

**STATEMENT
OF
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**BEFORE THE
U.S. FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
“APPROACH TO ADDRESSING DRUG SHORTAGE”
PUBLIC WORKSHOP
SEPTEMBER 26, 2011**

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On behalf of the 82,963 patients with chronic, debilitating and/or life-threatening illnesses, each facing an access to healthcare issue handled by professional case managers at Patient Advocate Foundation (PAF) in 2010 and more than 675,000 patients served since PAF's inception in 1996, we thank you for the opportunity to participate in today's workshop. National Patient Advocate Foundation (NPAF) is a non-profit organization policy office representing the voice of the patients served through PAF. The advocacy activities of NPAF are informed and influenced by the experience of patients who receive direct, sustained case management services from our companion organization, Patient Advocate Foundation.

We are deeply troubled and concerned with the recent drug shortage crisis, as effective life-saving medications are increasingly in short supply. According to the FDA, 178 drugs experienced shortages in 2010, an all-time high.¹ FDA reports an increasing number of shortages in 2011, especially for older, sterile injectable drugs². Even more alarming is that over the last six years, the number of prescription drug shortages has tripled.³ Shortages have been reported in historically effective oncologic agents such as Cytarabine and Cisplatin, forcing providers and hospitals into increasingly challenging decisions, such as prescribing alternative therapeutics, rationing or delaying care. Patients, especially those diagnosed with chronic, debilitating and life-threatening diseases such as cancer, may not have a therapeutic alternative available to them in their course of treatment and cannot simply delay their treatment.

Today's workshop is slated to address six topics relevant to drug shortages. I begin with the question of how FDA Center for Drug Evaluation and Research (CDER) becomes aware of drug shortages.

FDA cannot require manufacturers to provide notification of shortages except in the case of sole source drugs used to treat serious diseases or medical conditions⁴. Unfortunately, in circumstances where multiple manufacturers produce a drug, it is possible that the loss of production from one manufacturer may result in a drug shortage if the remaining manufacturers are unable or unwilling to satisfy demand through increased production. Without accurate and timely reporting of events that have caused or may cause a drug shortage, it is likely that any proposed drug shortage mitigation strategy will be hampered by lack of information. For a patient who is unable to receive a prescribed therapy or incurs additional cost from expensive alternatives, it is irrelevant that reporting of the shortage was not required.

An additional benefit of comprehensive reporting is that data may be used to thoroughly evaluate factors causing drug shortages. For a problem with so many contributing factors, the value of actionable data should not be underestimated. As timely and accurate reporting of potential and actual shortages is

¹ "FDA and Manufacturers Work to Prevent Drug Shortages." *Drugs*. U.S. Food and Drug Administration. 9 June 2011. Web. 21 September 2011. <<http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm257746.htm>>.

² Clarke, Patrick. "FDA Working to Lessen Patient Impact from Drug Shortages." *Drugs*. U.S. Food and Drug Administration. 9 June 2011. Web. 21 September 2011. <<http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm257745.htm>>.

³ "FDA and Manufacturers Work to Prevent Drug Shortages." *Drugs*. U.S. Food and Drug Administration. 9 June 2011. Web. 21 September 2011. <<http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm257746.htm>>.

⁴ "Drug Shortages." *Drugs*. U.S. Food and Drug Administration. 21 September 2011. Web. 21 September 2011. <<http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm>>.

necessary in order to develop and activate meaningful alternative drug supply measures, we believe that patient care may be positively impacted through more reliable and complete reporting of drug shortages.

Recommendation: NPAF would recommend that the Agency review the CDC process use of stockpiling vaccines to assure the public safety if the nation faced a life-threatening epidemic to determine if there are lessons to be learned that could inform the decision of whether this is a process that should be considered for the drugs that have proven to save lives and for which there is no equal alternative. NPAF would further recommend that the process of equitable distribution be reviewed concurrently to assure access to the stockpiled drugs by those who need them. Currently, there are reports of stockpiling that is occurring at many levels in the distribution, pharmacy and clinical levels. If these reports are reliable, the process of moving that procedure to a national level with regulatory oversight may indeed support a more equitable process of distribution.

As for the reasons behind drug shortages, numerous reports have shown that manufacturers routinely cease production of a drug for business reasons, among them being low profit margins. This is a problem known to particularly affect generic drugs. In an opinion article published in *The New York Times* on August 6, 2011, Dr. Ezekiel Emanuel noted that shortages are often the result of manufacturer decisions to end production or a consequence of financial or quality problems⁵. He further noted that the production volume decisions for generic drugs may be tied in some cases to unintended consequences of price increase limitations imposed by the Medicare Prescription Drug, Improvement and Modernization Act of 2003⁶. Generic chemotherapy drugs recently reported in tight supply by FDA include cisplatin, daunorubicin, doxorubicin, cytarabine and leucovorin⁷. Dr. Robert Mayer of the Dana-Farber Cancer Institute in Boston and a past president of American Society of Clinical Oncology notes that these are “incredibly important drugs which serve as the backbone for treating many of the most common and treatable cancers”⁸. We are deeply concerned that in the United States doctors must sometimes tell patients that proven, lifesaving drugs are simply are not available to them.

Recommendations: NPAF recommends that the FDA engage Centers for Medicare and Medicaid services in discussions to address reform of reimbursement for generics and older drugs to incent product production. Additionally, NPAF recommends that a process be developed within the FDA to grandfather approval for these legacy drugs that have been used for prolonged periods of time with

⁵ Emanuel, Ezekiel. “Shortchanging Cancer Patients.” *Sunday Review | The Opinion Pages*. The New York Times Company. 6 August 2011. Web. 20 September 2011.

<http://www.nytimes.com/2011/08/07/opinion/sunday/ezekiel-emanuel-cancer-patients.html?_r=1>.

⁶ Emanuel, Ezekiel. “Shortchanging Cancer Patients.” *Sunday Review | The Opinion Pages*. The New York Times Company. 6 August 2011. Web. 20 September 2011.

<http://www.nytimes.com/2011/08/07/opinion/sunday/ezekiel-emanuel-cancer-patients.html?_r=1>.

⁷ “Current Drug Shortages.” *Drugs*. U.S. Food and Drug Administration. 20 September 2011. Web. 20 September 2011. <<http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050792.htm>>.

⁸ Sherman, Debra and Steenhuisen, Julie. “U.S. cancer drugs shortage has doctors scrambling.” *Reuters*. Thomson Reuters. 7 June 2011. Web. 20 September 2011. <<http://www.reuters.com/article/2011/06/07/us-cancer-drugs-shortages-idUSTRE75653V20110607>>.

success. As well, the Agency is encouraged to review the safety database and hold the manufacturers of these legacy drugs to current production standards of drugs requiring them to meet purity-potency-safety standards.

NPAF recommends discussions with the FDA and appropriately designated stakeholders and federal agencies to discuss a process of defining what the Grey Market is, who comprises it, what is their process for procurement and subsequent sale and distribution of drugs at both the state and federal levels. Additionally, NPAF supports development of specific steps to limit this activity or to reform it in such a manner that it does not add additional costs to the system, nor does the Grey Market raid supplies from the legitimate markets.

There has also been recent attention to the pharmaceutical supply chain, including a U.S. Senate Health, Education, Labor & Pensions Committee hearing on September 14, 2011. The link between drug shortages and supply chain disruptions due to availability of active pharmaceutical ingredients (API), contamination and counterfeiting may not account for the majority of reported shortages, but patients and doctors deserve assurances that products are constituted as labeled. According to FDA, 80 percent of APIs for drugs manufactured in the United States and almost 40 percent of drugs taken by Americans are manufactured outside the country⁹. In light of the global nature of the pharmaceutical supply chain, cost effective measures that validate a product's identity, protect its integrity during transit and storage, and document the provenance of all ingredients seem appropriate.

Recommendation: NPAF recommends that the FDA consider measures during review of new drug applications to enhance surety of supply for drugs that may represent a patient's only viable therapeutic option. However, recognizing that access to necessary products is problematic for certain populations, we urge FDA to carefully consider and craft any proposed regulations to avoid reduced access to pharmaceutical agents for patients in rural and underserved areas. Further, NPAF recommends that the FDA when addressing surety of supply with minimum supply affirmed at not less than six months, NPAF further suggests that the current track and trace process be revisited to modify it, if necessary, to assist all federal agencies involved in drug distribution.

We recognize that federal agencies such as DEA and FTC must carry out their duties as stipulated by statute, but we encourage appropriate inter-agency communication and cooperation to ensure that drug shortages are alleviated, not exacerbated, by the actions of such agencies.

NPAF encourages FDA to explore incentives relative to sole source products and APIs. We are greatly concerned that a lack of redundant manufacturing locations and multiple API suppliers for such products can very quickly lead to devastating shortages. Noting that a sole source is better than no source, we strongly encourage an approach that provides incentives for market presence, including reasonable

⁹ Autor, Deborah. "Securing the Pharmaceutical Supply Chain." *Committee on Health, Education, Labor and Pensions*. United States Senate. 14 September 2011. Web. 20 September 2011. <<http://help.senate.gov/imo/media/doc/Autor.pdf>>.

market entry barriers, rather than requirements that discourage manufacturers from producing drugs with historically low profit margins.

Recommendations: NPAF recommends that the Agency work with appropriate stakeholders and federal Agencies to define an improved process of reimbursement for manufacturers that assures support for reasonable business models to support production and equitable distribution of drugs to be sold in the United States. Absent this process, NPAF anticipates continued erosion of available drugs for life-threatening illnesses.

NPAF recommends that the FDA establish an advisory group of stakeholders to include patients, providers, manufactures, and federal agencies to improve communications nationally identifying drug shortages early with a focus also on developing provider and patient information announcing the shortages with clarity as to what drugs, how long and what are the alternatives for getting to the drugs needed. NPAF must affirm that the long term goal is not to simply inform stakeholders of shortages but to address and eliminate the escalating growth of shortages; however, in the interim the issue of identifying shortages and informing consumers across a broad framework of available sources must be addressed.

Under current practice, when a shortage is projected for a medically necessary drug, FDA may look for and work with alternative manufacturers to ensure that an adequate supply is available¹⁰. In practice, doctors and patients may be frustrated by FDA's definition of a "medically necessary" drug, specifically the stipulation that no alternative drug is available. Since alternative drugs identified by FDA may not be efficacious for a particular patient's situation, the patient's care is adversely impacted when their prescribed drug is unavailable. Patients also encounter access issues when a designated alternative drug is not included in their insurance plan's formulary.

There are likely other participants in this workshop who are better able to address questions of current good manufacturing practice (CGMP) and other compliance issues. From a patient's perspective it is reasonable to expect that regulatory agencies maintain CGMP guidance that reflects current technology and the realities of a global supply chain.

Relative to actions taken when a drug shortage occurs, we recognize that immediate communication both with manufacturers and providers provides the greatest opportunity for successful alleviation of the shortage and management of patients' treatments through times of short supply. The limited shortage data that is often available under current reporting processes is distressingly inadequate for providers who must determine the best available course of treatment for their patients. Physician and pharmacists must spend significant amounts of time to ensure that a preferred therapeutic regimen will be available for the patient. As reported July 13, 2011 in the Wall Street Journal, a survey commissioned by the American Society of Health-System Pharmacists found that hospitals are estimated to spend \$216

¹⁰ "Drug Shortages." *Drugs*. U.S. Food and Drug Administration. 21 September 2011. Web. 21 September 2011. <<http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm>>.

million a year in additional labor costs to deal with drug shortages; it also found that “pharmacists and technicians spend about 17 hours a week managing drug shortages”¹¹.

In a 2010 drug shortage case handled by Patient Advocate Foundation, multiple conversations with a patient’s provider were necessary to arrange for an alternative treatment that resulted in slower resolution of an anemic condition.¹² In 2011, Patient Advocate Foundation worked a case involving a shortage of Doxil. Instead of receiving the chemotherapy drug during a three hour outpatient infusion, the endometrial cancer patient, an individual with limited income, was admitted to a hospital for three days to receive an alternative treatment consisting of at least three drugs. The patient was burdened not only with the hospitalization but with negative side effects on kidney function. While already experiencing financial hardship from treatment, the patient’s hospitalization resulted in a larger out of pocket expense than would have been incurred as an outpatient.¹³

By working with manufacturers to expedite any required regulatory processes to initiate production in alternate facilities, change suppliers of APIs and excipients, and, when necessary, import product from foreign sources, FDA positions industry to address and solve the shortage. Collection and publication of comprehensive shortage information by FDA or another authoritative entity will prove helpful to drug distributors who must determine whether measures such as allocation and emergency use only designations will be necessary.

The best possible outcomes of mitigated drug shortages are those that provide doctors with timely and relevant information regarding drug supplies, quickly restore adequate supplies to the market, result in no adverse patient events and help to diversify drug sources over the long term.

As patient advocates, we urgently ask FDA to take appropriate steps to ensure that highly effective, lifesaving drugs are available for critically ill patients in their time of need. National Patient Advocate Foundation and Patient Advocate Foundation are pleased to participate in this workshop and this initial step in the Agency’s effort to bring resolution to drug shortages in the United States of America.

¹¹ Dooren, Jennifer. “Most Hospitals Face Drug Shortages.” *The Wall Street Journal | Health*. Dow Jones & Company, Inc. 13 July 2011. Web. 20 September 2011. <<http://online.wsj.com/article/SB10001424052702304584404576442211187884744.html?KEYWORDS=Most+Hospitals+Face+Drug+Shortages>>.

¹² Case work. Patient Advocate Foundation. 2010.

¹³ Case work. Patient Advocate Foundation. 2011.