

January 11, 2019

Scott Gottlieb, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Docket No. FDA-2018-N-3272, Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions; Public Meeting; Request for Comments; Federal Register (Vol. 83, No. 175), September 10, 2018.

Dear Commissioner Gottlieb:

On behalf of our nearly 5,000 member hospitals, health systems and other health care organizations, and our clinician partners – including more than 270,000 affiliated physicians, 2 million nurses and other caregivers – and the 43,000 health care leaders who belong to our professional membership groups, the American Hospital Association (AHA) appreciates the opportunity to provide feedback on the Food and Drug Administration’s (FDA) request for comments on the public meeting, “Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions.”

New and chronic shortages of critical drugs are among the biggest challenges facing patients and hospitals. They threaten the quality of patient care, affect treatment options, and often require the use of alternative products that may be less appropriate/effective for the patient and/or less familiar to clinical staff, which can increase the potential for medical errors. Drug shortages also increase costs to hospitals and health care systems by, for example, diverting staff away from direct patient care in order to manage shortages, by substituting more expensive drugs or therapies for the shortage drugs, and by requiring adjustments to the management and documentation of the electronic health record (EHR). Moreover, drug shortages pose a threat to the public’s health and to national security by decreasing the preparedness and resilience of health care systems and communities for public health emergencies. **To that end, the AHA conducted extensive policy work on this issue and includes below our key legislative, regulatory and best practices recommendations derived from these discussions.**



BACKGROUND

The AHA has been actively engaged on the drug shortages issue since 2010, when the numbers of new shortages began to skyrocket. We have a close working relationship with the FDA's drug shortage staff, whose actions have successfully prevented, mitigated and resolved many drug shortages over the years. In particular, FDA's efforts have led to a significant decline in the number of new shortages since 2010. However, we have seen a troubling increase in the number of *persistent* shortages in recent years, such as for intravenous (IV) saline and other generic sterile injectable medications. Thus, the serious issues underlying drug shortages remain, and may be getting worse. Steps need to be taken to ensure that the right drugs are available to patients at the right time.

We applaud the FDA's leadership in addressing critical drug shortages, including the creation of a Drug Shortage Task Force, the prioritization of Abbreviated New Drug Applications (ANDAs) for drugs where there are fewer than three generic alternatives, the improved regulatory harmonization across global supply chains to facilitate expedited importation alternatives, and a reduction in the backlog of new ANDAs. We also appreciate the opportunities FDA has provided for hospitals and other stakeholders to share their perspectives and policy recommendations to address this daunting challenge, including convening listening sessions and holding the Nov. 27, 2018 public meeting. The AHA looks forward to continuing to work with the FDA on this challenging issue.

The AHA is a co-convening member of the National Drug Shortage Summit. Together with the other core members of the Summit – the American Society of Health-System Pharmacists (ASHP), the American Society of Clinical Oncologists, the American Society of Anesthesiologists and the Institute for Safe Medication Practices, we have worked to raise the profile of drugs shortages within the Executive Branch and Congress. The Summit has held several workshops, most recently a Sept. 20, 2018 [meeting](#) focused on the national security implications of drug shortages. In addition, the AHA helped plan a Sept. 5-6, 2018 [workshop](#), "Medical Product Shortages During Disasters: Opportunities to Predict, Prevent, and Respond," convened by the National Academies of Sciences, Engineering, and Medicine, at the request of the Health & Human Services Office of the Assistant Secretary for Preparedness and Response. Also, last spring the AHA joined a drug shortage working group organized by the Health Supply Chain Association to develop recommendations and policy proposals to help prevent and address drug shortages.

Finally, we surveyed AHA members to assess shortages and how they have impacted patient care and hospital operations. Most recently, the AHA, in collaboration with the Federation of America's Hospitals, conducted a study and will be releasing an independent report by the NORC at the University of Chicago in mid-January that details the specific experience of hospitals and health systems with drug purchasing

and drug shortages. While outside of the comment period for this docket, we will share the report when it is available, as the data may help inform the work of the Drug Shortages Task Force.

LEGISLATIVE RECOMMENDATIONS

Strengthen manufacturers' drug shortage disclosure requirements. Title X of the FDA Safety and Innovation Act (FDASIA), enacted in 2012, requires drug manufacturers to notify FDA "of any change in production that is reasonably likely to lead to reduction in supply," of a covered drug in the U.S., but does not require disclosure of the reason for a halt in production or an expected timeline to address it. Further, the only consequence for failing to comply with the drug shortage notification requirement is public disclosure of the failure by FDA. While this reporting requirement has helped the FDA to reduce the number of drug shortages, more must be done.

The AHA recommends that Congress strengthen the current drug manufacturer shortage reporting requirements to include disclosure of the problem that is causing the manufacturing interruption, the extent of the shortage, and the expected duration of the shortage. Failure to provide timely notice of an interruption should result in a monetary penalty for the manufacturer.

In addition, manufacturers should be required to report current or anticipated supply concerns, including issues pertaining to the production or acquisition of raw materials. The information provided should be easily accessible by the public on the FDA's website. Such enhanced reporting would allow FDA and providers to better prevent and manage shortages.

Incentivize manufacturing contingency plans and/or redundancies. Drug shortages can have negative impacts on patient safety and access to care; however, drug manufacturers cannot always predict when a shortage will occur. **Congress should enact incentives for drug manufacturers to establish contingency plans and/or redundant production lines to be used in the event of a shortage, specifically for drugs that have fewer than three manufacturers.** These plans should include prioritizing the most medically necessary products, qualifying third-party suppliers across their network, and increasing production and inventory for raw materials and finished goods.

Enhance production transparency requirements. **Congress should require manufacturers to disclose to the FDA the location of production, including situations where a contract manufacturer is used.** Further, there may be situations, such as when a natural disaster is imminent (e.g., Hurricane Maria in Puerto Rico), in which the FDA should release information simultaneously to the entire drug supply chain, including health care providers, about which drugs are produced at impacted locations so as to allow providers and others to engage in advance planning. To prevent

hoarding of inventory that could result from such communication, manufacturers could put products on an allocation list to ensure that the remaining supply is distributed equitably. This information is critical to ensure that all stakeholders take the most effective steps toward addressing drug shortages and ensuring uninterrupted, quality care for patients.

Enact shortage disclosure notification requirements for certain medical devices needed to administer drugs. Congress should enact legislation that requires medical device manufacturers to notify FDA in the event of an interruption or discontinuation for certain medical devices and equipment needed to administer drugs (e.g., containers needed to dilute drugs for IV infusion), similar to the 2012 FDASIA notification requirement for drug manufacturers.

Assess drug shortages as a national security threat. Require federal agencies 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.

Include potential risk for drug shortages as a factor in the Federal Trade Commission (FTC) reviews of drug company merger proposals. Congress should request the FTC consider the potential risk for drug shortages when reviewing drug company mergers and acquisitions.

REGULATORY RECOMMENDATIONS

Establish incentives to encourage manufacturers to produce drugs in shortage. When a drug is in shortage, it is often difficult to find a manufacturer willing to increase or begin production of the drug. Therefore, **the FDA should explore additional incentives to encourage other manufactures to begin producing drugs that are in shortage.**

Prevent manufacturing shutdowns. **The FDA should improve the process for enforcing the current good manufacturing practices (cGMP) regulations by shortening turnaround times and improving and standardizing processes of FDA reviews to identify problems prior to shutting down facilities.** Further, a more rapid review of corrective actions taken by manufacturers could help reduce the duration of supply interruptions.

Establish a quality manufacturing initiative. **The FDA should establish a manufacturing rating system where higher quality manufacturing receives the higher rating.** The FDA should consider incentives for manufacturers to participate in the program. The rating system should include factors such as whether the company has a contingency plan for production interruptions and disasters and whether the company has a plan for redundancy in production.

Enhance information on the quality of outsourcing facilities' compounding. Although outsourcing facilities registered with the FDA under section 503B are able to compound drugs that are in shortage, it is difficult for pharmacies to evaluate the quality of a 503B facility. This is especially true for an outsourcing facility that has been issued an FDA Form 483, indicating that the company has a problem with quality. **FDA should disclose more information regarding why a 483 was issued and remove the 483 in a timely way when the issue has been resolved.**

Expand and improve the FDA's drug shortages list. The FDA's drug shortage list does not take into account drugs that are in shortage based on their administration form and dosage, and does not include drugs that are experiencing significant regional shortages. Therefore, **the FDA should expand its list of drug shortages to incorporate drugs included on the ASHP's more comprehensive drug shortage list.** It also should include additional information that would be helpful to mitigate shortages, such as information on 503B compounders. This would help ensure that the drug shortages list is comprehensive, current and better able to be used to appropriately prioritize efforts to resolve shortages.

Develop a list of critical drugs. **The FDA should use the [World Health Organization's Model Lists of Essential Medicines](#) and other existing resources to develop a list of critical drugs needed for emergency response and for saving and preserving life.** The critical drug list could be used for a variety of purposes, including for: stabilizing the supply 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; assessing the quality of pharmaceutical manufacturers measured against the importance of drugs on the critical list; and providing greater transparency surrounding the sources of these drugs' raw materials and manufacturing locations so providers can more easily assess pharmaceutical product quality.

Consider how reducing the number of "unapproved" drugs¹ on the market might impact shortages. The FDA has been assisting drug manufacturers 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. **Before efforts to bring unapproved drugs into compliance are started, FDA should carefully balance the benefits of approval with the possibility that this process could result in shortages of these older, but often essential, drugs.**

¹ Pre-1938 drugs marketed prior to the enactment of the Food, Drug and Cosmetics Act.

Reduce drug waste. **The FDA should incentivize manufacturers to market repackaged sterile injectable drugs in the dosages commonly used in clinical care to reduce waste.**

Create an Office of Clinical Affairs within the Drug Enforcement Administration (DEA). Such an office would help ensure that DEA personnel are available to address the clinical implications of shortages of controlled substances, thereby better balancing the agency's current focus only on diversion control and enforcement.

MARKET RECOMMENDATIONS

Encourage early drug shortage alerts and multi-stakeholder communications. **All stakeholders in the market, including providers, manufacturers, wholesalers, group purchasing organizations and others should communicate with the FDA as soon as a potential shortage situation is identified, and continue to share information as available.** FDA and others should continue working to improve inter-agency communication and cross-agency coordination in shortage situations like the injectable narcotic shortage that occurred in 2018, which required involvement of both the FDA and the DEA. Encouraging early and ongoing communication is critical for mitigating risk and reducing the likelihood of shortage situations.

Develop drug shortage action plans. **Drug manufacturers should develop shortage action plans that would help prevent, identify and actively respond to drug shortage situations if they arise.** These remediation plans should be updated annually.

Establish best practices for critical drugs. **Best practices should be established for utilizing certain widely used and critical drugs.** This not only will be helpful in the event of a shortage, but if widely applied, also will reduce waste throughout health care systems, thus helping to prevent shortage situations. Focus specifically should be placed on limiting IV fluid waste. Once best practices are established, a multidisciplinary educational component should be implemented ensuring that all medical professionals are trained and educated in these best practices.

Encourage EHR vendors to make changes to their systems to ease the burden of making drug product changes. While increased automation in hospitals and other health care settings has improved patient safety and created efficiencies, these systems are often designed to use a certain product. When a shortage occurs it often takes countless hours and staff time to make a change to the EHR system to reflect the use of an alternative product. **EHR vendors should make changes to their systems to make it easier to switch products.** An example would be a 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).

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Page 7 of 7

We appreciate the opportunity to provide feedback and look forward to continuing to work with the FDA on finding enduring solutions to drug shortages. Please contact me if you have questions about our comments or feel free to have a member of your team contact Roslyne Schulman, director of policy, at 202-626-2273 or rschulman@aha.org.

Sincerely,

/s/

Thomas P. Nickels
Executive Vice President
Government Relations and Public Policy