

Drug Shortages & the Need for Action
February 9, 2012
Bill Greene, PharmD, BCPS, FASHP
Chief Pharmaceutical Officer
St Jude Children's Research Hospital
Memphis, TN

Summary of Testimony:

- The challenges that drug shortages are causing for patients and caregivers at St Jude and throughout the country are described
- The case of Lucy, a 5-year old brain tumor patient from Covington TN, is described to illustrate the patient impact of shortages
- The frequency of shortages has increased dramatically. From August 2008 to January 2012, St. Jude experienced a 10-fold increase in the number of shortages which required action
- Drug shortages make it difficult to provide the best possible **patient care**. Shortages cause delays or termination of **research** in important fields like pediatric oncology, including at least 85 Children's Oncology Group (COG) clinical trials. Shortages add **real costs** to the health care delivery system.
- Congress is urged to pass legislation (H.R. 2245 and S. 296) immediately to give the Food and Drug Administration (FDA) the tools it needs to prevent and minimize the impact these drug shortages have on pediatric care and research.
- Congress must give the FDA the resources and authority it needs to combat drug shortages in a proactive manner. Other relevant federal agencies, such as the DEA must collaborate with the FDA to combat drug shortages.
- Congress must ensure that in any solution it develops, pediatric protections are built in and pediatric experts are broadly engaged.
- The underlying causes of drug shortages are complex. Before enacting legislation to address those factors, Congress should carefully study and understand these factors and implications of proposed solutions

Chairman Pitts and other members of the Committee, I am grateful for the opportunity to speak before you – not only as a representative of St Jude Children’s Research Hospital, but as a representative of caregivers at children’s hospitals throughout the country. As you know, I am Chief Pharmaceutical Officer at my organization. St Jude is committed to developing research that leads to new cures for children with catastrophic diseases, and to providing unsurpassed clinical care of these patients. Thank you for letting me address you today.

St. Jude, located in Memphis, Tennessee, is internationally recognized for its pioneering research and treatment of children with cancer and other life-threatening diseases. The hospital’s research has helped push overall survival rates for childhood cancer from less than 20 percent when the institution opened in 1962 to almost 80 percent today. It is the first and only National Cancer Institute-designated Comprehensive Cancer Center devoted solely to children, and no family ever pays St. Jude for care.

In my short testimony today, I’d like to share 3 ways Congress can alleviate drug shortages for the pediatric community, but first I would like to begin by putting a face to my discussion. This is Lucy – a 5 year-old from Covington, TN. She and her family have given me permission to describe her case as a way of illustrating the challenges that drug shortages are causing for patients and caregivers at St Jude and throughout the country. Lucy is being treated for medulloblastoma – a type of brain cancer, and today she is doing well. Last spring, she was going through her prescribed course of therapy – supported through her treatment by the administration of intravenous nutrition. She began to deteriorate with blurred vision, random eye movements, and some visual changes; her family and physicians worried that her cancer was relapsing. She was admitted back into the hospital for evaluation. During this workup, her

physicians considered whether all of her new symptoms might be due to a simple vitamin insufficiency. She was treated with intravenous thiamine, and experienced a dramatic recovery and was able to continue treatment.

What was the cause of Lucy's thiamine deficiency that resulted in admission to the hospital?

Due to a drug shortage, her care team had been unable to add multivitamins to her nutrition solution for weeks – multivitamins containing thiamine. Despite all our efforts, there simply was no multivitamin solution available to be purchased. As a result, Lucy and her family worried about a relapse of her cancer, and she had to be readmitted to the hospital. This is unacceptable, and this is only one of many shortages that St Jude and other pediatric hospitals around the country have experienced in recent years.

You are aware that the number of drug shortages occurring in the United States has increased dramatically in recent years. A total of 267 shortages were noted in 2011 by the University of Utah Drug Information Service, up from 211 in 2010, which was dramatically higher than in previous years. While not all of these shortages have directly affected St Jude, our hospital has experienced a dramatic increase. **Figure 1** illustrates the number of drug shortages that have affected us since 2008; you will notice a 10-fold increase in the number of shortages which required action at St Jude. In the last 2 months alone, I have had to issue 14 different communications to clinical staff regarding shortages affecting our patients, and all of these notifications involved injectable sterile products. While chemotherapy drugs constitute a significant proportion of the affected drugs, many other types have been affected, including nutritionals, IV electrolytes, antibiotics, anesthesia drugs, and many others.

Drug shortages threaten our nation's healthcare system in three distinct ways. First, we know that we cannot always provide the best possible **patient care**, especially pediatric care for our most vulnerable patients like Lucy, who was dependent on injectable nutrition. Second, we know that shortages cause delays or termination of **research** in important fields like pediatric oncology, including at least 85 Children's Oncology Group (COG) clinical trials. And third, we know that all this adds **real costs** to the health care delivery system, as it did when Lucy had to be admitted for an extra stay at the hospital.

Patient care is affected because patients cannot receive medications that are necessary to most effectively treat their disorders. Chemotherapy shortages are a particular concern for St. Jude, and often alternative chemotherapy may not exist, or there may be little or no evidence that alternative drug therapies will be effective in pediatric cancer patients. The most common childhood cancer is acute lymphoblastic leukemia ("ALL"), with about 3,000 cases per year. Approximately 90 percent of patients with ALL can be cured using a combination of up to 10 drugs. **Over the last decade, however, eight of these 10 drugs have become difficult, and at times impossible, to obtain.** These frequent shortages insert additional and unnecessary complexity to curing children with ALL and other cancers.

While chemotherapy drug shortages have been an area of focus for St. Jude, shortages of other drugs important to pediatric patients have equally important implications. Drug shortages have most frequently occurred with sterile injectable drugs, which are often among the most complex and high risk therapies used in the hospital setting. Shortages of these products only add further

complexity to the use of these therapies and put patients at risk for a new source of medication errors and patient harm. For example, drug shortages often cause frequent shifts to alternate therapies and switching between available drugs, which can lead to errors and adverse patient outcomes.

When St. Jude opened in 1962, only 4% of children with ALL survived. About 90% of children with ALL are cured today due to discoveries made through basic and clinical research. Clinical research at St. Jude and across the country is negatively impacted by drug shortages.ⁱ At least 85 Children's Oncology Group ("COG") and 150 National Cancer Institute ("NCI") clinical trials for cancer have been affected by drug shortages. In some cases, clinical trials for cancer patients have been suspended due to drug shortages. At St. Jude, we have not had to discontinue any of our clinical trials due to drug shortages, but there have been times when we have had to carefully consider whether we could continue to enroll patients for certain protocols. Besides limiting clinical trial enrollment, drug shortages have added complexity and additional work to the conduct of clinical trials. St. Jude developed guidance for our investigators about how to handle the impact of drug shortages on existing trials, and in some cases, investigators were forced to make substantial protocol amendments.

Drug shortages add costs to the system in many ways. Selection of alternative therapy may result in use of drugs that are more expensive than the originally selected drug. Errors may require additional hospital stay or require unplanned admissions. At the very minimum, busy clinicians devote literally thousands of hours to gather information on shortages, assess the organization's specific situation, create and plan, and communicate this to colleagues.

Obviously, this work does little to improve health care and diverts effort away from important patient care and research activities.

Now, I know that the Subcommittee has likely heard similar testimony before from others. Much data on drug shortages has been shared, and many hearings have been conducted. It is now time for immediate action. So I have 3 points I'd like to make about what Congress can do to help.

First, I urge Congress to pass legislation immediately to give the Food and Drug Administration (FDA) the tools it needs to prevent and minimize the impact these drug shortages have on pediatric care and research. Despite extremely limited resources, the FDA has been effective in minimizing the impact of drug shortages when appropriate communication is made to the agency. Despite a largely voluntary reporting system FDA's efforts avoided almost 200 shortages in 2011., Congress can strengthen the reporting system by enacting H.R. 2245 and S. 296, to give the FDA more complete knowledge of permanent and temporary supply chain disruptions in advance. Once that early-warning system is in place, the FDA can streamline its communication with pharmacists like me so that I can more effectively work to mitigate the impact of drug shortages on patients like Lucy at St. Jude.

These resources should specifically include:

- **Manufacturer notification when a company is leaving the market or curtailing production.** While manufacturer notification to FDA would not be a permanent solution to the current drug shortage crisis, FDA has demonstrated that it has the ability to help avoid shortages when it is notified of conditions that tend to lead to—or at least

exacerbate—shortages. FDA has proven its ability to avoid shortages in recent years. In 2010, FDA averted 38 shortages when manufacturers voluntarily communicated potential issues, and as already noted FDA avoided nearly 200 shortages in 2011. In a September 2011 FDA Public Workshop on drug shortages, FDA officials noted that additional information from manufacturers has been critical to their improved efforts to prevent shortages.ⁱⁱ

- **Mandatory manufacturer notification to FDA of conditions that could result in a drug shortage.** Notification should occur when there is a single provider of the active pharmaceutical ingredient (“API”), which indicates a drug is at a higher risk of shortage and that FDA should monitor it more closely. St. Jude further supports notification to FDA when there is any interruption in the supply of raw materials, API or manufacturing processes. Increasing manufacturer and FDA communication will provide FDA more tools to manage and prevent drugs shortages. The October 2011 Executive Order on drug shortagesⁱⁱⁱ enhances FDA’s ability to prevent and mitigate drug shortages, consistent with current law, but legislation is necessary to codify and formalize FDA’s authority to take action to prevent drug shortages.

Second, I urge Congress to give the FDA the resources and authority it needs to combat drug shortages in a proactive manner. While the FDA’s efforts have been laudable, these efforts have been largely reactive and once a shortage has evolved, patients **will be** affected. The agency must have what it needs to develop proactive approaches to predict and prevent shortages before they affect organizations like St. Jude and patients like Lucy. The FDA should have sophisticated systems in place, such as a database of all foreign and domestic manufacturers producing critical

medications, and should develop the ability to forecast supply and demand levels. This technology exists in the private sector and should be expanded nationwide to enable the FDA to work more proactively with suppliers and purchasers to prevent shortages from ever occurring.^{iv} Further, other relevant federal agencies such as the DEA must collaborate with the FDA to combat drug shortages. At the end of calendar year 2011, St. Jude experienced serious drug shortages of controlled substances such as intravenous fentanyl, and concerns have been expressed that the DEA quota system may be inflexible and contribute to drug shortages.

Third, Congress must ensure that in any solution it develops, pediatric protections are built in and pediatric experts are broadly engaged. Children are not just small adults; rather they need specialized care and medications. Children require medications in special strengths, packaged in smaller dose sizes, dye-free and preservative-free when possible. Hospitalized children frequently require intravenous medications, and as you know the majority of drug shortages have been sterile injectable medications. In many cases, fewer alternatives exist for children when a drug is in short supply. For these reasons, the expertise of pediatric practitioners who are familiar with the nuances and intricacies of pediatric care must be included in developing solutions for drug shortages.

Finally, I'd like to conclude by recognizing that the underlying causes of drug shortages are complex. I have offered three possible solutions today that will help address this growing public health crisis in the United States. These solutions alone will not solve the many reasons drug shortages exist and continue to increase. Before enacting legislation to address those factors, I urge Congress to carefully and comprehensively study and understand all the underlying factors

and implications of proposed solutions, with input from health care professionals and other stakeholders. Remember that data from the FDA and other sources point to two major factors as the most common underlying contributors to shortages: manufacturing issues, and quality issues resulting in temporary closure of production facilities.

We must return to a state where a consistent, reliable, and safe supply chain of needed pharmaceutical products exists to protect patients like Lucy. Nothing less is acceptable. Thank you for your dedication to this issue and for allowing me these few minutes to speak as a provider and caregiver, representing children throughout this country who have been affected by these shortages.

References

¹ Ledford H. Drug shortages slow clinical trials. *Nature*, October 3, 2011, *available at*:

<http://www.nature.com/news/2011/111003/full/news.2011.570.html>.

¹ See Food and Drug Administration Center for Drug Evaluation and Research, "Approach to Addressing Drug Shortage; Public Workshop." *available at* <http://www.fda.gov/Drugs/NewsEvents/ucm265968.htm>

¹ Executive Order 13588: Reducing Prescription Drug Shortages, Oct. 31, 2011, *available at*

<http://www.whitehouse.gov/the-press-office/2011/10/31/executive-order-13588-reducing-prescription-drug-shortages>.

¹ "Drug shortages: a closer look at products, suppliers, and volume volatility," IMS Institute for Healthcare Informatics (November 2011), *available at*:

<http://www.imshealth.com/portal/site/ims/menuitem.edb2b81823f67dab41d84b903208c22a/?vgnextoid=a6fbcc0f68f73310VgnVCM100000ed152ca2RCRD>.

Figure 1: Drug Shortages Affecting St Jude Patient Care

