

Statement of

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**Before the
United States House of Representatives Committee on Energy and Commerce
Health Sub-Committee**

“Examining The Increase In Drug Shortages”

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Introduction

Good morning and thank you for the opportunity to participate in this hearing today. My name is Rich Paoletti and I am a pharmacist and Vice President of Operations at Lancaster General Health in Lancaster, PA. My comments today will address the daily challenges hospitals, patients, and providers are experiencing as a result of the increasing drug shortages occurring nationwide. On behalf of Lancaster General Health, I applaud the Committee for holding this hearing.

Background

Lancaster General Health is an acute care community hospital and level II trauma center with over 600 beds and 7000 employees, located in a county with a population just over 500,000. With a current annual drug budget of approximately \$43.5 million, our institution dispenses an estimated 12,000 doses of medication per day and receives daily shipments of medications six days per week. Although our organization has always focused on quality and safety, the IOM Report “To Err is Human,” was a catalyst for an improved focus on a culture of safety developed over the past decade. The fundamental building blocks to this culture are largely based on standardization and elimination of waste and variability. The requirement for safe, secure, and efficient medication management in our institution relies heavily on intelligent leveraging of automation and technology including, but not limited to, electronic order management software, automated storage and retrieval systems, decentralized dispensing cabinets, barcode-medication administration, and intelligent infusion devices.

In the current healthcare climate, hospitals are being asked to re-structure to meet the quality, safety, fiscal constraint, and community benefit standards expected in today’s world. Our resources are being stretched to the limit. At the same time, the number of documented drug shortages has nearly quadrupled in the United States over the past five years and presently, there are at least 198 drug shortages^{1,2}, spanning multiple therapeutic classes, ranging from nutritional supplements to chemotherapy agents and many other categories in between.

Ongoing drug shortage challenges at Lancaster General Health are increasingly becoming the norm and are resonating across hospitals, physician practices, emergency responders - and most importantly – patients every day. At Lancaster General Health, we strive to maintain a culture of quality and patient safety largely based on the fundamental building blocks of standardization through elimination of waste and variability. In direct conflict with

these safety practices, drug shortages add variability, complexity and additional burden, increasing the possibility of medication misadventure, poor outcomes and patient harm.

The lack of an early warning system regarding impending shortages is one of the greatest challenges we face as healthcare providers, such that we sometimes learn about shortages or their severity when products are not received in our daily shipments.

A review of our drug wholesaler ordering patterns last month (August 2011) demonstrated a 79.5% raw service level; of 4,344 line items ordered, only 3,452 were supplied; 892 line items were not available and, of those 892, only 25 were temporary issues within the control of the wholesaler.

Aug-11	Lines Ordered	Wholesaler Out	All Other Exception Lines	Lines Filled	Raw Service Level %
ACCT 1	3292	19	572	2701	82.05%
ACCT 2	731	4	280	447	61.15%
ACCT 3	321	2	15	304	94.70%
TOTAL	4344	25	867	3452	79.47%

Every disruption to medication supply creates new responsibilities to investigate alternative treatments and evidence, and to update protocols, procedures, and various technologies. Additionally, the hospital must disseminate effective education on alternatives not always readily familiar to frontline caregivers. In our fast-paced, complex environment, every substitution adds variation and risk.

Manufacturer consolidations, in some cases, have exacerbated this problem by reducing the number of facilities that produce critical drugs to one or two sources worldwide. As a result, even a small shift in a facility's production lines can eliminate the availability of drugs for days. Hospitals are also unable to buffer the impact of drug shortages due to the need for just-in-time inventory controls that are necessary in today's fiscal environment.

Some examples of how these decisions and realities impact patients include the following:

Causes:

- Increased demand for a product (can be due to sole source suppliers, other manufacturers exiting the market on a particular product)
- Natural disasters
- Raw materials shortages
- Manufacturing / Regulatory issues
- Recalls
- Changes in licensing and/or changes in formulation

Challenges

- The lack of an advance warning system (often, hospital staff are only able to detect a shortage when they receive fewer units than expected from a wholesale order)
- Communications by manufacturer and FDA often lag behind the discovery of shortages at the point of care
- Current FDA authority is inadequate to ensure a consistent supply of medications
- Institutions must stretch their resources in order to adequately manage shortages

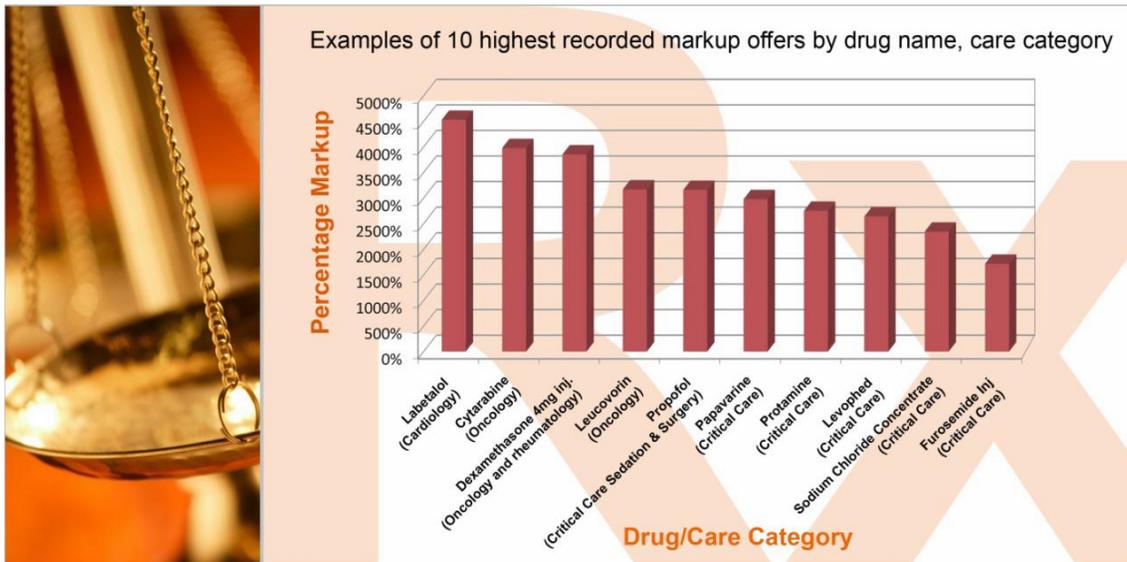
Impact

Financial

Drug shortages can have a significant financial impact on hospitals by affecting market prices and adding administrative costs in order to adapt to shortages. The enormous amount of time required to mitigate drug shortages also takes hard-working employees away from patient-centered activities. Healthcare organizations, as a result of this time-consuming activity, must bear additional administrative and wage costs, as well.

For example, when a shortage of a niche product arises, the price of that product can rise rapidly upon reintroduction into the market. This type of shortage can occur when pharmaceutical companies sell the rights to these products to smaller firms. When the new owners of the drug reintroduce it to the market, acquisition costs can sometimes be 100% higher than the cost of the original products (e.g., Chlorothiazide [Diuril], indomethacin [Indocin], mechlorethamine [Mustargen], and dactinomycin [Cosmegen]).³

The use of gray market suppliers also increases acquisition costs during drug shortages. A study conducted by Premier Inc. in August of 2011 recorded 1,745 gray market offers to providers, with an average markup of 650 percent.⁴ Many items, including those used in the treatment of critically ill patients, had markups even higher.



Adapted from Premier Gray Market analysis⁴

Drug shortages may force institutions to use higher-cost medications. For example, a hospital may have to purchase brand name Unasyn when generic ampicillin sulbactam is unavailable, or purchase branded oncology drugs such as levoleucovorin (Fusilev) during a leucovorin shortage.

Even more alarming, shortages of certain intravenous medications may jeopardize surgeries, interrupt cancer treatment and other medical procedures. Beyond the life-threatening impact that these situations can have on patients, they also mean lost revenue for hospitals that serve their communities.

Additionally, after a drug shortage ends, hospitals may experience a large surplus of the previously-scarce drug, resulting in higher inventory costs. During a shortage, hospitals often continue to order a product through wholesalers or manufacturers to fulfill contractual “failure to supply” clauses or to have a standing order on hand when the medication is available. When the medication shortage is over, suppliers sometimes fill backorders and standing orders, resulting in excessive supply and additional resources spent managing this new inventory. Lancaster

General Health has experienced this situation after resolution of backorders in vancomycin injection, dextrose 50% prefilled syringes, and phenylephrine, resulting in over a year's supply of medication on hand which in some instances was not returnable.

Finally, drug shortages often cause hospitals to rely on alternate suppliers which charge extremely high prices for critical medications. In each instance, Lancaster General Health first exhausted all other supply options and then evaluated the credibility of the alternate market supplier before resorting to this high-cost solution. Examples of alternate market supplier medication prices, compared to normal wholesaler acquisition prices, appear below:

Medication	Wholesale Acquisition Cost (WAC)	Alternate Supplier Pricing
Aminocaproic Acid 250mg/mL 25 x 20mL	\$ 17.13	\$ 375.00
Cisplatin 100mg Vial	\$ 17.23	\$ 120.00
Diltiazem 25mg/5mL SDV x 10	\$ 11.58	\$ 129.00
Hydralazine 20mg/mL 10 x 1 mL	\$ 114.62	\$ 295.00
L-Cysteine 50mg/mL SDV x 5	\$ 60.30	\$ 355.00
MultiTrace - 5 Concentrate 25 x 10mL	\$ 78.39	\$ 425.00
Paclitaxel 300mg/50mL Vial	\$ 52.78	\$ 695.00
Potassium Phosphate 4.4meq 25 x 50mL	\$ 55.48	\$ 325.00
Sodium Acetate 2meq 25 x 50mL	\$ 57.89	\$ 235.00
Valproate 500mg/5mL 10 x 5mL	\$ 64.60	\$ 275.00

Personnel

Drug shortages place a heavy logistical and administrative burden on hospitals. To combat these shortages, hospitals such as Lancaster General Health must reallocate existing staff to acquire medications, manage inventory, administer rapid changes to information systems, communicate to clinical staff, and develop alternative measures. Personnel may spend minutes to hours managing shortages, depending on the nature of the shortage.

Dealing with a drug shortage may require the work of a full range of providers, including pharmacy managers, technicians, front-line pharmacists, informatics and clinical pharmacists, pharmacy buyers, nurses, and physicians.

- **Pharmacy managers and supervisors:** daily review of current shortages, communication with front-line and clinical staff, patient/medication management determinations, development of alternative treatment strategies.
- **Pharmacy technicians:** management of inventory, including reallocation of supply to areas of need and monitoring of current supply.
- **Front-line pharmacists:** One-on-one communications with providers in acute situations who may not realize the shortage, ensuring an alternative therapy is available when needed, often with only a few minute notice (ex. OR).
- **Informatics pharmacist:** making necessary changes in information systems to accommodate alternative products or patient treatment strategies.
- **Clinical pharmacists:** development/implementation of alternative patient management strategies and patient education.
- **Pharmacy buyer or pharmacy purchasing department liaison:** daily review of current shortages, communication of shortage(s), researching strategy to manage including establishment of direct

order/allocation arrangements, bulk buying opportunities, compounding pharmacy opportunities, or gray market acquisitions.

- **Nursing:** patient education and implementation of alternative strategies.
- **Physicians:** decision making with regard to patient management and alternative treatments.

Patient Care / Safety

- Over the past year, medication shortages have resulted in delayed treatment, changes in therapy, and the omission of certain medications for many patients.

Some examples affecting Lancaster General Health include:

Bleomycin – This drug is critical to curative therapies for Hodgkin's lymphoma (ABVD regimen) and testicular cancer (BEP regimen), especially for young adult patients with curative diseases and good performance status. We receive medication via an allocation program by the manufacturer, which increases paperwork and results in delayed initiation of treatment as well as rescheduling of patient appointments. Alternative regimens are more toxic and impair fertility in young patients.

Leucovorin – Due to a shortage of this drug within the past year, for about two months, this drug was either omitted from regimens or patients were moved to alternative regimens that were potentially less effective or not well-tolerated. The biggest concern with regard to this drug is the unknown and potentially negative effect on patients with colorectal cancer who receive curative/adjuvant therapy through Oxaliplatin and Irinotecan + fluorouracil based regimens. This drug has a synergistic effect with fluorouracil and increases the cancer-fighting ability of the fluorouracil.

Doxil (Liposomal Based Doxorubicin) – Lancaster General Health experienced a shortage of this drug due to manufacturing issues. The manufacturer also established an allocation program (Doxil C.A.R.E.S) to assist in supplying medication to patients currently in need. Due to difficulties that Lancaster General Health has experienced in enrolling patients in this program, we are currently experiencing patient treatment delays. Since the allocation supply has been available, we have had one patient accepted and at least 10 more waitlisted indefinitely. Substitute treatment medications/regimens which have been required to be used in some cases run a higher risk of toxicity (including cardiac and/or hematologic events).

Taxol (paclitaxel) – This drug is effective in the treatment of numerous cancers, including breast cancer, ovarian cancer, lung cancer, and gastric cancer. While shortages have not caused us to withhold care, other physician offices in our community have been unable to obtain this medication. Few affordable alternatives exist, because many providers use this drug as an alternative therapy in place of other medications that are currently on back-order.

Fluorouracil – This drug is standard in numerous treatment regimens, the largest group being FOLFOX and FOLFIRI for colorectal cancer. While Lancaster General Health has not yet experienced a shortage of this drug to the point of withholding care, other provider offices in our community have, as well as subsequent home infusion services.

L-Cysteine – This non-essential amino acid, which improves the solubility of calcium and phosphorus, is in short supply due to manufacturing issues. Presently, we are unable to obtain this ingredient from any source, forcing us to omit it from patient regimens. Intravenous nutrition supplementation is often necessary in premature infants due to inadequate nutrient stores. Without L-Cysteine, providers must monitor the solubility of calcium and phosphorus in patients in order to ensure their safety.

Prochlorperazine – This injection, which is used for the treatment of nausea and vomiting, is presently unavailable. Prochlorperazine is a safer alternative to promethazine injections in patients with contraindications to several different medications.

Electrolytes, including injectable calcium gluconate and magnesium sulfate, are presently in short supply and increasingly difficult to obtain from any supplier. Providers use electrolytes in situations where urgent supplementation is necessary, to treat conditions or side effects from other medications, and in customized intravenous nutrition formulas. *The limited availability of electrolytes has resulted in rationing/restricting utilization and the use of higher-cost premixed intravenous nutrition formulas. Higher-cost alternatives carry potential safety concerns.*

Protamine is the reversal agent for heparin and is imperative in surgical and procedural settings. While Lancaster General Health has not yet had to deny the use of this agent to patients, our supply levels have been down to having only a few days supply in inventory. A lack of protamine at Lancaster General Health would threaten the scheduling of important surgeries and other procedures.

Additional examples that previously affected Lancaster General Hospital:

Epinephrine is an essential cardiac medication used in emergency code blue situations. We were unable to obtain the standard concentration of 1:10,000 1 mg/10 ml pre-filled syringes, which is supplied as a universally recognized single-use package in our emergency code carts. Our inability to obtain any product forced us to substitute epinephrine with a different concentration, 1 ml of the 1:1000 (1mg/ml) ampules (note: 10x greater concentration). The potential for medication errors was high, given that only 1 mL was required instead of 10 mL in these high-stress circumstances.

Propofol is a sedative and anesthetic agent with many advantages, including fast onset, short half-life once infusion is discontinued, and predictable clinical effects reached critical lows. The use of pre-filled syringes avoids waste. We required obtainment of Fresenius propofol, an alternative manufactured in the United Kingdom. The package insert cautioned against the use of this agent in individuals with soy or milk allergies, which is not a concern with the product we typically stock. Since many children and adults have milk or soy allergies, this represented a major safety concern.

Succinylcholine and Vecuronium are neuromuscular blocking agents that anesthesia providers use to induce and maintain anesthesia. Succinylcholine is particularly advantageous as a short-acting paralytic, a first-line choice for many surgical interventions. The shortage of succinylcholine led to our anesthesia department developing specific criteria and restricting the use of this agent. This resulted in the substitution of a longer-acting paralytic agent in place of this drug of choice for many operating room cases, which increased the risk for respiratory compromise due to prolonged paralysis. We were close to cancelling surgical procedures because of these risks, and surgeons threatened to cancel cases due to lack of availability of these agents.

Neostigmine was also in critical supply, which is required to reverse the effects of paralytic agents at the conclusion of a surgical intervention, which led to much anxiety in our anesthesia group.

Dexamethasone is most potent intravenous steroid specifically utilized for certain conditions. We were forced to stock a 10 mg/ml concentration of this drug, due to our inability to obtain any of our standard 4 mg/ml concentration. The potential for medication errors from the same total volume (1ml) were high.

Other concerns include:

- Utilization of gray market suppliers is concerning, as these are unofficial, unauthorized, or unintended suppliers of manufactured items. It is not always possible to obtain medication pedigrees to be certain of where the supplier obtained the medication from, or that it is not a counterfeit item.
- There is potential that substitution of similar medications if available may lead to medication errors or adverse events, especially if the prescriber is unfamiliar with the alternative's dosing or drug interactions.
- Medication shortages in procedural areas have the potential to cause delays in procedures and surgeries.

These logistical tasks consume significant dedicated hours from multiple stakeholders and staff working collaboratively on detailed plans to maintain safety, while requiring execution in limited timeframes.

During the past year, these collaborative discussions have included me personally, clinical pharmacy staff, nurses, and countless other caregivers working with:

- anesthesiologists and emergency physicians in contemplating how to maintain the airway of a patient presenting to the trauma center without the availability of a paralyzing agent;
- neonatologists considering how to best provide nutritional care to compromised premature infants;
- infectious disease specialists searching for alternative anti-infectives;
- oncologists discussing alternative treatment regimens midway through a course of therapy; and
- most significantly, how providers will explain to patients that we may not have the medication necessary to treat their disease.

I'd like to share a story relayed to me from our medical director of oncology concerning an 80 year old lady being treated for metastatic lung cancer. She was treated for three months with no side effects and in complete remission. One year later, her cancer returned and repeat treatment was planned, consented, and ordered. The drug was not available and an alternative was selected. The patient, who does not drive, needed to return so that we could re-consent, re-order and re-schedule treatment using an alternate agent. The patient subsequently suffered severe side effects, leading to the discontinuation of treatment until she recovers.

In our opinion, drug shortages are a national healthcare crisis.

Recommendations

Relieving and minimizing avoidable drug shortages requires both short-term interventions and longer-term, permanent solutions. We believe multiple opportunities exist and suggest the following actions:

First, we recommend the bipartisan legislation currently in both houses of Congress that requires drug manufacturers to report potential or existing production problems to the FDA. This key communication requirement would allow for appropriate planning and mitigation strategies to facilitate early identification, resolution and prevention of drug shortages. We believe this legislation will create greater collaboration and transparency between drug manufacturers and the FDA, which would facilitate more proactive approaches to avoiding critical situations.

Next, we recommend further collaborative requirements between the FDA and manufacturers to establish evidence-based allocation plans for critical drug therapies. Executed carefully, these actions could secure the pharmaceutical supply chain and direct available supplies to our most critical patient populations, making certain a drug is available in situations without reasonable alternatives.

Finally, we would encourage an exploration of incentive programs to encourage drug manufacturers to stay in, re-enter or initially enter the market, specific to critical drugs in short supply. These incentives could include creation of a fast track for approval of ANDA's, unapproved drugs, new production lines, alternate manufacturing sites or new suppliers of raw materials for drugs vulnerable to shortage, without compromising quality and safety.

Closing

Again, I want to thank the Committee for holding this hearing. Lancaster General Health offers its continued support and commitment to assist in the development of solutions that will help to prevent and mitigate risks caused by drug shortages. Thank you.

I will close with a statement made by Dr. Jacqueline Evans, from Cancer Care for Women:

“The entire oncology community, as a whole, has been kept in the dark as to the exact causes for the shortages of these medications...our patients and their families are the ones suffering. Their diseases are progressing, and they are actively dying, while we wait for the medications that could save their lives.”

Thank you.

References

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