

REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

CSAPH Report 2-A-19

Subject: Drug Shortages: 2019 Update

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1 INTRODUCTION

2

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 (see Appendix 1 for policy). This report provides an update on
7 continuing trends in national drug shortages and ongoing efforts to further evaluate and address this
8 critical public health issue.

9

10 METHODS

11

12 English-language reports were selected from a PubMed and Google Scholar search from
13 September 2017 to February 2019, using the text term “drug shortages.” Additional articles were
14 identified by manual review of the references cited in these publications. Further information was
15 obtained from the Internet sites of the US Food and Drug Administration (FDA), National
16 Academies of Sciences, Engineering, and Medicine (NASEM), American Society of Health-
17 System Pharmacists (ASHP), Pew Charitable Trusts, Duke Margolis Center for Health Policy, the
18 Institute for Safe Medication Practices (ISMP), and by direct contact with key FDA, ASHP, and
19 Utah Drug Information Service staff who monitor drug shortages and related issues daily.

20

21 BACKGROUND

22

23 The CSAPH has issued nine reports on drug shortages.¹⁻⁹ The findings and conclusions of the first
24 five reports are summarized in CSAPH Report 2-I-15, “National Drug Shortages: Update.”⁴ The
25 remainder of this report will update information on drug shortages since the 2018 report was
26 developed, specifically commenting on the new initiatives to identify the root causes of drug
27 shortages.

28

29 CURRENT TRENDS IN DRUG SHORTAGES

30

31 Drug shortages remain an ongoing public health concern in the United States. The rate of new
32 shortages is increasing and common shortages are severely impacting patient care and pharmacy
33 operations. Ongoing supply challenges of certain medications, typically older, generic, injectable
34 products that are off-patent and have few suppliers (usually three or fewer), persist. Long-term
35 active and ongoing shortages are not resolving and the most basic products required for patient care
36 are in shortage, including bupivacaine, lidocaine, hydromorphone, morphine, fentanyl, ketamine,
37 ondansetron, saline, and sterile water. Causes of shortages continue to remain largely unchanged
38 and are mostly triggered by quality problems during manufacturing processes.

1 The two primary data sources for information on drug shortages in the United States continue to be
2 the Drug Shortage Program at the FDA and the Drug Shortage Resource Center maintained by
3 ASHP in cooperation with the University of Utah Drug Information Service (UUDIS). According
4 to the most recent data compiled by ASHP and UUDIS, in 2018 there were a total of 306 active
5 shortages, with 186 of those being new (compared to 2017 which saw 303 active and 146 new
6 shortages). Each quarter since the third quarter of 2017 saw an increase in drug shortages. The top
7 five classes of drugs implicated in active drug shortages include CNS medications (43);
8 antimicrobials (33); electrolytes, nutrition, and fluids (31); cardiovascular medications (23); and
9 chemotherapy agents (16). The reasons for drug shortages vary and unknown/unreported reasons
10 account for 51 percent of drug shortages. Manufacturing issues account for 30 percent of shortage
11 issues and drug discontinuation increased to 10 percent of shortage issues in 2018 compared to 4
12 percent in 2017. (See Appendix 2 for ASHP/UUDIS data).¹⁰

13
14 The fifth annual report on drug shortages from the FDA to Congress published in June 2018,
15 summarizes the major actions the FDA took in calendar year 2017 related to drug shortages.¹¹
16 Notably, using a range of available tools, the FDA worked with manufacturers to successfully
17 prevent 145 shortages during 2017.¹¹

18
19 The FDA continues to utilize a mobile app to provide up-to-date access to drugs in shortage as well
20 as notifications about new and resolved drug shortages and gives physicians the ability to report a
21 drug shortage. The FDA Drug Shortages webpage includes a current shortages list, mobile app, and
22 additional information (Box 1).¹² The ASHP Shortage Resource Center provides a list of shortages,
23 guidance on managing critical shortages, as well as shortage metrics (Box 1).¹³ Additionally, a
24 recent publication details ASHP guidelines for managing drug product shortages and provides a
25 framework for healthcare teams in patient care to develop policies and procedures that minimize
26 the effects of drug shortages on quality of care.¹⁴

27 28 CURRENT DRUG SHORTAGE ACTIVITIES

29
30 *National Academies of Sciences Engineering Medicine Workshop, Medical Product Shortages*
31 *during Disasters: Opportunities to Predict, Prevent, and Respond*

32
33 In September 2018, the AMA participated in a NASEM-convended workshop, Medical Product
34 Shortages during Disasters: Opportunities to Predict, Prevent, and Respond, to better understand
35 the gaps that lead to cascading effects in patient care throughout the U.S. health care system when
36 shortages of medical devices, drugs, and supplies occur in the context of disaster (not day-to-day
37 shortages).

38
39 Discussion topics included the importance of public-private partnerships and a collaborative effort;
40 situational awareness about all elements of the supply chain; the need to identify useful metrics,
41 collect sufficient data, and share it accordingly; the strategic national stockpile; issues with “just-
42 in-time stocking” and shortage cascades; the issues involved in frequent staff (re)training, learning,
43 and alert fatigue; and the impact on patient care including “regression of care” when physicians
44 need to find solutions other than the standard of care. The detailed proceedings from the workshop
45 have been published.¹⁵

1 *Multi-stakeholder Summit, Drug Shortages as a Matter of National Security: Improving the*
2 *Resilience of the Nation’s Healthcare Critical Infrastructure*

3
4 In September 2018, the AMA participated in a summit regarding drug shortages as a matter of
5 national security, sponsored by several stakeholders including ASHP, ISMP, the American
6 Hospital Association, American Society of Anesthesiologists, and American Society of Clinical
7 Oncology.

8
9 The objectives of the summit were to identify the vulnerabilities of the supply chain that result in
10 drug shortages; define the roles and responsibilities of the public and private sectors for planning
11 and responding to national security events; and identify recommendations to strengthen the current
12 healthcare infrastructure to prevent drug shortages that may result in patient harm.

13
14 The meeting brought together representatives from clinician groups, industry and supply chain, and
15 public-sector members to discuss drug shortages as a national security priority. Several
16 recommendations were offered after the discussion as potential policy and marketplace changes
17 that may help prevent and mitigate drug shortages.¹⁶

18
19 Some of the recommendations discussed at length included:

- 20
21 1. The need for greater understanding of the drug supply chain from beginning to end,
22 including clarity of raw material sources, overall quality of production, and greater
23 transparency from manufacturers;
24 2. Development of management models using data science as well as the need to identify the
25 relevant metrics related to the drug supply chain and how to collect and share it
26 3. Development of an “essential drugs” list;
27 4. Incentives for manufacturers;
28 5. Standardization of medication dose, preparations, and size.

29
30 *U.S. Food and Drug Administration Activities*

31
32 In a statement from July 2018, FDA Commissioner Scott Gottlieb, MD, and FDA Center for Drug
33 Evaluation and Research Director Janet Woodcock, MD, outlined new efforts the FDA is
34 advancing to address drug shortages – a three-pronged approach that focuses on preventing
35 shortages, early identification of anticipated shortages, and responding to shortages using their
36 current authorities, as well as the creation of an Interagency Drug Shortage Task Force.^{17,18}

37
38 Interagency Drug Shortage Task Force. An Interagency Drug Shortage Task Force was established
39 by the FDA to identify the root causes of drug shortages and advance potential long-term solutions
40 in a report to Congress. The Task Force will be led by FDA’s Associate Commissioner for
41 Strategic Initiatives and will include federal officials from several agencies concerned with drug
42 shortages including the FDA, the Centers for Medicare & Medicaid Services (CMS), the Office of
43 the Assistant Secretary for Preparedness and Response, the Department of Veterans Affairs, the
44 Department of Defense, and the Federal Trade Commission.¹⁹

45
46 Currently, in cases of drug shortages, the FDA has a variety of tools to employ to minimize the
47 impact. These include expediting the inspection of a new drug manufacturing facility so it can
48 become operational as soon as possible; expediting the review of a new or generic drug application
49 that, if approved, may help mitigate or prevent a shortage; urging manufacturers of similar or
50 alternative products to ramp up production to meet an anticipated increased demand; and exercising
51 discretion with respect to temporary importation of a product from a foreign manufacturing source

1 until a shortage is resolved. FDA officials have stated that the work of the Task Force will be
2 “forward-leaning and extensive” with the goal of complementing and strengthening the ongoing
3 efforts of the Agency to establish long-term solutions. Some of the considerations include
4 proposals for possible additions to FDA authorities, evaluation of reimbursement policies of
5 payors, exploration of possible incentives to encourage manufacturing that can expand and ensure a
6 stable drug supply, evaluation of the need for an essential drugs list, and incentives for
7 manufacturing critical drugs.

8
9 FDA Listening Session on Drug Shortages. In October 2018, the FDA held a series of invitation-
10 only listening sessions at the FDA. Invitations were extended to a diverse group of stakeholders
11 including medical organizations (such as AMA), pharmacies and hospitals, manufacturing groups,
12 group purchasing organizations (GPOs) and distributors, and experts and think tanks. The goal of
13 the sessions was for the FDA to gather information concerning the economic and clinical impact of
14 drug shortages and to inform the newly formed Interagency Drug Shortage Task Force. AMA staff
15 in attendance provided comprehensive comments regarding AMA policy and the most recent
16 Council on Science and Public Health report from A-18.

17
18 The FDA lists four general themes that came from the series of listening sessions:

- 19
20 1. The impacts of drug shortages affect every level of the health care system, ultimately
21 compromising the standard of care, producing waste, and increasing costs.
- 22 2. Multiple market factors such as buyer and seller consolidation, low margins, and
23 contracting practices contribute to drug shortages.
- 24 3. It is unclear what the right level of transparency is based on manufacturing security
25 concerns, and hospital, pharmacy, and GPO needs. The health care community would like
26 more transparency throughout the supply chain.
- 27 4. Multiple federal agencies such as the FDA, Drug Enforcement Administration, and CMS,
28 have different authorities on drugs, which makes it hard for both industry and hospitals to
29 manage. Ideas have been put forth on how agencies can mitigate – but may unintentionally
30 exacerbate – the issues.

31
32 FDA Public Meeting: Identifying the Root Causes of Drug Shortages and Finding Enduring
33 Solutions. In November 2018, the FDA Interagency Task Force under a cooperative agreement
34 with the Robert J. Margolis, MD, Center for Health Policy at Duke University, hosted a public
35 meeting for open discussion of the root causes of drug shortages and solutions, which AMA staff
36 attended. The speakers at the day-long public meeting included a broad range of stakeholders.

37
38 The FDA’s efforts to date have addressed the immediate causes of drug shortages such as
39 manufacturing quality issues, raw material sourcing, business decisions to discontinue products,
40 and marketplace changes. This initiative aims to focus on identifying and remedying systemic, root
41 causes that drive and sustain product shortages and developing enduring solutions to mitigate and
42 prevent drug shortages from occurring.

43
44 Little consensus exists regarding the most significant and the largest contributing root causes of
45 drug shortages. A useful discussion guide from this public meeting outlines some of the
46 hypothesized root causes of drug shortages including lacking information to assess drug supply
47 reliability; low profit margins, particularly among generic drugs, causing decreased production and
48 quality; barriers to market entry from manufacturers to address shortages; and additional
49 contributing factors including “just-in-time” manufacturing, contracts and agreements, stockpiling,
50 and increased globalization/limited supply chain options.²⁰

1 Input from this meeting, as well as from listening sessions with stakeholders, and the public docket
2 will be considered during the drafting of a report providing recommendations/guidance that the
3 Task Force plans to submit to Congress by the end of 2019. Potential areas of action might include,
4 but would not be limited to, contracting, tax incentives, increased transparency of manufacturing
5 quality, reimbursement or regulatory changes, as well as any other proposed solutions as
6 appropriate.

7
8 Public Docket. FDA had a public docket open to receive stakeholder comments regarding the root
9 causes of drug shortages and possible solutions which closed on January 11, 2019. The AMA
10 submitted comments to the docket outlining our policy and recommendations (Appendix 3).²¹

11
12 Quality Metrics. Appropriate quality metrics provide elements of assurance and oversight
13 necessary for pharmaceutical manufacturing and quality control; however, the complexity of the
14 manufacturing process makes the collection and use of metrics difficult. The FDA has taken steps
15 within its regulatory authority to address this issue as it relates to drug shortages by developing a
16 quality metrics program for pharmaceutical manufacturers.²² Information generated could be used
17 by the FDA to identify drugs at greater risk of shortage and proactively reduce that risk before a
18 disruption occurs.

19
20 Manufacturing Modernization. Another FDA initiative encourages manufacturers to adopt
21 advanced manufacturing technologies, such as continuous manufacturing, that increase production
22 reliability and capacity and can assist in medical product shortage mitigation. To support this
23 initiative, the FDA established an Emerging Technology Program to foster dialogue between FDA
24 and manufacturers as they work to develop and implement these approaches.²³ Additionally, a
25 recent workshop at NASEM, and sponsored by the FDA and the Biomedical Advanced Research
26 and Development Authority, focused on the status of, and research opportunities for, continuous
27 manufacturing in the pharmaceutical industry.²⁴

28
29 Generic Drugs. As previously mentioned, medical product shortages typically involve older,
30 generic products. In January of 2018, the FDA announced a Drug Competition Action Plan aimed
31 at promoting competition and access, especially in the development of generic drugs in
32 pharmaceutical categories that lack competition.²⁵

33 34 *New Companies to Mitigate Drug Shortages*

35
36 Civica Rx. Recently, more than 120 health organizations have been involved in the creation of a
37 not-for-profit generic drug company, Civica RX, that will manufacture, or sub-contract
38 manufacturing of, critical hospital-administered drugs.²⁶ Martin VanTrieste, Civica Rx CEO, has
39 stated that "All drug shortages are the result of economics, financial and management decisions."
40 The organization will initially seek to stabilize the supply of essential generic medications
41 administered in hospitals (including sterile injectables), many of which have fallen into chronic
42 shortage situations, putting patients at risk. The organization is focusing on fair and sustainable
43 prices for medications and predicts this initiative will ultimately result in overall lower costs and
44 more predictable supplies of essential generic medicines. Civica Rx expects to have its first
45 products on the market in 2019.

46
47 ProvideGx. In January 2019, Premier Inc. announced that it has formed a company intended to
48 help address drug shortages, ProvideGx, and has partnered with five generic drug makers to
49 address a targeted pipeline of 60 crucial drugs that will be available through Premier's GPO.

1 SUMMARY

2

3 The rate of new medical product shortages is increasing and shortages of essential medications are
4 severely impacting patient care and pharmacy operations. The ongoing supply challenges of mostly
5 generic medications, typically injectable products, that are off-patent persist.

6

7 A recent FDA data analysis of the scope and scale of drug shortages evaluated the occurrence,
8 duration, intensity, and public health impact medical product shortages.²⁷ The analysis revealed
9 that the occurrence of active and ongoing shortages is increasing; the duration is longer; shortages
10 are more persistent; intensity is high, as some shortages have been ongoing for >8 years; and the
11 public health impact is high because of an increase in patient harm and health care losses.
12 Congruent with these findings, the FDA has undertaken new initiatives to address the systemic root
13 causes and contributing factors that lead to shortages and determine enduring solutions. Our AMA
14 has been involved in conversations with the FDA and other stakeholders and remains committed to
15 addressing this critical issue. Beyond activity at the federal agency level, the marketplace in 2019
16 saw the emergence of two new companies, Civica Rx and ProvideGx, which may directly address
17 shortages by bringing into the market supplies of drugs and drug vehicles critically needed by
18 hospitals and the patients they serve.

19

20 The AMA's drug shortage policy is timely and already addresses a variety of issues that are under
21 consideration by the FDA and other stakeholder including the improvement quality systems;
22 expedited facility inspections and manufacturing changes/improvements; necessary resiliency and
23 redundancy in manufacturing capability; evaluation of root causes of drug shortages; transparent
24 analysis of economic drivers and reasonable and sustainable payment rates for prescription drugs;
25 greater transparency of the manufacturing process; and including drug manufacturing sites as part
26 of the nation's critical infrastructure plan. Therefore, the Council feels that an update to AMA
27 policy is not warranted at 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. ASHP and University of Utah [guidance](#) on small-volume parenteral solutions shortages
4. ASHP and University of Utah [guidance](#) on injectable opioid shortages
5. [FDA Drug Shortages Page](#) (includes current shortages list, mobile app, and additional information)

APPENDIX 1

AMA Drug Shortage Policy

H-100.956, “National Drug Shortages”

1. Our AMA considers drug shortages to be an urgent public health crisis, and recent shortages have had a dramatic and negative impact on the delivery and safety of appropriate health care to patients.
2. Our AMA supports recommendations that have been developed by multiple stakeholders to improve manufacturing quality systems, identify efficiencies in regulatory review that can mitigate drug shortages, and explore measures designed to drive greater investment in production capacity for products that are in short supply, and will work in a collaborative fashion with these and other stakeholders to implement these recommendations in an urgent fashion.
3. Our AMA supports authorizing the Secretary of the U.S. Department of Health and Human Services (DHHS) to expedite facility inspections and the review of manufacturing changes, drug applications and supplements that would help mitigate or prevent a drug shortage.
4. Our AMA will advocate that the US Food and Drug Administration (FDA) and/or Congress require drug manufacturers to establish a plan for continuity of supply of vital and life-sustaining medications and vaccines to avoid production shortages whenever possible. This plan should include establishing the necessary resiliency and redundancy in manufacturing capability to minimize disruptions of supplies in foreseeable circumstances including the possibility of a disaster affecting a plant.
5. The Council on Science and Public Health shall continue to evaluate the drug shortage issue, including the impact of group purchasing organizations on drug shortages, and report back at least annually to the House of Delegates on progress made in addressing drug shortages.
6. Our AMA urges the development of a comprehensive independent report on the root causes of drug shortages. Such an analysis should consider federal actions, the number of manufacturers, economic factors including federal reimbursement practices, as well as contracting practices by market participants on competition, access to drugs, and pricing. In particular, further transparent analysis of economic drivers is warranted. The federal Centers for Medicare & Medicaid Services (CMS) should review and evaluate its 2003 Medicare reimbursement formula of average sales price plus 6% for unintended consequences including serving as a root cause of drug shortages.
7. Our AMA urges regulatory relief designed to improve the availability of prescription drugs by ensuring that such products are not removed from the market due to compliance issues unless such removal is clearly required for significant and obvious safety reasons.

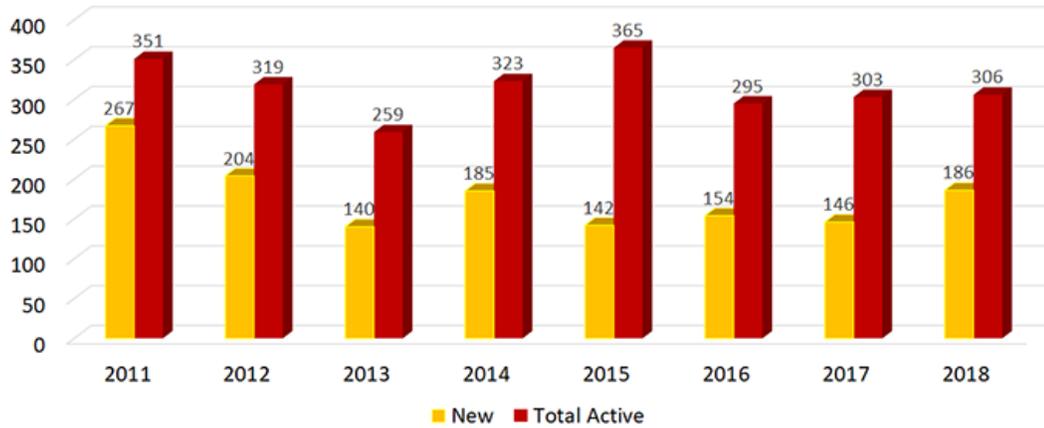
8. Our AMA supports the view that wholesalers should routinely institute an allocation system that attempts to fairly distribute drugs in short supply based on remaining inventory and considering the customer's purchase history.
9. Our AMA will collaborate with medical specialty society partners and other stakeholders in identifying and supporting legislative remedies to allow for more reasonable and sustainable payment rates for prescription drugs.
10. Our AMA urges that during the evaluation of potential mergers and acquisitions involving pharmaceutical manufacturers, the Federal Trade Commission consult with the FDA to determine whether such an activity has the potential to worsen drug shortages.
11. Our AMA urges the FDA to require manufacturers to provide greater transparency regarding production locations of drugs and provide more detailed information regarding the causes and anticipated duration of drug shortages.
12. Our AMA encourages electronic health records (EHR) vendors to make changes to their systems to ease the burden of making drug product changes.
13. Our AMA urges the FDA to evaluate and provide current information regarding the quality of outsourcer compounding facilities.
14. Our AMA urges DHHS and the U.S. Department of Homeland Security (DHS) to examine and consider drug shortages as a national security initiative and include vital drug production sites in the critical infrastructure plan.

APPENDIX 2

ASHP/University of Utah Drug Information Service Drug Shortage Data

Figure 1.

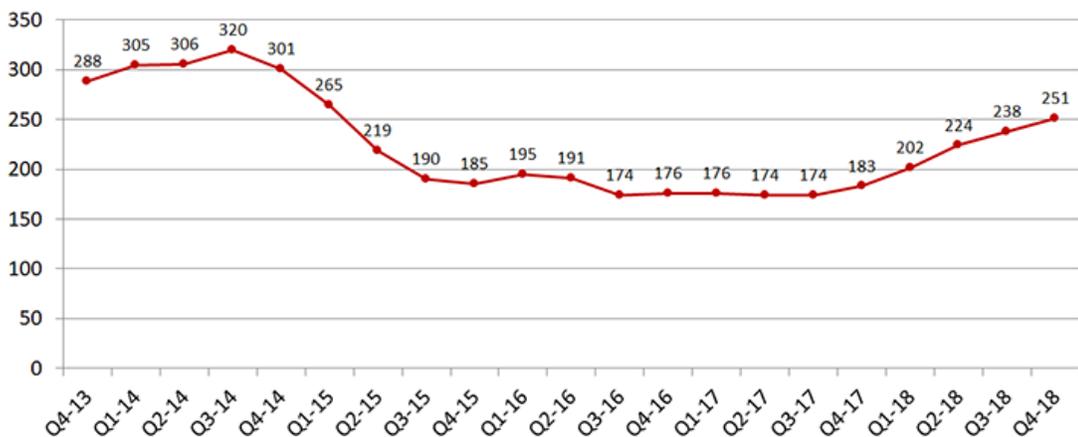
National Drug Shortages: Annual New Shortages and Total Active Shortages
2011 to 2018



University of Utah Drug Information Service
Contact: Erin.Fox@hsc.utah.edu, [@foxeirin](https://twitter.com/foxeirin) for more information.

Figure 2.

National Drug Shortages: Active Shortages by Quarter
October 1, 2013 to December 31, 2018

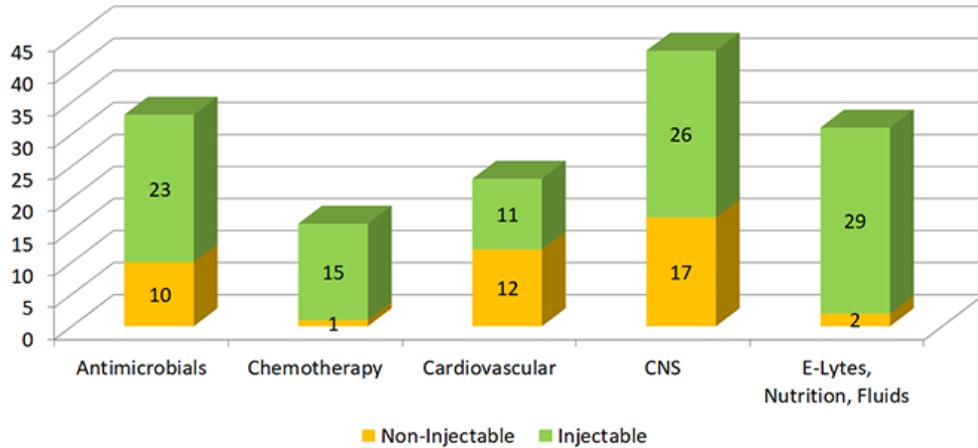


Note: These data represent the count of active shortages on the last day of each quarter, and should not be interpreted as total shortages for that period.

University of Utah Drug Information Service
Contact: Erin.Fox@hsc.utah.edu, [@foxeirin](https://twitter.com/foxeirin) for more information.

Figure 3.

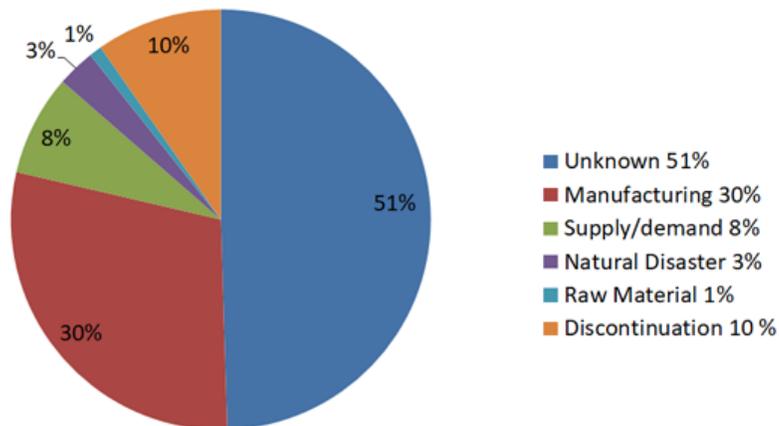
National Drug Shortages: Active Shortages-Top Five Drug Classes
December 31, 2018



University of Utah Drug Information Service
Contact: Erin.Fox@hsc.utah.edu, [@foxerinr](https://twitter.com/foxerinr) for more information.

Figure 4.

National Drug Shortages
Reasons for Shortages* – 2018



*Based on information provided by manufacturers to the University of Utah Drug Information Service

University of Utah Drug Information Service
Contact: Erin.Fox@hsc.utah.edu, [@foxerinr](https://twitter.com/foxerinr) for more information.

APPENDIX 3

AMA Comment Letter: Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions; Docket No. FDA-2018-N-3272



JAMES L. MADARA, MD
EXECUTIVE VICE PRESIDENT, CEO

ama-assn.org
t (312) 464-5000

January 11, 2019

The Honorable Scott Gottlieb, MD
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions; Docket No. FDA-2018-N-3272

Dear Commissioner Gottlieb:

On behalf of the physician and medical student members of the American Medical Association (AMA), I appreciate the opportunity to provide comments in response to *Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions*. We applaud the U.S. Food and Drug Administration's (FDA) establishment of a Drug Shortages Task Force in order to identify the root causes of drug shortages and recommend sustainable and structural policy solutions in a report to Congress. The persistence and pervasiveness of drug shortages have consequences for patient care and require an ongoing comprehensive examination of the systemic causes and drivers.

Drug shortages are an urgent public health crisis. Recent shortages have had a negative impact on the delivery and safety of appropriate health care to patients. Long-term shortages have been persistent and critical shortages of basic products such as saline are driving poor patient health outcomes, increasing the potential for medication errors, re-directing scarce administrative and clinical staff time and resources to the identification of alternative treatment options, or delaying patient treatment (such as surgeries). Several commonly used products required for patient care are in shortage, including sterile infusion solutions and injectable products that are off-patent and have few suppliers.^{1,2}

To address the drug shortage issue, AMA supports policy, legislation, and/or regulation that:

- Encourages stakeholders in the drug supply chain to increase **collaboration**.
- **Increases transparency** along the pharmaceutical supply chain.
- Establishes plans for **continuity of supply** of vital medications, including the establishment of resiliency and redundancy in manufacturing capability.
- Reduces or **removes regulatory hurdles** and barriers while enhancing flexibilities.
- **Incentivizes investment** in expanded manufacturing production capacity for vital products.

¹ U.S. Government Accountability Office (GAO). Drug Shortages: Certain Factors Are Strongly Associated with This Persistent Public Health Challenge. July 2016.

² Mazer-Amirshahi M, Fox ER. Saline Shortages — Many Causes, No Simple Solution. *New England Journal of Medicine*. 2018; 378:1472-1474

Collaboration

The AMA applauds the FDA's efforts thus far in engaging with a broad range of stakeholders in public meetings and listening sessions and remains committed to participating and assisting. The AMA supports recommendations that have been developed by multiple stakeholders to improve manufacturing quality systems, identify efficiencies in regulatory review that can mitigate drug shortages, and explore measures designed to drive greater investment in production capacity for products that are in short supply.³ We urge stakeholders from the entirety of the drug supply chain and the FDA to work in a collaborative fashion to implement these recommendations.

Increase Transparency

The AMA strongly urges the FDA to require manufacturers to provide greater transparency regarding the drug manufacturing process from start to finish. Knowledge of the entire supply chain, including raw material suppliers, active pharmaceutical ingredient manufacturers and suppliers, distributors and distribution sites, as well as production locations of drugs, can provide the necessary metrics for much-needed quality analysis and information regarding supply chain disruptions that contribute to medical product shortages and their causes. More information about the manufacturing process can inform the causes and anticipated duration of drug shortages and assist in shortage mitigation.

Continuity of Drug Supply

The AMA strongly supports conferring the FDA with enforcement authorities to ensure that drug manufacturers establish a plan for continuity of supply of vital medications and vaccines to avoid production shortages whenever possible. The continuity of supply plan should include the establishment of the necessary resiliency and redundancy in manufacturing capability to minimize disruptions of supplies in foreseeable circumstances including the possibility of a disaster affecting a plant.

The AMA strongly supports the designation of drug shortages as a national security priority and the inclusion of vital drug production sites in the critical infrastructure plan. Several manufacturers were impacted by cyber events over the past year and product shortages were worsened by the recent hurricanes impacting Puerto Rico which demonstrate the need to evaluate risk and hazard and disaster response for drug and medical product manufacturing. The AMA urges the application of critical infrastructure policies to the drug shortage challenges clinicians, their patients, and families face each day.

Reduction in Regulatory Burden

The AMA strongly supports the FDA's effort to provide increased flexibilities and engagement when manufacturers have notified the Agency of a potential or actual drug shortage. The AMA continues to specifically support expedited facility inspections and the review of manufacturing changes, drug applications, and supplements that would assist manufacturers in mitigating or preventing a drug shortage. We urge the FDA to consider whether innovative portals, technologies, or collaborations involving big data and augmented intelligence systems (also referred to as artificial intelligence) could be

³ ASHP Drug Shortages Roundtable Report, November 2018. <https://www.ashp.org/drug-shortages/shortage-resources/roundtable-report>

deployed by the FDA to forecast potential shortages and root causes including, but not limited, to regulatory policies.

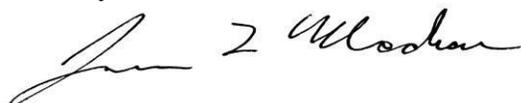
Federal Policies, Market Forces, Investment Incentives

The AMA strongly supports the development of a comprehensive report on the root causes that also analyzes current manufacturing capacity, the number of manufacturers, mergers and consolidations, economic factors including federal reimbursement practices, as well as contracting practices by market participants on competition, access to drugs, and pricing. The AMA also urges careful consideration of federal health care program payment rates for drugs that are vulnerable to shortage. The Government Accountability Office identified low profit margins for drugs in shortage as a relevant contributing factor to persistent shortages. Carefully targeted policies to address potential underinvestment in vital products subject to intractable shortages should be evaluated.

The AMA strongly supports collaboration between the Federal Trade Commission (FTC) and the FDA during the evaluation of potential mergers and acquisitions involving pharmaceutical manufacturers. FTC consultation with the FDA can aid in determining the public health implications of mergers and acquisitions, including the potential impact on drug shortages. Related to the foregoing, the AMA has expressed support for expanded resources and capacity at the FTC to more fully assess and evaluate the impact of mergers and consolidations on competition as well as consumer access as part of the FTC's charge to advance consumer protection. Without oversight and intervention, drug shortages will exist into the foreseeable future if further consolidations occur reducing production capacity.

Our physician members and their patients are negatively impacted by the persistent and ongoing shortages of necessary and often basic medical products. We look forward to working closely with you and other federal agencies to take rapid, direct action where opportunity exists to permanently resolve or mitigate drug shortages. If you have questions, please contact Shannon Curtis, Assistant Director, Division of Federal Affairs at shannon.curtis@ama-assn.org or 202-789-8510.

Sincerely,

A handwritten signature in black ink, appearing to read "James L. Madara". The signature is fluid and cursive, with a large initial "J" and "M".

James L. Madara, MD