INTRODUCTION

American Medical Association (AMA) Policy H-100.956, “National Drug Shortages,” directs the Council on Science and Public Health (CSAPH) to continue to evaluate the drug shortage issue and report back at least annually to the House of Delegates (HOD) on progress made in addressing drug shortages in the United States. This report provides an update on continuing trends in national drug shortages and ongoing efforts to further evaluate and address this critical public health issue.

METHODS

English-language reports were selected from a PubMed and Google Scholar search from September 2018 to August 2021, using the text term “drug shortages.” Additional articles were identified by manual review of the references cited in these publications. Further information was obtained from the Internet sites of the U.S. Food and Drug Administration (FDA), National Academies of Sciences, Engineering, and Medicine (NASEM), U.S. Department of Health and Human Services (HHS), American Society of Health-System Pharmacists (ASHP), Duke Margolis Center for Health Policy, and by direct contact with key FDA, ASHP, and University of Utah Drug Information Service (UUDIS) staff who monitor drug shortages and related issues daily.

BACKGROUND

CSAPH has issued eleven reports on drug shortages. The findings and conclusions of the first five reports are summarized in CSAPH Report 2-I-15, “National Drug Shortages: Update.” The remainder of this informational report will provide an update on drug shortages since the 2020 report was developed, specifically commenting on issues associated with the drug supply chain that lead to drug shortages.

CURRENT TRENDS IN DRUG SHORTAGES

Drug shortages remain an ongoing public health concern in the United States and the AMA continues to monitor the situation and take action when appropriate. Overall, new drug shortages are decreasing; however, a large number of shortages are still ongoing and pose continued problems for patient care. Additionally, new shortages may occur as manufacturing capacity in the pharmaceutical industry is prioritized during the continuing COVID-19 public health emergency, specifically for the production of COVID-19 vaccines and treatments.

The two primary data sources for information on drug shortages in the United States continue to be the Drug Shortage Program at the FDA and the Drug Shortage Resource Center maintained by ASHP in cooperation with the UUDIS (see Box 1 for links to these resources).
According to the most recent data compiled by ASHP and UUDIS, provided in Appendix 1 of this report, there were 129 new shortages reported in 2020 and 38 new shortages reported as of June 30, 2021; this is compared to the 166 new shortages reported for 2019. The number of active drug shortages has decreased to 236 in the second quarter of 2021 from 271 in quarter one of this year. In 2019, 39 percent of shortages were in injectable drugs; this increased to 50 percent in 2020 and is currently at 47 percent for 2021. The top five classes of drugs implicated in active drug shortages include CNS medications (43); cardiovascular medications (31); antimicrobials (26); chemotherapy agents (19); and hormonal agents (19).

The reasons for drug shortages vary and unknown/unreported reasons account for 57 percent of drug shortages in 2020, down from 82 percent in 2019 (See Appendix for ASHP/UUDIS data). In the past year, significantly more suppliers did provide a reason for shortages. Additionally, “business decision” is included as a reason in 2020, with 14 percent of manufacturers reporting this as the reason for a shortage.

The ASHP Shortage Resource Center provides a list of shortages, guidance on managing critical shortages, as well as shortage metrics (Box 1).

The FDA continues to utilize a mobile app to provide up-to-date access to information about drugs in shortage as well as notifications about new and resolved drug shortages. This mobile app also gives physicians the ability to report a drug shortage. The FDA Drug Shortages webpage includes a current shortages list, a link to the mobile app, and additional information (Box 1).

The eighth annual report on drug shortages from the FDA to Congress published in early 2021 summarizes the major actions the FDA took in calendar year 2020 related to drug shortages. During the COVID-19 pandemic in 2020, FDA continued to closely monitor the medical product supply chain and, as expected, the supply chain was impacted by the pandemic, leading to supply disruptions or shortages of drug products in the United States. Appendix 2 includes a breakdown of the FDA’s calendar year 2020 metrics, including the number of expedited reviews (471) and expedited inspections (19).

The Coronavirus Aid, Relief, and Economic Security Act (CARES Act) was signed into law on March 27, 2020, to aid response efforts to the COVID-19 pandemic and to ease the economic impact of COVID-19. In addition, the CARES Act amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) to include authorities intended to enhance FDA’s ability to identify, prevent, and mitigate possible drug shortages by, among other things, enhancing FDA’s view into drug supply chains. Specific authorities to enhance FDA’s ability to identify, prevent, and mitigate drug shortages took effect on September 23, 2020 and include the following:

- Amendments to expand the requirement for manufacturers of certain drugs to provide information on permanent discontinuances and interruptions in manufacturing that may lead to a meaningful disruption in supply to FDA.
- Amendments to require FDA to prioritize and expedite, as appropriate, the review of certain applications and inspections that could help mitigate or prevent a shortage of a drug covered by section 506C(a).
- The addition of a section of the code of federal regulations requiring manufacturers of drugs described in section 506C(a) of the FD&C Act or of any active pharmaceutical ingredient (API) or any associated medical device used for preparation or administration.
included in the drug to develop, maintain, and implement, as appropriate, a redundancy
risk management plan that identifies and evaluates the risks to the supply of the drug, as
applicable, for each establishment in which the drug or API of the drug is manufactured.

• Amendments to require drug manufacturers registered under section 510 of the FD&C Act
to annually report on the amount of each drug that they have “manufactured, prepared,
propagated, compounded, or processed” for commercial distribution.

DRUG SHORTAGES AND COVID-19

The FDA reports that it has been closely monitoring the supply chain with the expectation that the
COVID-19 pandemic would likely impact the medical product supply chain, including potential
disruptions to supply or shortages of critical medical products in the United States. The COVID-19
pandemic has also increased the risks of shortages due to sudden increases in demand for drugs
used in hospitalized patients, particularly the most critically ill. To respond to this risk, Drug
Shortage Staff within the FDA’s Center for Drug Evaluation and Research (CDER) has asked
manufacturers to evaluate their entire supply chain, including key starting materials, APIs, finished
dose forms, packaging components, and any other components that may be impacted in any area of
the supply chain due to the COVID-19 outbreak.

FDA reports proactively reaching out to manufacturers as part of an approach to identify potential
disruptions or shortages and notes that the Agency will use all available tools to react swiftly and
mitigate the impact to U.S. patients and health care professionals when a potential disruption or
shortage is identified.

Actemra/RoActemra (tocilizumab)

Recently, Roche reported that the demand for Actemra/RoActemra (tocilizumab), a drug widely
used to treat hospitalized patients with severe or critical COVID-19 around the world, has
increased to unprecedented levels globally. Actemra/RoActemra is not approved for the treatment
of COVID-19 in any country but was recently granted an Emergency Use Authorization in the
United States for hospitalized adults and pediatric patients (2 years of age and older) who are
receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive
mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). Additionally,
tocilizumab has also now been included in the World Health Organization (WHO) Therapeutics
and COVID-19 Living Guideline, based on the body of evidence that has been generated
throughout the last 18 months. A statement from Roche acknowledges the increase in demand and
the global shortage of the drug and also details the company’s efforts to minimize the impact of
global supply constraints. ASHP has developed an information sheet regarding the tocilizumab
shortage.

DRUG SUPPLY CHAIN AND DRUG SHORTAGES

Over the last several years, natural disasters, quality problems, manufacturer consolidation, and
other issues have disrupted pharmaceutical manufacturing and have left the U.S. healthcare system
on the brink of a significant public health crisis multiple times. The COVID-19 public health
emergency further underscored the vulnerability of our nation’s healthcare supply chain and stressed-
tested supply chains, highlighting the fragilities and deficiencies.

Considerable attention has been focused on supply chain resilience in the past several months. This
year, the FDA has published several guidance documents related to supply chain security, the
White House released a report and fact sheet on policies to support the creation of resilient supply
chains,23,24 and The Duke-Margolis Center for Health Policy and the COVID Collaborative released a new white paper on challenges and potential solutions for resilient drug supply chains that complements the White House reports.25 All of these publications address aspects of AMA policy regarding drug shortage, including calls for increased transparency, global cooperation, resiliency and redundancy in manufacturing capability, and the creation of a quality rating system.

CURRENT AMA DRUG SHORTAGE ACTIVITIES

AMA staff continue to remain engaged in drug shortage activities. Staff are involved in a multi-stakeholder effort to remain current on policies, drug shortage and supply chain issues, and to develop group recommendations on the topics. The effort includes the AMA, the ASHP, the American Hospital Association (AHA), the United States Pharmacopeia (USP), the American Society of Anesthesiologists (ASA), and the American Society of Clinical Oncology (ASCO). Earlier this year, the group sent a letter to the Secretary of Health and Human Services and leaders in the office of the Assistant Secretary for Preparedness and Response (ASPR) offering to assist the administration in its efforts to improve our nation’s healthcare supply chains and specifically noting that:

For a number of years, we have worked collaboratively to address drug shortages. Recently, our organizations have begun developing consensus recommendations on a number of other supply chain issues, including Strategic National Stockpile (SNS) enhancement, visibility into supply chains, quality and manufacturing improvement (e.g., reducing contamination in finished pharmaceuticals), and medical supply and medical device supply chain reinforcement. We would welcome the opportunity to meet with you to share these recommendations, which are drawn from our members’ expertise and their real-world experience with utilizing complex, and sometimes fragile, medical supply chains. We greatly appreciate the work ASPR and FDA are already undertaking on EO 14017, and we look forward to continuing to work closely with you.

SUMMARY

The rate of new medical product shortages is decreasing, but the current COVID-19 public health emergency requires continued diligence in monitoring any shortage or supply chain issues due to manufacturing capacity prioritization for COVID-19 vaccines and treatments.

The AMA’s drug shortage policy is timely and already addresses a variety of issues that are under consideration by the White House, FDA, and other stakeholders including the improvement of quality assurance systems; expedited facility inspections and manufacturing changes/improvements; necessary resiliency and redundancy in manufacturing capability; evaluation of root causes of drug shortages; transparent analysis of economic drivers and reasonable and sustainable payment rates for prescription drugs; greater transparency of the manufacturing process; and including drug manufacturing sites as part of the nation’s critical infrastructure plan. Therefore, the Council feels that an update to AMA policy is not warranted at this time.
REFERENCES


Box 1. Resources available to assist in mitigation of drug shortages.

1. ASHP Resource Center
2. ASHP list of current shortages
3. FDA Drug Shortages Page (includes current shortages list, mobile app, and additional information)
APPENDIX 1

ASHP/University of Utah Drug Information Service Drug Shortage Data

Figure 1.

**National Drug Shortages: New Shortages by Year**

January 2001 to June 30, 2021

![Bar chart showing national drug shortages by year from 2001 to 2021.](chart1.png)

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

University of Utah Drug Information Service

Contact: Erin.Fox@hsc.utah.edu, @foxerinr for more information.

Figure 2.

**National Drug Shortages: Active Shortages by Quarter**

![Line chart showing active drug shortages by quarter from Q2-15 to Q2-21.](chart2.png)

*Note:* Each point represents the number of active shortages at the end of each quarter.

University of Utah Drug Information Service

Contact: Erin.Fox@hsc.utah.edu, @foxerinr for more information.
Figure 3.

National Drug Shortages: Active Shortages Top 5 Drug Classes

![Graph showing active shortages by drug class as of June 30, 2021.](image)

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Contact: Erin.Fox@hsc.utah.edu, @foxerinr for more information.

Figure 4.

National Drug Shortages

Reasons for Shortages as Determined by UUDIS During Investigation — 2020

![Pie chart showing reasons for shortages in 2020.](image)

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APPENDIX 2

FDA Drug Shortage Data

### Breakdown of CDER’s and CBER’s Shortage Numbers, CY 2020

<table>
<thead>
<tr>
<th></th>
<th>CDER</th>
<th>CBER</th>
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<td>New Shortages</td>
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<tr>
<td>Prevented Shortages</td>
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<td>20</td>
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<td>Ongoing Shortages</td>
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<td>8</td>
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<tr>
<td>Notifications</td>
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<td>39</td>
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<tr>
<td>No. of Manufacturers Notifying</td>
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<td>29</td>
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**ACTIONS TAKEN TO MITIGATE SHORTAGES**

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<tr>
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<th>CDER</th>
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<td>1</td>
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<tr>
<td>Expedited Reviews</td>
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<td>18*</td>
</tr>
<tr>
<td>Expedited Inspections</td>
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<td>0</td>
</tr>
</tbody>
</table>

* This number includes expedited reviews for nine biologics license application (BLA)/BLA supplements and nine lot-release submissions for CBER-regulated products.