American Hospital Association

Liberty Place, Suite 700
325 Seventh Street, NW
Washington, DC 20004-2802
(202) 638-1100 Phone
www.aha.org

March 14, 2013

Margaret A. Hamburg, M.D.
Commissioner
Food and Drug Administration
Division of Dockets Management (HFA-305)
Docket No. FDA-2013-N-0124
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket No. FDA–2013–N–0124, Food and Drug Administration Drug Shortages Task Force and Strategic Plan; Request for Comments; (Vol. 78, No. 29), February 12, 2013.

Dear Dr. Hamburg:

On behalf of our more than 5,000 member hospitals, health systems and other health care organizations, and our 42,000 individual members, the American Hospital Association (AHA) appreciates the opportunity to provide comments to selected questions regarding the Food and Drug Administration's (FDA) Drug Shortages Task Force and Strategic Plan related to drug and biological product shortages. Hospitals are committed to providing every patient with the right care, at the right time, in the right setting. Timely access to the right drugs is an essential element in that equation. However, the number of drug shortages has more than tripled in the past five years, seriously impacting patient care.

The AHA is strongly supportive of the drug shortage and other related provisions contained in the *Food and Drug Administration Safety and Innovation Act of 2012* (FDASIA). We understand that it may take time for the new FDA authorities included in this legislation to begin to show a significant impact; however, the nation's hospitals and health care systems continue to experience drug shortages – both in the number of drug products and in the duration of the shortages. While the numbers of drugs *newly* in shortage began to decline in 2012, many of the *existing* shortages have not been resolved. There were 299 active drug shortages in the last quarter of 2012, the highest quarterly number to date. Nearly half of these shortages involve generic sterile injectible drugs, including critical hospital drugs such as succinylcholine and propophol, emergency syringes, preservative free morphine and electrolytes. These drug shortages continue in 2013, making the delivery of patient care more difficult and dangerous by

causing delays in treatment and forcing the use of alternative drugs that may be less familiar to the provider. Shortages also are costly to hospitals in terms of staff time and other resources needed to manage the shortages, as well as the increased cost of buying alternative drugs "off contract."

The FDA's formation of a Task Force and Strategic Plan on this issue comes at a critical time and is welcome news for both hospitals and patients. We are hopeful that the task force, with help from the private sector stakeholders contributing to its work, will be successful in developing and implementing a strategic plan to enhance the FDA's ability to prevent and mitigate drug shortages. Along these lines, we are happy to share our responses to several selected questions posed by FDA in this request for comment.

Question 1c: Are there incentives that FDA can provide to encourage manufacturers to establish and maintain high-quality manufacturing practices, to develop redundancy in manufacturing operations, to expand capacity, and/or to create other conditions to prevent or mitigate shortages?

Inadequate investments in upgrading quality systems and a lack of redundancy in manufacturing operations are the Achilles heels of drug shortages. Particularly in the generic drug market, where price competition is the primary way to gain market share, economic incentives are stacked firmly against investing in plant improvements or redundancies. In the short term, there is little that the FDA can do to counteract these economic disincentives, other than provide for expedited inspections and certification of manufacturers who voluntarily expand their operations to produce drugs vulnerable to or in a shortage, or to reduce or waive required user fees. However, in the longer term, we recommend that the FDA and Congress collaborate with the pharmaceutical industry to identify appropriate incentives that would encourage drugmakers to establish manufacturing redundancies and invest in their quality systems. Among the possible areas for incentives are those that involve preferential tax or patent policy for manufacturers of drugs vulnerable to shortage, the development of quality metrics to support purchasing and reimbursement decisions, and increases in Medicare payment rates for providers who utilize such drugs in order to remove some of the existing barriers that make these drugs financially unattractive to drugmakers. All of these incentives could have a variety of possible consequences for the pharmaceutical industry and should be explored further.

In addition, some shortages are related to an inadequate range of commercially available concentrations, forms or vial sizes of particular drugs. For instance, pediatric doses of drugs are often in short supply. Accordingly, the FDA could help mitigate these kinds of shortages, as well as reduce the need for hospitals to obtain such products through compounding pharmacies, by working with manufacturers to identify appropriate incentives to make a wider range of formulations available. This could include expedited processing of applications and inspections for different concentrations or forms of already-approved drugs.

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? Are there changes to the public shortage Web sites that would help enhance their utility for patients, prescribers, and others in managing shortages?

Hospitals and physicians have expressed a desire for more timely information about disruptions in the supply of critical drugs. Earlier notification about a disruption or an interruption in the supply of a drug, including information about its cause and expected duration, allows the provider time to plan, to seek out alternate sources of the drug or similar drugs, and to develop and implement strategies to conserve their existing supply.

The FDA's public drug shortage website, with its options for email notification and Rich Site Summary (RSS) feeds, offers some ability for providers to receive regular updates on the products included on the national drug shortage list. However, the list of drugs on the website is long and email updates are not sent out often enough to alert providers about changes in the status of particular drugs in shortage. Therefore, the AHA believes that this process could be better targeted by adding some optional features. Interested stakeholders, for instance cancer hospitals or physician specialty societies, should be able to receive customized RSS feeds that would allow them to be updated more frequently regarding specific drugs or classes of drugs in shortage that are relevant to their area of practice. That way, whenever the FDA updates the status of a particular drug in shortage, that update could be immediately pushed to providers who have requested the specific information.

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

There have been a number of reports of clinical trials that have been adversely impacted due to unexpected shortages in the supply of one or more drugs involved in the research. Older generic drugs, the type of drugs that are now commonly in short supply, are often used in clinical trials either as controls or in combination with experimental medicines. Shortages of these drugs can result in a sudden change in the study's protocol involving the substitution of an alternate, often less-attractive drug or can shut down a clinical trial altogether. These situations confound research findings and delay the development of new drug therapies. For instance, a shortage of doxorubicin, an older chemotherapy drug, delayed a trial for a new cancer drug by five months (Ledford, Heidi, "Drug shortage slows clinical trials," *Nature*, Oct. 3, 2011, http://www.nature.com/news/2011/031011/full/news.2011.570.html).

The actions that can be pursued to mitigate the impact of drug shortages on research are similar to what can be done in clinical medicine, which is employing contingency planning and seeking more timely information. The FDA, in collaboration with the National Institutes of Health (NIH), should encourage researchers to incorporate into their clinical protocols contingency plans for addressing how the trial will proceed in the event of a shortage of a study drug, including other sources for the drug or alternative drugs that could be used as substitutes. In addition, processes should be established to inform researchers rapidly about disruptions in the supply of study drugs.

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

The AHA encourages FDA to continue to apply the tools and strategies it has used in the past to prevent or mitigate drug shortages, including employing its myriad communication tools, regulatory authorities and use of enforcement discretion.

In addition, the AHA believes that the generic pharmaceutical industry's Accelerated Recovery Initiative (ARI), a multi-stakeholder initiative intended to accelerate the recovery of drugs in short supply, holds promise, and we look forward to learning more about ARI in the near future. As we understand it, ARI involves voluntary communication among the FDA, IMS Health and stakeholders involved in the manufacturing and distribution of critical generic medications currently in shortage. It will use real-time supply and distribution information, as well as manufacturers' production and release forecasts, to give the FDA a better understanding of current conditions and abilities to expand the supply of critical medications and potentially avert future shortages.

We are hopeful that this voluntary initiative, together with the work being done by the FDA, will increase early visibility and communication between the FDA and the field relating to current and potential drug shortages and lead to mitigating the impact of existing shortages and possibly preventing new shortages. The AHA encourages the FDA, in conjunction with the generic pharmaceutical industry, to provide regular updates to interested stakeholders about the progress made through the ARI.

We are also hopeful that the *Generic Drug User Fee Act*, enacted as part of FDASIA, will fulfill its promise to provide the FDA with additional resources and reduce the average time it takes to review generic drug and supplement applications by nearly two years. These provisions should support the timely approval of generic drug applications and future availability of a broader supply of generic drugs as well as provide a way to expedite federal approval for new sources of drugs for which a nationwide shortage has been identified.

Thank you again for the opportunity to comment. The AHA appreciates the FDA's time and efforts, particularly through the Drug Shortage Program, to resolve and reduce collaboratively the impact of drug shortages. If you have any questions, please contact me or Roslyne Schulman, director for policy development, at (202) 626-2273 or rschulman@aha.org.

Sincerely,

/s/

Rick Pollack
Executive Vice President