American Society of Anesthesiologists

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March 14, 2013

Margaret Hamburg, M.D.
Commissioner
Food and Drug Administration
U.S. Department of Health & Human Services
5630 Fishers Lane
Rockville, MD 20852

Re: Docket No. **FDA-2013-N-0124**; Food and Drug Administration Drug Shortages Task Force and Strategic Plan; Request for Comments

Dear Commissioner Hamburg:

The American Society of Anesthesiologists (ASA), on behalf of its over 50,000 members, appreciates the opportunity to provide comments in response to the Food and Drug Administration's (FDA) February 12, 2013 Federal Register Notice regarding the Drug Shortages Task Force and strategic plan. As the recognized leader in patient safety, anesthesiologists are seriously concerned about the toll drug shortages are having on our ability to care for our patients. In March 2012, ASA conducted a survey of 3,063 anesthesiologists to quantify the impact of drug shortages on our patients and practices. Our survey results demonstrated that as a result of drug shortages, 97.6% of respondents reported that they are currently experiencing a shortage of at least one anesthesia drug, 96.3% had to use alternative drugs, 66.7% of patients experienced a less optimal outcome (e.g. prolonged recovery, increased pain, post-op nausea and vomiting, increased costs), and 0.2% resulted in the death of a patient.

The bipartisan passage of the Food and Drug Administration Safety and Innovation Act (FDASIA) was an important step in helping to prevent and mitigate drug shortages, but critical anesthesia drugs are still in shortage. ASA is pleased that the FDA is drafting a strategic plan on drug shortages and we believe the recommendations offered below will help the Agency address this public health problem.

Question 1(a): To what extent do purchasers and prescribers use information about manufacturing quality when deciding how to purchase or utilize products? What kinds of manufacturing quality metrics might be valuable for purchasers and prescribers when determining which manufacturers to purchase from or which manufacturers' products to prescribe?

Anesthesiologists currently do not use information about manufacturing quality when deciding how to purchase or prescribe products because the majority of anesthesiologists assume that all FDA-approved drugs have met requisite safety standards. If the FDA determines that manufacturing quality metrics would be helpful to relieve drug shortages, manufacturers should make available information on the identity of the claimed content, absence of microbiological or chemical contamination, and precision of

drug concentration. In addition, manufacturers should update this information with every batch or shipment entering the United States.

Question 4: Are there other communication tools that FDA should use or additional information the Agency should share to help health care professionals, manufacturers, distributors, patients, and others manage shortages more effectively?

The FDA should offer relevant up-to-the-minute drug shortage information through an RSS-feed or similar web feed format that can be automatically posted and updated on medical societies' and patient advocacy organizations' websites. This one central location will provide physicians up-to-date information on the medications they use to treat their patients. RSS-feeds are particularly attractive since physicians and patients can subscribe to the feed and this information will then be automatically forwarded to them.

The FDA should also establish a mechanism where physicians and patients can sign up for email updates on shortages of specific drugs or drug classes. It can be burdensome for physicians and patients to search through information on all of the drugs in shortage when many physicians and patients only need information on specific drugs. This mechanism will allow physicians and patients to receive targeted emails on pertinent shortages so they only receive the information they need. In designing this mechanism, the FDA should ensure that physicians and patients receive information on new drug shortages so they can elect to sign up for future updates on those drugs.

Information offered to medical societies and patient advocacy organizations through RSS-feed and to physicians and patients through targeted emails should include the name and manufacturer of the drug, the dosage form affected, the date of the expected shortage, the cause of the shortage, if known, and the length of the expected shortage. The FDA should also notify physicians and patients whether there are FDA approved strategies to mitigate shortages, such as the use of filters to draw up a drug or extension of the expiration date on a lot of a drug.

Question 5: What impact do drug and biological shortages have on research and clinical trials? What actions can FDA take to mitigate any negative impact of shortages on research and clinical trials?

The FDA, prior to the start of a research or clinical trial, should help clinicians and researchers design contingency plans to assure that critical research projects that employ generic drugs as comparisons have an assured supply of such drugs to complete the project.

Question 6: What other actions or activities should FDA consider including in the strategic plan to help prevent or mitigate shortages?

The bipartisan passage of FDASIA was an important step in helping to prevent and mitigate drug shortages, but shortages of critical anesthesia drugs still exist. To prevent and mitigate drug shortages, ASA recommends that FDA adopt the remaining Drug Shortage Summit Steering Group recommendations that were not addressed by FDASIA. ASA presented these recommendations to the FDA at the Agency's Drug Shortage Workshop in September 2011. Specifically, the Steering Group recommends that FDA work with manufacturers to develop contingency plans for critical drugs that are vulnerable to shortages and help create incentives to manufacture pre-1938 generic injectables. Finally, the FDA should develop incentives for manufacturers to develop smaller vial sizes and alternative concentrations.

In November of 2010, ASA along with the American Society of Clinical Oncology, the American Society of Health-System Pharmacists, the Institute for Safe Medication Practices and the American Hospital Association co-convened a Drug Shortage Workshop Summit. This Drug Shortage Summit Steering Group, consisting of the co-conveners, manufacturers, distributors and group purchasers, released initial findings and continued to meet over the course of the next ten months producing a series of five recommendations for regulatory and legislative action.

The work group made the following recommendations:

1) Reallocate resources within FDA and for the Congress to authorize and appropriate funding for FDA activities that prevent or mitigate shortages;

2) Require manufacturers to report product discontinuations and manufacturing interruptions six months in advance or upon determining that production will not meet average historical demand. Establish communications methods to provide accurate and timely information to health care providers. Establish methods to better predict the seriousness and duration of drug shortages;

3) Establish criteria for determining whether a drug is vulnerable to shortage. Designate drugs that are vulnerable to shortage as part of the FDA approval process. Establish appropriate incentives for manufacturing redundancies or other means of producing emergency supplies for drugs that are deemed vulnerable to shortages. The pharmaceutical industry should collaborate with regulatory and legislative entities to identify these incentives;

4) Require collaboration between the FDA Center for Drug Evaluation and Research divisions and the Attorney General to establish a process that would expedite the increase in manufacturing production quotas when needed in response to drug shortages of controlled substances;

5) Leverage current FDA pathways to expedite the approval process for medically necessary unapproved drugs that are vulnerable to shortages without compromising the safety of the drug.

Pursuant to FDASIA, manufacturers are now required to report to the FDA a permanent discontinuance or interruption of the manufacture of a wide array of drugs, including those used by anesthesiologists in emergency medical care or during surgery and by physicians who treat patients with chronic pain. FDASIA also addressed the Steering Group's recommendation that the FDA and DEA collaborate on shortages of controlled substances. In addition, ASA is pleased that the FDA increased the number of staff who work on drug shortages.

The FDA, however, should adopt the remaining two recommendations that were not addressed by FDASIA. First, the FDA should work with manufacturers to develop contingency plans for critical drugs that are vulnerable to shortages. Pharmaceutical manufacturing is highly efficient in order to maximize the capacity of the facility and equipment. The same production line is often used to make multiple drug products, and changing a line to a different drug or set of drugs requires a great deal of time and planning on the part of the firm as well as inspection and certification by FDA. In addition, manufacturers do not make more product than the usual demand requires. Without redundancies in manufacturing processes or

other continuity of supply plans for drugs that are vulnerable to shortage, there is limited capacity to respond to unexpected increased demand.

To help firms develop contingency plans for critical drugs vulnerable to shortages, the FDA should establish criteria for determining whether a drug falls in this category. Criteria might include factors such as availability of therapeutic alternatives, supply chain characteristics, and other elements that determine products' vulnerability to shortages. Using these criteria, the FDA should designate drugs that are vulnerable to shortages as part of the FDA approval process and create a procedure to identify FDA-approved drugs that become vulnerable to shortages because of changed circumstances. For example, FDA-approved drugs may become vulnerable to shortages if manufacturers consolidate or stop production.

Second, the FDA should help create incentives for firms to manufacture pre-1938 generic injectables. Many of the current critical shortages involve pre-1938 drugs that are essential to anesthesiologists' ability to safely care for patients. Approval requires submission of a new drug application (NDA), which is a disincentive for manufacturers to continue their production. The NDA submission and approval process can be lengthy and expensive and is unlikely to be offset by the profitability of older generic products. FDA should leverage current pathways to expedite the approval process for medically necessary pre-1938 drugs that are vulnerable to shortages without compromising the quality and safety of the drug. Quicker approval for medically necessary pre-1938 drugs may incentivize manufacturers to initially enter, re-enter or remain in the market and produce such critical therapies.

Finally, the FDA should work with manufacturers to create incentives to develop smaller sized vials and alternative concentrations of FDA-approved medications. Some sterile injectable generics, like propofol, are produced in single dose vials. The Centers for Disease Control and Prevention (CDC) has stated that if single-dose vials are to be used for more than one patient, providers must adhere to *U.S. Pharmacopeia* standards to minimize risk. ASA supports CDC's position, and adopted CDC's Safe Injection Practices in the *Recommendations for Infection Control for the Practice of Anesthesiology* (3d ed.), located here: http://www.asahq.org/For-Members/Standards-Guidelines-and-Statements.aspx . However, many physicians practice in facilities that do not have access to the equipment necessary to repackage drugs pursuant to USP 797 and must discard the unused portion of a drug, which is particularly problematic when the drug is in short supply. For that reason, ASA encourages FDA to work with manufacturers to develop incentives to make vial sizes and concentrations of FDA-approved drugs that physicians use most frequently to treat their patients.

We look forward to continue working with the FDA on this important issue. Please feel free to contact Lisa Pearlstein, J.D., Pain Medicine and Regulatory Lobbyist at l.pearlstein@asawash.org or 202-289-2222 if you have any questions or need additional information regarding this issue.

Sincerely,

John Zerwas, M.D.
President
American Society of Anesthesiologists