



February 8, 2012

Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane,
Room 1061
Rockville, MD 20852

Re: FDA-2011-N-0898; Applications for Food and Drug Administration Approval to Market a New Drug; Revision of Postmarketing Reporting Requirements – Discontinuance

Dear Sir/Madam:

The American Society of Health-System Pharmacists (ASHP) is pleased to submit comments to the Food and Drug Administration (FDA) on the Interim Final Rule (IFR) modifying or clarifying certain terms with respect to notification of discontinuance requirements as announced in the Federal Register on December 19, 2011.¹ For more than 60 years, ASHP has helped pharmacists who practice in hospitals and health systems improve medication use and enhance patient safety. The Society's 35,000 members include pharmacists and pharmacy technicians who practice in inpatient, outpatient, home-care, and long-term-care settings, as well as pharmacy students. Pharmacists in hospitals and health systems are experts in medication use who serve on interdisciplinary patient-care teams. They work with physicians, nurses, and other health care professionals to ensure that medicines are used safely and effectively.

Since 2006, shortages of primarily generic injectable drugs have dramatically escalated, increasing from 70 five years ago to over 230 as of November 2011. These drugs, which are fundamental and essential to care, affect this nation's hospitalized and most vulnerable patients. Without access to the preferred or most clinically appropriate drug treatment, healthcare professionals must use alternatives, which may be less effective or associated with increased risk of adverse outcomes.

Drug shortages also add to the cost of providing care. A study by the Premier Healthcare Alliance in March of last year suggested the cost of purchasing alternative therapeutic products to those in shortage to be \$200 million. In addition, a survey conducted by ASHP and the University of Michigan indicated that hospital pharmacists are spending

eight to twelve additional hours per week dealing with shortages – time taken away from direct patient care. Further, the study estimated that additional annual labor costs to hospitals of managing shortages to be \$216 million.

ASHP partnered with several healthcare, provider and safety-related groups to hold a drug shortages summit in November 2010 that was aimed at defining the causes of drug shortages and identifying potential avenues to address the problem through legislation, regulation and within the marketplace itself.² One finding was that the causes of drug shortages are many and complex. The causes of a vast number of drug shortages can be traced to manufacturing issues that include product quality issues that result in production halts or recalls, product discontinuations, and unavailability of active pharmaceutical ingredients (APIs) or other raw materials. When manufacturers report production issues to the FDA, the Agency has demonstrated that it is able to work with the producers to prevent a shortage, if possible. ASHP continues to work with FDA, other health care provider groups and members of the supply chain to address the issue. According to FDA, in 2011 the Agency was able to avoid 195 shortages when they were made aware of production interruptions ahead of time, and so far this year, 12 shortages have been avoided.³

Under current law and regulation, manufacturers are not required to report to FDA when they experience an interruption in the production of their products, unless that drug is “life supporting, life sustaining, or intended for use in the prevention of a debilitating disease or condition.”⁴ The same holds true when manufacturers choose to discontinue a product.

Under this IFR, the FDA is defining “discontinuance” to “include both permanent and temporary interruptions in the manufacturing of a drug product, if the interruption could lead to a disruption in supply of the product.”⁵ The Agency clarifies that the following situations, for example, would trigger a “discontinuance” reporting requirement under the new definition:

- Delay in acquiring APIs or inactive ingredients that may lead to an interruption in manufacturing; and
- Suspension in production for maintenance or other routine services if the period of shut-down exceeds expectations.

The FDA makes note that notification of temporary suspension in production is not required if the shut-down is expected, planned for, and/or will not result in a product shortage. For example, a planned maintenance period would not necessarily be reported to the FDA if it is not expected to impact production and does not exceed scheduled down-time. Conversely, an unexpected suspension in production, such as a

power outage or other unplanned event would not need to be reported to the FDA should it too, not be expected to impact available product. ASHP strongly supports the Agency's clarification of this definition as it should increase the number of instances in which sole manufacturers are required to notify the FDA of product discontinuance, both permanent and temporary in nature, without being overly burdensome.

Further, the FDA clarifies its definition of a "sole manufacturer" by defining the term to mean "an applicant that is the only entity currently manufacturing a drug product of a specific strength, dosage form, or route of administration for sale in the United States, whether the product is manufactured by the applicant or for the applicant under contract with one or more different entities." The Agency further clarifies that a manufacturer will be considered a "sole manufacturer even if other manufacturers hold an approved NDA or ANDA for the same product, if the other applicants are no longer manufacturing (or have never manufactured) the product for sale in the United States."⁶ Our members have cited issues with patient safety if the correct strengths are not readily available to appropriately treat a patient even when other forms of the drug may be available in the market. ASHP strongly agrees with this definition and believes that these clarifications should also increase the number of entities required to report discontinuance to the FDA, giving the Agency more advanced notification of an impending shortage. This information could be extremely useful to FDA where the Agency could work with alternate suppliers to approve accelerated applications for different dosages, strengths, or routes of administration to offset the decrease in supply due to the interruption or discontinuation of the initial product.

While ASHP supports this IFR, we note that even with these clarifications, the FDA currently has no meaningful enforcement mechanism to penalize a drug maker for failing to report these problems. ASHP has long supported bipartisan legislation (S. 296, H.R. 2245) that would require drug manufacturers to notify the Agency when they experience an interruption in the production of a drug product potentially resulting in a shortage situation and are pleased that the Obama administration supports passage of this legislation as noted in the October 31, 2011 Executive Order.⁷

U.S. Department of Health and Human Services
Food and Drug Administration
February 8, 2012
Page 4

The Society appreciates the opportunity to comment on the FDA's Interim Final Rule. Please contact me if you have any questions or wish to discuss our comments further. I can be reached by telephone at 301-664-8806, or by e-mail at ctopoleski@ashp.org.

Sincerely,



Christopher J. Topoleski
Director, Federal Regulatory Affairs

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- ¹ Federal Register, Volume 76, No. 243. Page 78530 - 78540.
 - ² American Society of Anesthesiologists, American Society of Clinical Oncology, American Society of Health-System Pharmacists, and the Institute for Safe Medication Practices, Drug Shortages Summit Summary Report: November 5, 2011 (issued Jan. 10, 2011), available at <http://www.ashp.org/drugshortages/summitreport>.
 - ³ According to the FDA, of the 195 shortages prevented in 2011, 86 were from one firm that required an expedited review of a manufacturing change that affected 86 different drugs.
 - ⁴ 21 U.S.C. § 356c; C.F.R. § 314.81(b)(3)(iii).
 - ⁵ Federal Register, Volume 76, No. 243. Page 78531.
 - ⁶ Federal Register, Volume 76, No. 243. Page 78532.
 - ⁷ Executive Order 13588 -- Reducing Prescription Drug Shortages; <http://www.whitehouse.gov/the-press-office/2011/10/31/executive-order-reducing-prescription-drug-shortages>