

REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

CSAPH Report 01-N-21

Subject: Drug Shortages: 2021 Update

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1 INTRODUCTION

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

8

9 METHODS

10

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

19

20 BACKGROUND

21

22 CSAPH has issued eleven reports on drug shortages.¹⁻¹¹ The findings and conclusions of the first
23 five reports are summarized in CSAPH Report 2-I-15, “National Drug Shortages: Update.”⁴ The
24 remainder of this informational report will provide an update on drug shortages since the 2020
25 report was developed, specifically commenting on issues associated with the drug supply chain that
26 lead to drug shortages.

27

28 CURRENT TRENDS IN DRUG SHORTAGES

29

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

36

37 The two primary data sources for information on drug shortages in the United States continue to be
38 the Drug Shortage Program at the FDA and the Drug Shortage Resource Center maintained by
39 ASHP in cooperation with the UUDIS (see Box 1 for links to these resources).^{12,13}

1 *ASHP and UUDIS*

2
3 According to the most recent data compiled by ASHP and UUDIS, provided in Appendix 1 of this
4 report, there were 129 new shortages reported in 2020 and 38 new shortages reported as of June 30,
5 2021; this is compared to the 166 new shortages reported for 2019. The number of active drug
6 shortages has decreased to 236 in the second quarter of 2021 from 271 in quarter one of this year.
7 In 2019, 39 percent of shortages were in injectable drugs; this increased to 50 percent in 2020 and
8 is currently at 47 percent for 2021. The top five classes of drugs implicated in active drug shortages
9 include CNS medications (43); cardiovascular medications (31); antimicrobials (26); chemotherapy
10 agents (19); and hormonal agents (19).¹⁴

11
12 The reasons for drug shortages vary and unknown/unreported reasons account for 57 percent of
13 drug shortages in 2020, down from 82 percent in 2019 (See Appendix for ASHP/UUDIS data).¹⁴ In
14 the past year, significantly more suppliers did provide a reason for shortages. Additionally,
15 “business decision” is included as a reason in 2020, with 14 percent of manufacturers reporting this
16 as the reason for a shortage.

17
18 The ASHP Shortage Resource Center provides a list of shortages, guidance on managing critical
19 shortages, as well as shortage metrics (Box 1).¹²

20
21 *FDA*

22
23 The FDA continues to utilize a mobile app to provide up-to-date access to information about drugs
24 in shortage as well as notifications about new and resolved drug shortages. This mobile app also
25 gives physicians the ability to report a drug shortage. The FDA Drug Shortages webpage includes a
26 current shortages list, a link to the mobile app, and additional information (Box 1).¹³

27
28 The eighth annual report on drug shortages from the FDA to Congress published in early 2021
29 summarizes the major actions the FDA took in calendar year 2020 related to drug shortages.¹⁵
30 During the COVID-19 pandemic in 2020, FDA continued to closely monitor the medical product
31 supply chain and, as expected, the supply chain was impacted by the pandemic, leading to supply
32 disruptions or shortages of drug products in the United States. Appendix 2 includes a breakdown of
33 the FDA’s calendar year 2020 metrics, including the number of expedited reviews (471) and
34 expedited inspections (19).¹⁵

35
36 The Coronavirus Aid, Relief, and Economic Security Act (CARES Act) was signed into law on
37 March 27, 2020, to aid response efforts to the COVID-19 pandemic and to ease the economic
38 impact of COVID-19.¹⁶ In addition, the CARES Act amended the Federal Food, Drug, and
39 Cosmetic Act (FD&C Act) to include authorities intended to enhance FDA’s ability to identify,
40 prevent, and mitigate possible drug shortages by, among other things, enhancing FDA’s view into
41 drug supply chains.¹⁷ Specific authorities to enhance FDA’s ability to identify, prevent, and
42 mitigate drug shortages took effect on September 23, 2020 and include the following:¹⁸

- 43 • Amendments to expand the requirement for manufacturers of certain drugs to provide
44 information on permanent discontinuances and interruptions in manufacturing that may
45 lead to a meaningful disruption in supply to FDA.
- 46 • Amendments to require FDA to prioritize and expedite, as appropriate, the review of
47 certain applications and inspections that could help mitigate or prevent a shortage of a drug
48 covered by section 506C(a).
- 49 • The addition of a section of the code of federal regulations requiring manufacturers of
50 drugs described in section 506C(a) of the FD&C Act or of any active pharmaceutical
51 ingredient (API) or any associated medical device used for preparation or administration

1 included in the drug to develop, maintain, and implement, as appropriate, a redundancy
2 risk management plan that identifies and evaluates the risks to the supply of the drug, as
3 applicable, for each establishment in which the drug or API of the drug is manufactured.

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

7 8 DRUG SHORTAGES AND COVID-19

9
10 The FDA reports that it has been closely monitoring the supply chain with the expectation that the
11 COVID-19 pandemic would likely impact the medical product supply chain, including potential
12 disruptions to supply or shortages of critical medical products in the United States. The COVID-19
13 pandemic has also increased the risks of shortages due to sudden increases in demand for drugs
14 used in hospitalized patients, particularly the most critically ill. To respond to this risk, Drug
15 Shortage Staff within the FDA’s Center for Drug Evaluation and Research (CDER) has asked
16 manufacturers to evaluate their entire supply chain, including key starting materials, APIs, finished
17 dose forms, packaging components, and any other components that may be impacted in any area of
18 the supply chain due to the COVID-19 outbreak.

19
20 FDA reports proactively reaching out to manufacturers as part of an approach to identify potential
21 disruptions or shortages and notes that the Agency will use all available tools to react swiftly and
22 mitigate the impact to U.S. patients and health care professionals when a potential disruption or
23 shortage is identified.

24 25 *Actemra/RoActemra (tocilizumab)*

26
27 Recently, Roche reported that the demand for Actemra/RoActemra (tocilizumab), a drug widely
28 used to treat hospitalized patients with severe or critical COVID-19 around the world, has
29 increased to unprecedented levels globally.¹⁹ Actemra/RoActemra is not approved for the treatment
30 of COVID-19 in any country but was recently granted an Emergency Use Authorization in the
31 United States for hospitalized adults and pediatric patients (2 years of age and older) who are
32 receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive
33 mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).²⁰ Additionally,
34 tocilizumab has also now been included in the World Health Organization (WHO) Therapeutics
35 and COVID-19 Living Guideline, based on the body of evidence that has been generated
36 throughout the last 18 months. A statement from Roche acknowledges the increase in demand and
37 the global shortage of the drug and also details the company’s efforts to minimize the impact of
38 global supply constraints.¹⁹ ASHP has developed an information sheet regarding the tocilizumab
39 shortage.²¹

40 41 DRUG SUPPLY CHAIN AND DRUG SHORTAGES

42
43 Over the last several years, natural disasters, quality problems, manufacturer consolidation, and
44 other issues have disrupted pharmaceutical manufacturing and have left the U.S. healthcare system
45 on the brink of a significant public health crisis multiple times. The COVID-19 public health
46 emergency further underscored the vulnerability of our nation’s healthcare supply chain and stress-
47 tested supply chains, highlighting the fragilities and deficiencies.

48
49 Considerable attention has been focused on supply chain resilience in the past several months. This
50 year, the FDA has published several guidance documents related to supply chain security,²² the
51 White House released a report and fact sheet on policies to support the creation of resilient supply

1 chains,^{23,24} and The Duke-Margolis Center for Health Policy and the COVID Collaborative
2 released a new white paper on challenges and potential solutions for resilient drug supply chains
3 that complements the White House reports.²⁵ All of these publications address aspects of AMA
4 policy regarding drug shortage, including calls for increased transparency, global cooperation,
5 resiliency and redundancy in manufacturing capability, and the creation of a quality rating system.
6

7 CURRENT AMA DRUG SHORTAGE ACTIVITIES

8
9 AMA staff continue to remain engaged in drug shortage activities. Staff are involved in a multi-
10 stakeholder effort to remain current on policies, drug shortage and supply chain issues, and to
11 develop group recommendations on the topics. The effort includes the AMA, the ASHP, the
12 American Hospital Association (AHA), the United States Pharmacopeia (USP), the American
13 Society of Anesthesiologists (ASA), and the American Society of Clinical Oncology (ASCO).
14 Earlier this year, the group sent a letter to the Secretary of Health and Human Services and leaders
15 in the office of the Assistant Secretary for Preparedness and Response (ASPR) offering to assist the
16 administration in its efforts to improve our nation's healthcare supply chains and specifically
17 noting that:

18
19 For a number of years, we have worked collaboratively to address drug shortages. Recently,
20 our organizations have begun developing consensus recommendations on a number of other
21 supply chain issues, including Strategic National Stockpile (SNS) enhancement, visibility into
22 supply chains, quality and manufacturing improvement (e.g., reducing contamination in
23 finished pharmaceuticals), and medical supply and medical device supply chain reinforcement.
24 We would welcome the opportunity to meet with you to share these recommendations, which
25 are drawn from our members' expertise and their real-world experience with utilizing complex,
26 and sometimes fragile, medical supply chains. We greatly appreciate the work ASPR and FDA
27 are already undertaking on EO 14017, and we look forward to continuing to work closely with
28 you.
29

30 SUMMARY

31
32 The rate of new medical product shortages is decreasing, but the current COVID-19 public health
33 emergency requires continued diligence in monitoring any shortage or supply chain issues due to
34 manufacturing capacity prioritization for COVID-19 vaccines and treatments.
35

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

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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)

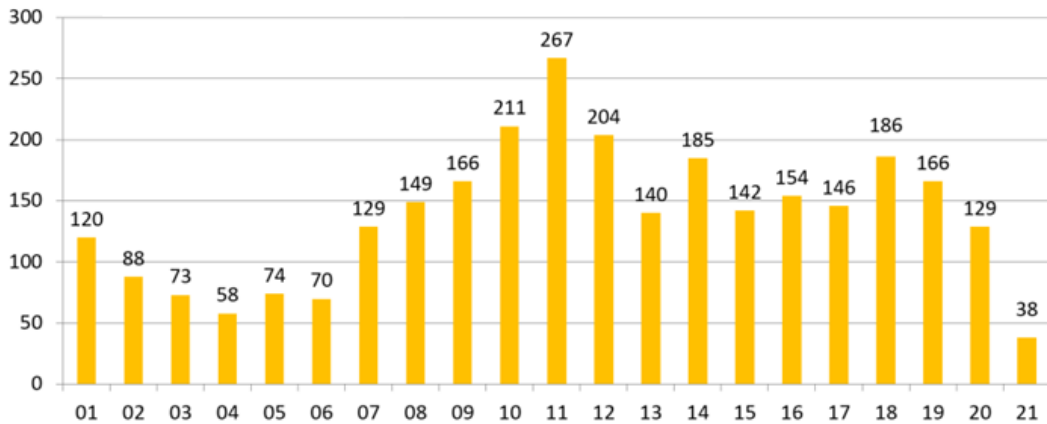
APPENDIX 1

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



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



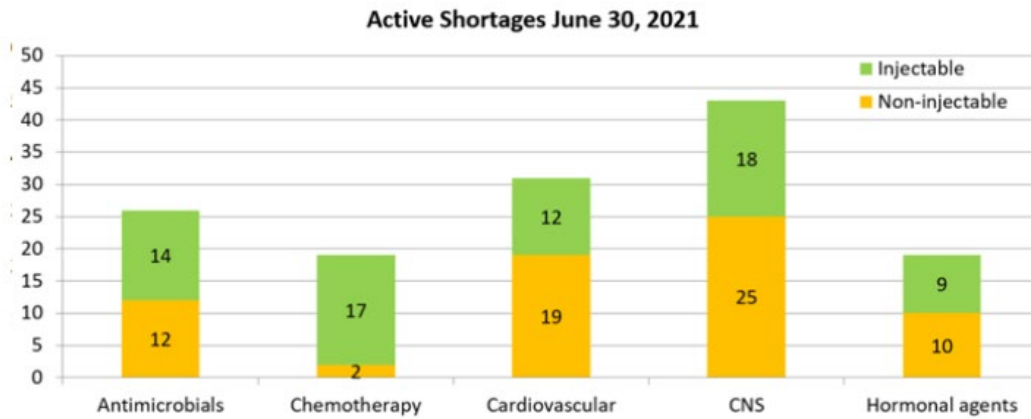
Note: Each point represents the number of active shortages at the end of each quarter.

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

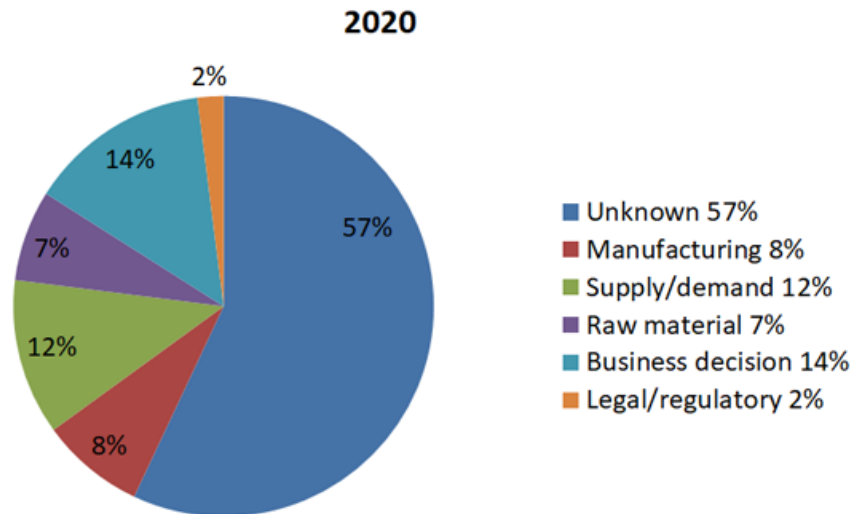


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Figure 4.

National Drug Shortages

Reasons for Shortages as Determined by UUDIS During Investigation — 2020



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

APPENDIX 2

FDA Drug Shortage Data

Breakdown of CDER's and CBER's Shortage Numbers, CY 2020

	CDER	CBER
New Shortages	43	0
Prevented Shortages	179	20
Ongoing Shortages	78	8
Notifications	473	39
No. of Manufacturers Notifying	93	29
ACTIONS TAKEN TO MITIGATE SHORTAGES		
Regulatory Flexibility and Discretion	110	1
Expedited Reviews	471	18*
Expedited Inspections	19	0

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