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**Statement prepared for:
U.S. House Committee on Energy and Commerce Subcommittee on Oversight
and Investigations**

**Examining the Root Causes of Drug Shortages: Challenges in Pharmaceutical
Drug Supply Chains**

May 11, 2023

The Association for Clinical Oncology (ASCO) is pleased to submit this statement for the record of the hearing entitled, “Examining the Root Causes of Drug Shortages: Challenges in Pharmaceutical Drug Supply Chains.” ASCO is grateful that the subcommittee has provided the medical community the opportunity to share our concerns regarding drug shortages and the risk they pose to our national security. We strongly believe that Congress and policymakers within U.S. federal agencies need to intervene to secure the pharmaceutical pipeline to mitigate drug shortages and protect the U.S. from vulnerabilities that risk our national security.

ASCO is the national organization representing more than 45,000 physicians and other health care professionals who care for people with cancer. ASCO members are dedicated to conducting research that leads to improved patient outcomes, and we are also committed to ensuring that evidence-based practices for the prevention, diagnosis and treatment of cancer are available to all Americans, including Medicare beneficiaries.

For years, the medical community has experienced shortages of critical drugs that are used to treat a variety of conditions. These shortages are caused by a multitude of factors, including quality issues, manufacturer business decisions, disruptions to raw ingredient and excipient supplies, natural disasters, and other emergencies that take place in countries that house critical drug manufacturing facilities. In recent years, the U.S. has experienced shortages in broadly used essential products such as saline, morphine, and fentanyl, in addition to products critical to smaller patient populations.

In 2010 and 2011, our affiliate organization, the American Society of Clinical Oncology (the Society) began hearing concerns regarding drug shortages from its members. The oncology community rapidly identified drug shortages as a

serious issue directly impacting patient care; as early as 2013 we were highlighting the effect of these shortages at our Annual Meeting.^{1,2,3} Since that time, we have engaged with lawmakers, federal agencies, and stakeholder organizations to raise awareness and pass legislation providing the Food and Drug Administration (FDA) with necessary tools to help mitigate drug shortages.⁴ In partnership with other major national organizations, we have held summits, released reports and recommendations, and advocated for policy changes aiming to get to the root of the problem.^{5,6,7} Along with collaborating organizations, we were amongst the first groups to identify drug shortages as a matter of national security.⁸

In response to Executive Order 14017,⁹ ASCO and other organizations highlighted in a letter to the U.S. Department of Health and Human Services (HHS) Secretary that the COVID-19 public health emergency further underscored the vulnerability of our nation's healthcare supply chain. During the pandemic, health care providers struggled to obtain medications and supplies essential to patient care, including the sedatives necessary to mechanically ventilate patients, personal protective equipment (PPE) such as gloves and masks, and ancillary devices and supplies, such as syringes and swabs. The pandemic stress-tested our supply chains, highlighting their fragilities and deficiencies, throwing the need for immediate corrective action into sharp relief.

Oncology Drug Shortages

Within the oncology pharmaceutical supply chain, patients and providers continue to face shortages of potentially life-saving treatments. A recent survey of U.S. oncology pharmacists found that oncology drug shortages occurred frequently in 2020 and led to delays in chemotherapy and changes in treatment or omission, complicated clinical research, and increased risk of medication errors and adverse outcomes.¹⁰ The study also reported that the most difficult oncology drugs to obtain at the time were vincristine, vinblastine, intravenous immunoglobulin, leucovorin, and Bacillus Calmette-Guerin. Currently, the cytotoxic chemotherapy drug fludarabine remains on the FDA drug shortage list and has been on the list throughout the COVID-19 pandemic. Many large volume cancer centers across the U.S. have completely run out of the drug, which is a critical component of induction prior to CAR T-cell therapy. The centers have been forced to choose between offering an inferior replacement induction chemotherapy, or potentially ineffective CAR T-cell therapy. Because the CAR T-cell treatment is a genetically modified cellular product from the immune system of the patient who receives the treatment, this treatment can often not be repeated due to cost, logistics, and cancer related factors. Thus, the lack of this critical chemotherapy drug could result in patients, who would otherwise be cured

¹ https://journals.lww.com/oncology-times/fulltext/2013/07100/new_surveys_document__cancer_drug_shortages.5.aspx

² <https://www.ajmc.com/view/-drug-shortages-persist-in-months-after-surveys-make-headlines-at-asco>

³ https://www.youtube.com/watch?v=eX_l3rFLUx0

⁴ <https://www.ashp.org/advocacy-and-issues/key-issues/drug-shortages/meds-act>

⁵ <https://www.ashp.org/drug-shortages/shortage-resources/roundtable-report?loginreturnUrl=SSOCheckOnly>

⁶ <https://www.ashp.org/news/2018/09/19/summit-on-drug-shortages-to-examine-impact-on-national-security-and-health-care-infrastructure>

⁷ <https://www.ashp.org/-/media/assets/advocacy-issues/docs/Recommendations-Drug-Shortages-as-Matter-of-Natl-security.ashx>

⁸ <https://www.ashp.org/news/2018/09/19/summit-on-drug-shortages-to-examine-impact-on-national-security-and-health-care-infrastructure>

⁹ <https://www.whitehouse.gov/wp-content/uploads/2021/06/100-day-supply-chain-review-report.pdf>

¹⁰ <https://ascopubs.org/doi/full/10.1200/OP.21.00883>

if fludarabine was available, having poorer outcomes from their cancer. Currently, there are 15 oncology drug shortages according to the FDA's website.¹¹

We appreciate Congress' efforts thus far to secure the drug supply chain, especially with the inclusion of key policy provisions from the Mitigating Emergency Drug Shortages (MEDS) Act in the enacted Coronavirus Aid, Relief, and Economic Security (CARES) Act. However, more action is necessary.

Recommendations to Mitigate Drug Shortages

ASCO and other stakeholders have long collaborated on efforts to improve our nation's drug supply chain and mitigate shortages. As such, we worked together to put forth the following recommendations¹² to improve the resilience of the nation's health care infrastructure. These recommendations are meant to provide a range of potential policy and marketplace changes to guide policymakers in their efforts to address these challenges.

Regulatory

1. Develop a comprehensive list of critical drugs. Use the World Health Organization Model Lists of Essential Medicines and other existing resources as a starting point to define what a shortage is and develop a list of critical drugs needed for 1) emergency response and 2) saving and preserving life. Using historical data and manufacturing input, address why these drugs have been on the shortage list. The critical list can be used to:
 - a. Stabilize the availability of critical drugs by working with manufacturers and the FDA to create redundant product in multiple locations in anticipation of natural disasters and other supply chain threats.
 - b. Assess the quality of pharmaceutical manufacturers measured against the importance of drugs on the critical list.
 - c. Work with the private sector for greater transparency surrounding the source of raw materials and manufacturing locations so providers can more easily assess pharmaceutical product quality. The FDA has proposed a star rating system for pharmaceutical manufacturers, which could increase transparency.
2. Create a multi-stakeholder advisory panel with the FDA to address key issues, such as the possibility of creating a stockpile of critical drugs, the logistics of warehousing such excess pharmaceutical inventory and where the excess inventory should be stored.
3. Enhance communication with the entire drug supply chain, including healthcare providers during, or in advance of, a public health emergency or other event that may create a drug shortage. FDA should provide the healthcare community with information simultaneously on the type of products that may be impacted and the expected duration of the impact. To prevent hoarding of inventory that could result from such communication, manufacturers could put product on allocation to ensure that remaining supply is distributed equitably.
4. Streamline regulations to incentivize increased manufacturing production.
 - a. Compounding regulations: 503(b) outsourcers need incentives to make drugs in short supply; it is costly to ramp up for only a short duration.

¹¹ <https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>

¹² <https://www.ashp.org/-/media/assets/advocacy-issues/docs/Recommendations-Drug-Shortages-as-Matter-of-Natl-security.ashx>

- b. Global regulatory environment: there are multiple agencies internationally, all with competing requirements for manufacturers.
 - c. Aligns with FDA's initiative to harmonize international technical standards for approval of generic drugs.
- 5. Engage the Centers for Medicare and Medicaid Services (CMS) to discuss the practice of citing hospitals that use medications after the guaranteed stability period in product labeling. This may, for example, address a powder after it is solubilized, which can contribute to unnecessary medical waste.
 - a. There are situations where evidence exists in the literature that stability goes well beyond the period of time listed in product labeling. However, CMS and the Joint Commission will cite a hospital even though the organization has evaluated this evidence and revised the date based on that. This warrants further discussion with CMS to see what might be needed to avoid or address drug shortage situations.
- 6. Encourage FDA to consider how reducing the number of unapproved (pre-1938 Federal Food, Drug, and Cosmetic Act) drugs on the market might impact shortages.
 - a. FDA has been assisting companies with finding opportunities to legally market older "grandfathered" products that are currently marketed without the required FDA approval. While the FDA approval process ensures that marketed drugs meet current FDA standards for safety, efficacy, quality, and labeling, there have been concerns that these efforts to bring widely used but unapproved drugs into compliance with current FDA requirements have resulted in drug shortages. For context, it may cost drug manufacturers more to invest in obtaining formal drug approval. As such, some may drop out of the market rather than make the investment, thus leading to potential drug shortages.

Legislative

1. Enact legislation that requires a notification requirement for medical product devices and equipment needed to administer medications, similar to the legislation enacted in 2012 that requires drug manufacturers to notify the FDA "of any changes in production that is reasonably likely to lead to reduction in supply" of a covered drug in the U.S.
 - a. E.g. fluid containers to dilute medications for infusion.
2. Enact legislation requiring a risk assessment of foreign source active pharmaceutical ingredients (APIs).
 - a. Relying predominantly on other countries for the necessary ingredients to manufacture crucial drugs puts the U.S. at risk. This was especially evident during the COVID-19 pandemic. With U.S.-China relations strained, the Chinese government used its posture as a main source of U.S. APIs to gain the upper hand on foreign relations issues tied to the pandemic.
3. Require federal government authorities with jurisdiction over national security to conduct an analysis of domestic drug and medical device manufacturing capability and capacity for critical products to assess whether a threat to national security exists.
4. Require a U.S. Government Accountability Office study to examine all aspects of the drug supply chain to see if there are any new issues exacerbating drug shortages.

Legislative and Regulatory

1. Develop incentives for drug manufacturers to have contingency or redundant production plans for their pharmaceutical products on the critical drug list. The back-up plan should include

- prioritizing the most medically necessary products, qualifying third party suppliers across their network, and increasing production and inventory for API and finished goods.
2. Investigate developing a system of paying suppliers to hold inventory, perhaps similar to the system employed by the U.S. Department of Defense (DoD) Defense Logistics Agency. Consider partnering with the DoD to create contractual leverage with drug manufacturers for civilian hospitals.
 3. Incentivize manufacturers and work with the FDA to repackage pharmaceuticals according to the amount of medication commonly used to reduce waste.
 - a. E.g. only a 30 mL vial of a drug is available when most common volume needed is 5 mL.
 4. Create an Office of Clinical Affairs within the Drug Enforcement Agency (DEA), so DEA personnel will be available to address the clinical side of medication shortages of controlled substances, rather than just the diversion enforcement aspect.

Market/Non-Legislative or Regulatory

1. Standardize medical concentration, containers, and sizes to stabilize pharmaceutical supply and reduce the probability of patient harm due to constantly needing to change concentrations and associated technology. Standardizing products reduces the risk of adverse drug events when shortage products are substituted. Standardizing the concentration of compounded products within organizations also helps provide a critical mass for industry to consider making previously unavailable products available.
2. Identify tools that address supply access, such as Pfizer's web access tool, which provides information about happenings at Pfizer's facilities, latest product updates and a Q&A forum.
3. Ensure hospital staff, healthcare providers and pharmacies have the capacity to manage drug shortages.
 - a. Ensure early notification of predictable medication shortages and medication substitutes so staff can build necessary information into communication efforts.
 - b. Work with medical and specialty organizations to ensure necessary information is built into educational efforts, such as national guidelines and continuing education.
4. Examine how changes in United States Pharmacopeia (USP) standards for drugs with a solid historical safety record can affect supply, and whether these changes are necessary.
 - a. Consult with USP representatives about pharmaceutical regulations that may lack an evidence base.
5. Request that electronic health record (EHR) vendors amend their systems to ease the burden of making drug product changes when a shortage occurs. An example would be some sort of tool that makes changes to various integrated technology databases at the same time (like EHR and smart pump drug libraries, or automated dispensing cabinets and pharmacy inventory systems).

Thank you for the opportunity to provide ASCO's comments, concerns, and solutions to address drug shortages. We would welcome the opportunity to engage with Congress in a meaningful dialogue about these issues. Please contact Megan Tweed at Megan.Tweed@asco.org with any questions.