

# REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

CSAPH Report 2-I-16

Subject: National Drug Shortages: Update

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## 1 INTRODUCTION

2  
3 Policy H-100.956, “National Drug Shortages,” directs the Council on Science and Public Health  
4 (CSAPH) to continue to evaluate the drug shortage issue and report back at least annually to the  
5 House of Delegates (HOD) on progress made in addressing drug shortages in the U.S. This  
6 informational report provides an update on continuing trends in national drug shortages and  
7 ongoing efforts to further evaluate and address this critical public health issue.

## 9 METHODS

10  
11 English-language reports were selected from a PubMed and Google Scholar search from  
12 September 2015 to August 2016, using the text term “drug shortages” combined with “impact,”  
13 “crisis,” “oncology,” “chemotherapy,” “antibacterial,” “pediatric(s),” “nutrition,” and “parenteral.”  
14 Additional articles were identified by manual review of the references cited in these publications.  
15 Further information was obtained from the Internet sites of the U.S. Food and Drug Administration  
16 (FDA), American Society of Health-System Pharmacists (ASHP), Government Accountability  
17 Office (GAO), Pew Charitable Trusts, Generic Pharmaceutical Association, the Pharmaceutical and  
18 Research Manufacturers of America (PhRMA) and by direct contact with key FDA and ASHP staff  
19 who manage drug shortage issues on a daily basis.

## 21 BACKGROUND

22  
23 The Council has issued six previous reports on drug shortages.<sup>1-6</sup> The findings and conclusions  
24 from these reports are summarized in CSAPH Report 2-I-15.<sup>6</sup> The remainder of this report will  
25 update current information on drug shortages since that report was developed.

## 27 CURRENT TRENDS IN DRUG SHORTAGES

28  
29 The two primary data sources for information on drug shortages in the United States continue to be  
30 the Drug Shortage Resource Center maintained by ASHP in cooperation with the University of  
31 Utah Drug Information Service and the Drug Shortage Program at the FDA.<sup>7,8</sup> For a reminder on  
32 how the ASHP and FDA information and statistics on drug shortages are developed, see Table 1.  
33 The ASHP defines a drug shortage as “a supply issue that affects how the pharmacy prepares or  
34 dispenses a drug product or influences patient care when prescribers must use an alternative agent.”  
35 The FDA defines shortages as a period of time when the demand or projected demand for a  
36 medically necessary drug in the United States exceeds its supply. Medically necessary drugs are  
37 defined by FDA as “any drug product used to diagnose, treat, or prevent a serious disease or

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Action of the AMA House of Delegates 2016 Interim Meeting: Council on Science and Public Health Report 2 Filed for Information.

1 medical condition for which there is no other drug that is judged to be an appropriate substitute or  
2 there is an inadequate supply of an acceptable alternative.”

3 Because their criteria differ (the main distinction being the FDA’s definition of a “medically  
4 necessary drug”), the ASHP site lists more drug shortages than the FDA site.

5  
6 *American Society of Health-System Pharmacists*

7  
8 As of September 13, 2016, ASHP’s Drug Shortage Resource Center identified 135 drugs in  
9 shortage, down from 180 at the same time in 2015. Among these drug shortages, 17 products were  
10 not commercially available at all.<sup>8</sup> Sixty-nine manufactured drugs have been discontinued since  
11 2010, an increase of 9 from a year ago. The top active shortages by drug class remain central  
12 nervous system agents, electrolytes and nutritional components, antimicrobials, cardiovascular  
13 drugs, and chemotherapeutic agents. For a longitudinal view of new drug shortages on an annual  
14 basis, and the number of active drugs shortages quarterly, see the Appendix. Active shortages  
15 include both new and unresolved drug shortages. According to ASHP, the number of new  
16 shortages continues to decrease, while the number of active shortages has stabilized to a certain  
17 degree.

18  
19 *Food and Drug Administration*

20  
21 As of September 13, 2016, the FDA reported that 61 drugs were currently in shortage (compared  
22 with 67 one year ago), and 10 had been resolved.<sup>8</sup> The latter are closely monitored because they  
23 may be at risk for falling back into shortage. Based on passage of the Food and Drug  
24 Administration Safety and Innovation Act (FDASIA) in 2012, companies are required to notify  
25 FDA of a permanent discontinuance or an interruption in manufacturing of certain drug products  
26 six months in advance, or if that is not possible, as soon as practicable. The shortage notification  
27 requirement has apparently reduced the number of new shortages by allowing FDA additional time  
28 to work with manufacturers to prevent shortages. The FDA’s drug shortages website lists drugs that  
29 meet these criteria, reflecting shortage information supplied by manufacturers.<sup>8</sup> A Final Rule  
30 published on July 27, 2015 provides further guidance on the notification process and adds biologic  
31 products to the requirements for notification about potential supply disruptions.<sup>9</sup>

32  
33 Drug Shortages Metrics Reported by FDA. The FDA’s third annual report on drug shortages  
34 (required by FDASIA) noted the following metrics during the first three quarters of calendar year  
35 2015.<sup>10</sup>

- 36  
37
- 38 • FDA was notified of 131 potential shortage situations by 47 different manufacturers,  
39 comparable to the numbers reported in 2014.
  - 40 • 128 new drug shortages were prevented in the first three quarters of 2015, a 64% increase  
41 over the comparable time period for 2014.
  - 42 • The review of 102 generic abbreviated new drug or supplemental applications was  
43 expedited, comparable to the numbers reported in 2014.
  - 44 • 11 inspections were prioritized to address a drug shortage, comparable to the number  
45 reported in 2014.
  - 46 • 11 fewer new drug shortages occurred in the first three quarters of 2015 (22) compared  
47 with the same period in 2014 (33).
  - 48 • FDA exercised regulatory flexibility and discretion in 19 instances affecting 37 medically  
49 necessary products. Most of these involved measures to mitigate risks such as removing  
particulate matter, extra testing for quality, third-party oversight of production, provision

1 of special instructions to prescribers and/or patients, or approval of foreign sources. With  
2 respect to the last of these mitigation strategies, the FDA now conducts regular virtual  
3 meetings with their international regulatory counterparts to share information on drug  
4 shortages and mitigation strategies impacting patients in other countries.

5  
6 The FDA also has developed apps for both the iPhone and Android operating systems that provide  
7 access to drug shortage information as well as notifications about new and resolved drug shortages.

#### 8 9 *Reporting a Drug Shortage*

10  
11 Physicians can directly [report](#) a drug shortage via the ASHP drug shortage website. Physicians can  
12 directly report a drug shortage to the Center for Drug Evaluation and Research via email  
13 ([drugshortages@fda.hhs.gov](mailto:drugshortages@fda.hhs.gov)) or by phone at 240-402-7770.

#### 14 15 GAO REPORT

16  
17 In a follow-up to its 2014 report on drug shortages, the Government Accountability Office (GAO)  
18 evaluated trends in drug shortages from 2010-2015 in an effort to identify influential factors.<sup>11</sup> This  
19 evaluation confirmed that the FDA had prioritized 383 new, abbreviated, and supplemental drug  
20 applications to address drug shortages, mostly for sterile injectable products. The use of this  
21 prioritization scheme was temporally associated with reductions in active and ongoing shortages.  
22 Analysis of selected categories (i.e., sterile injectable anti-infective and cardiovascular drugs)  
23 confirmed that shortages were strongly associated with previously identified key drivers, namely a  
24 decline in the number of manufacturers, existence of a generic product, and an emergent problem  
25 with manufacturing capability in at least one manufacturer that was sufficiently serious to cause a  
26 warning letter to be issued. Shortages were more likely to affect generic drugs with low profit  
27 margins, although drug price itself was not predictive in this study.

#### 28 29 GENERIC PHARMACEUTICAL ASSOCIATION

30  
31 Given that the majority of drug shortages involve generic products, the GPhA created a voluntary  
32 approach called the Accelerated Recovery Initiative in 2013 intended to accelerate the recovery of  
33 certain critical drugs in short supply.<sup>4,12</sup> This multi-stakeholder approach relies on voluntary,  
34 confidential communication between an independent third party (IMS Health) and pharmaceutical  
35 companies involved in the manufacturing of generic injectable drugs in shortage. Additionally,  
36 wholesalers, distributors, and the FDA can provide information to assist companies with making  
37 timely decisions to help avert or mitigate a shortage. While this program is apparently still  
38 operational, there are no publicly available reports evaluating its degree of success.<sup>12</sup>

#### 39 40 CLINICAL IMPLICATIONS

41  
42 Despite increasing success in preventing or mitigating drug shortages and an overall decrease in the  
43 number of new drug shortages, critical drug shortages continue to occur across multiple therapeutic  
44 categories. While the existence of a sole source manufacturer is a risk factor for shortages, it also  
45 has been the focus of some recent exorbitant drug price escalations. Reviews of shortages affecting  
46 the operation of emergency departments identified several intravenous formulations that remain in  
47 short supply and are affecting patient care including certain opioid analgesics, antiemetics, selected  
48 antimicrobials, benzodiazepines and other drugs used for rapid induction of anesthesia,  
49 electrolytes, and local anesthetics.<sup>13,14</sup> Shortages of various antidotes also have been noted, and the  
50 implications of drug shortages for pediatric patients, those with cardiovascular disease or those

1 who are acutely ill have been studied.<sup>15-18</sup> In some cases, work-arounds have been successful in  
2 maintaining patient safety and achieving satisfactory clinical outcomes.<sup>19</sup>

3 SUMMARY

4  
5 Manufacturers are notifying the FDA about potential disruptions in supply or shortages earlier than  
6 in the past and the FDA is expediting the review of new applications intended to address shortages.  
7 Accordingly, the total number of new drug shortages continues to decline and the extent of ongoing  
8 shortages has stabilized over the past two years. However, the drug supply for many acutely and  
9 critically ill patients in the United States remains vulnerable despite federal efforts.<sup>20</sup> Some  
10 progress is being made, but permanent solutions remain elusive and beyond the control of  
11 individual practitioners and the health care system.

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Table 1. Contrasting the FDA (CDER) and ASHP Drug Shortage Websites

	FDA	ASHP
Purpose	Provides information obtained from manufacturers about current shortages, estimated duration, and discontinuations and provides information about FDA’s and other stakeholders’ roles in addressing and preventing shortages	Notification of new shortages and status of ongoing shortages; drug shortage management resources
Audience	Public	Healthcare practitioners
Scope of shortage list	All drugs are listed that are confirmed to be a national shortage by FDA. A shortage is considered to be the period of time when the demand for the drug within the United States exceeds the supply of the drug. <sup>a</sup>	All drug and biologic shortages reported and confirmed with manufacturer that are national in impact.
Source of shortage report	Manufacturers notify FDA of production disruption and voluntarily provide updates. Reports are also received from ASHP and from public via <a href="mailto:drugshortages@cder.fda.gov">drugshortages@cder.fda.gov</a> Note: Manufacturer-provided information represents shortage status at drug firm level.	Voluntary reports from practitioners, patients, pharmaceutical industry representatives and others <b>Note 1:</b> Information is updated based on release dates from manufacturers. <b>Note 2:</b> Reports reflect status at healthcare provider level.
Criteria for inclusion on list	Manufacturers cannot meet current market demand for the drug based on information provided by manufacturers and market sales research. Drug listed are defined as “medically necessary.”	(1) Shortage is verified with manufacturers and (2) affects how pharmacy prepares or dispenses a product, or (3) requires use of alternative drugs, which may affect patient care.
Criteria for resolving shortage	One or more manufacturers are in production and able to meet full market demand.	All manufacturers of the drug restore all formulations and dosage sizes to full availability. Note: Products are listed despite partial or restricted availability as supply chain disruptions can result in intermittent shortages at the provider or patient level.
Reason for shortage	Provided by manufacturers using reasons required by legislation. <sup>b</sup> FDA encourages firms to provide additional information about reasons and other information which, if proprietary, is nondisclosable without the firm’s permission.	Provided by manufacturer, if willing to disclose. Note: May differ from FDA’s due to different sources of information and legislation requiring FDA to use specified reasons
Other information	Estimated duration, links to regulatory information such as recalls and Dear Healthcare Provider Letters	Estimated duration, list of available products, implications for patient care and safety, shortage management strategies, therapeutic alternatives

<sup>a</sup> Note: A separate shortage webpage for vaccines and some biologics is maintained by the Center for Biologics Evaluation and Research.

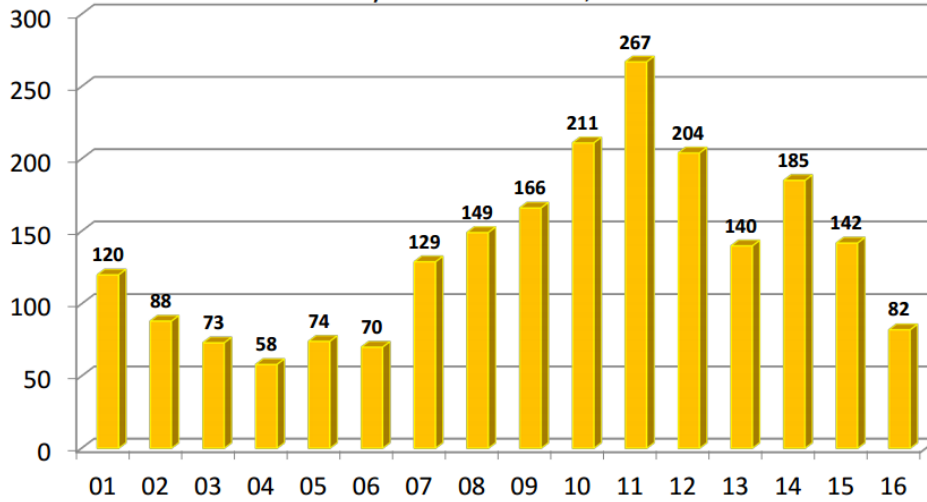
<sup>b</sup> Categories include (a) requirement related to complying with good manufacturing practices; (b) regulatory delay; (c) shortage of an active ingredient

APPENDIX

National Drug Shortages

**Annual New Shortages by Year**

January 2001 to June 30, 2016

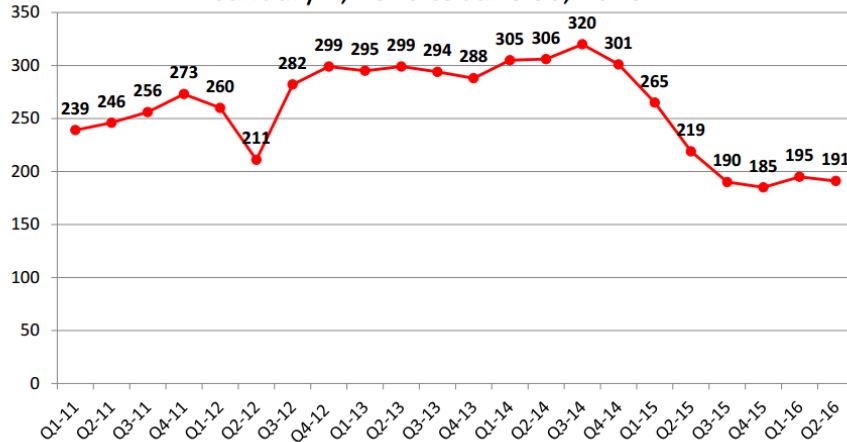


University of Utah Drug Information Service  
 Contact [Erin.Fox@hsc.utah.edu](mailto:Erin.Fox@hsc.utah.edu), @foxerinr for more information

National Drug Shortages

**Active Shortages by Quarter**

January 1, 2010 to June 30, 2016



**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.

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 Contact [Erin.Fox@hsc.utah.edu](mailto:Erin.Fox@hsc.utah.edu), @foxerinr for more information