the drug shortage problem, and is open to exploring multi-stakeholder solutions. As an industry, GPOs are committed to alleviating the harmful impacts of scarcity in the U.S. drug market. Collectively, the GPO industry is committed to:

- 1) Working with manufacturers to ensure timely and appropriate supply of products.
- 2) Working with its supplier partners to communicate and forecast the product demands of provider members. Manufacturers that receive this information from GPOs in a timely fashion are better positioned to have more advance notice about demand and better able to plan their production capacity.
- 3) Supporting entities that facilitate reporting on shortages and alert members of potential access issues. GPOs use various modes of communication to provide this information, including webinars, conferences, newsletters, and electronic alerts as issues warrant.

In addition to these efforts, the HSCA is calling on all relevant stakeholders to address the drug shortage crisis. The GPO industry has identified specific recommendations that aim to mitigate drug shortages through the following means:

Improving FDA’s approval processes

- Supporting necessary FDA resources to ensure timely responses to market entry and production issues
- Encouraging the FDA to institute an accelerated approval process for new sources of supply or manufacturing for items listed as in short supply

Adopting early notification systems and public communication

- Having manufacturers provide GPOs with early, advanced warning of potential drug shortages and/or notable increases in product demand
- Strengthening current FDA six-month notification rule
- Developing a broader definition of how FDA defines “medically-necessary” drugs
- Improving FDA website to enhance communication
- Evaluating, and where appropriate, applying, best practices from other countries experiencing shortages
- Requiring immediate allocation of products in shortage by the manufacturer and its authorized distributors to minimize speculative purchasing and hoarding (while recognizing previously existing contractual relationships needing to be respected)

Implementing market and operational efficiencies

- Improving FDA regulatory violation process
- Advocating for FDA to ensure quality in the sterile pharmacy compounding space through regular inspections of compounding outsourcing facilities, with or without additional regulatory authority
- Working with FDA to develop a score card that would allow the market to observe and reward quality

HSCA members are also committed to partnering with all participants in the distribution chain to find proactive, novel, and flexible means to ensure patient access to critical medications. Finding solutions to the interconnected issues causing drug shortages will require coordination from all levels of the supply chain including FDA, manufacturers, and healthcare providers, many of whom are beyond HSCA’s membership, but with whom ongoing communication can be invaluable. Meanwhile, HSCA and its members are identifying specific recommendations aimed at mitigating drug shortages by improving FDA’s approval processes; refining early notification systems and public communication; and implementing market and operational efficiencies.

Responsible Party	Recommendation
Improving FDA’s Approval Processes	
Federal Government	Institute an accelerated approval process: Implement an abbreviated approval process to speed production of therapeutically equivalent products that are in short supply.
Adopting Early Notification System and Public Communication	

Responsible Party	Recommendation
Manufacturers	<p>Provide GPOs with early, advanced warning: Manufacturer notification to GPOs can assist GPO and member facilities in preparing for a drug shortage. With earlier warnings, alternative policies, procedures, and/or order sets, and physician education, facilities will be better prepared to withstand a drug shortage. Early warnings will allow GPOs to assist members by providing guidance documents to members regarding the length and severity of the anticipated shortage, as well as information on alternative therapies.</p>
Federal Government	<p>Borrow best practices from other countries experiencing shortages: FDA should approach the resolution of shortages as a global phenomenon. The Agency's Office of Global Regulatory Operations and Policy should lead on this issue and exchange best practices, formally or informally, with agencies from countries that also need to monitor and resolve shortages.</p>
All stakeholders	<p>Develop a broader definition of how FDA defines medically necessary drugs: FDA, ASHP, and physician organizations should develop a single critical drug list. Currently, FDA does not consider many drug therapies in shortage to be medically necessary. This list would determine which medications are considered critical for healthcare facilities. The drug list would consist of drugs that have limited treatments available for a given indication, are used in surgery or catheter labs, or treat life-threatening conditions (cancer, myocardial infarction, etc.).</p>
Manufacturers	<p>Participate in Accelerated Recovery Initiative's (ARI) pilot program: A pilot program has been underway since March 2013 for ARI – an FDA/industry partnership being coordinated by IMS to forecast, prevent, and mitigate the impact of drug shortages. HSCA fully supports the ARI initiative and encourages manufacturers to participate in the voluntary pilot.</p>
Federal Government	<p>Improve FDA's website to enhance communication: Through collaboration with industry and clinicians, improve CDER's drug shortage website to: make updates clear; highlight new material; make notifications downloadable or printable; make website alphabetically linked; provide alternative drug guidance and dosing assistance associated with drugs in short supply; provide better estimations of shortage resolution so facilities can develop their contingency strategies; include clinical references where information was obtained from and links to these references.</p>
<p>Implementing Market and Operational Efficiencies</p>	

Responsible Party	Recommendation
Federal Government	<p>Improve FDA’s regulatory violation process: Various inefficiencies in the FDA regulatory process for evaluating current Good Manufacturing Practices (cGMPs) have been exposed during this drug shortage crisis. The prolonged turnaround time in re-reviewing a site, extended delays in releasing improved products, and confusing or missing guidance to assist manufacturers in returning to regular production have contributed to shortages. FDA should standardize turnaround times, improve and standardize reviews and frequency of FDA reviews to identify problems prior to shutting down facilities. FDA should work with industry to develop a score card that allows the market to observe and reward quality.</p>
Federal Government	<p>FDA should continue to ensure quality in the pharmaceutical sterile compounding space through regular inspections of compounding outsourcing facilities, to keep a crucial, alternative source of production viable: Pharmaceutical compounders perform a vital service for providers and patients, by compounding medically necessary products, including copies of FDA-approved products, when manufacturers are unable to meet the demand for medically necessary drugs. Problems with quality and sterility in the compounding space jeopardize the safety and efficacy of this alternative supply source for drugs in shortage. HSCA supports the Agency continuing its quality inspections.</p>
Developing Policies to Ensure Fair Allocation of Drugs in Shortage	
Institute of Medicine/ Healthcare Providers	<p>IOM should form a committee to guide institutions in choosing priority populations for scarce drugs: Physicians often have no formal institutional guidance for making allocation decisions. A survey conducted by researchers at the Abramson Cancer Center and the Perelman School of Medicine at the University of Pennsylvania found that as many as 70 percent of oncologists made difficult decisions in the absence of guiding policies. HSCA recommends that the Institute of Medicine form a committee to develop a decision-making template that would guide clinicians and healthcare administrators in selecting priority populations for scarce drugs among equally vulnerable patients. This template could subsequently be incorporated in hospital policies nationwide.</p>
Federal Government	<p>Prepare a report or hold a public meeting on ethical challenges raised by drug shortages: The Presidential Commission for the Study of Bioethical Issues acts as an advisory panel to the President on bioethical issues related to scientific research, healthcare delivery, and technological innovation. The Commission should hold a public meeting and focus its next report on allocating resources during shortages in an ethically and socially responsible manner.</p>