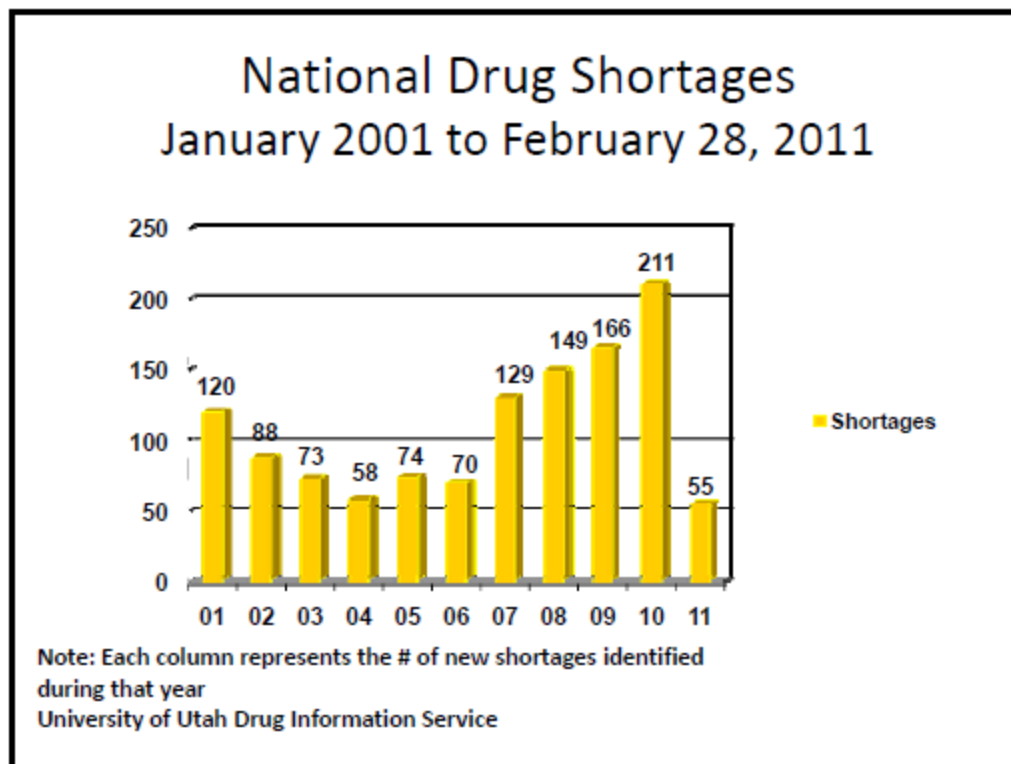




## Unprecedented Drug Shortages in the United States: What it means for Children's Hospitals by John VanEckhout, Pharm.D., Vice President, Clinical Services, CHCA

Drug shortages are at their highest level in a decade. Some experts believe we are experiencing the worst shortage in 30 years and it will probably not improve anytime soon. What does this mean for your hospital and what efforts are underway to plug the holes in the dam?



The University of Utah Drug Information Service (UUDIS) tracked a record 211 shortages in 2010—the highest in 10 years of monitoring shortages. In the first two months of 2011, more than 50 drug shortages have been reported. UUDIS provides drug shortage information and content to the American Society of Health-System Pharmacists (ASHP) and Novation and works closely with the FDA.

### Drug Shortage Side Effects

There are several serious side effects from drug shortages but none more important than patient safety and care standards. According to an Institute for Safe Medication Practices (ISMP) survey last summer, there were more than 1,000 drug shortage-related "near misses," errors and adverse patient outcomes, including at least two deaths and several extended hospitalizations reported by 1,800 respondents. Therapeutic drug substitutions with infrequently used products can create medication errors, unknown side effects and dosage errors. In some cases different sizes and concentrations of drug preparations can lead to patient harm when the shortage forces a substitute for a frequently prescribed dose and/or pre-loaded syringes.

Hospitals also report substantial drug shortage-related costs including the administrative burden to investigate and locate alternate supplies, create and implement crisis plans for shortages, and prepare and administer dosing and drug alternatives. Direct costs for procurement of drugs are increased dramatically if the pharmaceutical product in short supply is only available through alternate suppliers or other vendor relationships.

### **No Single Cause=No Easy Solution**

There is no single solution to the problem. According to the FDA, about 54 percent of the shortages in 2010 were due to product quality problems. Two of the largest manufacturers of sterile injectables, such as propofol, had product recalls last year after the FDA found particulates in the syringes. Another 21 percent of the shortages stemmed from production delays, while 11 percent were caused from discontinuing a product, usually for business reasons. The rest were due to increased demand, raw material shortages and manufacturing sites' consolidation or closure.

Consolidation in the drug industry is one cause. The number of generics and ethical drug manufacturers has decreased over time. Many Generic drug manufacturers have a small number of products or niches in the marketplace. When one or more of them is forced to exit the market place due to recalls or regulatory issues, the remaining entities are unable to respond to the need due to limited capacity. If there is a problem with any of them, the shortage is felt immediately. If a competing manufacturer withdraws due to shortage or exiting the market, they do not notify other manufacturers producing the same drug, which could allow for lead time to ramp up. Increasing production capacity also takes time. Additionally, generic drugs may be discontinued to produce more profitable drugs. The FDA only has authority for safety and efficacy and has no regulator authority over what drugs are produced by the manufacturers.

Historically, some shortages have been attributed to pharmaceutical manufacturing issues—loss of experienced staff, outdated equipment, or the unavailability of bulk and raw materials. Stockpiling (hoarding) may also occur when providers buy in excess of their immediate and short-term needs following a rumor of impending shortage. More recently, drug recalls have grown significantly and greatly contributed to drug shortages.

The increase in the number of drug recalls directly correlates to the number of drug shortages. In 2009, there were 157 drug shortages documented by the FDA which stemmed from the 1,742 recalls. Many of these drugs continue to be in short supply as the FDA and manufacturers work together to find solutions to supply the U.S. market. *(The FDA tracks drug shortages in medically necessary drugs only; not all biologics as does UUDIS.)*

The large number of injectable drugs having supply issues in the U.S. is an even heavier burden on pediatric institutions which primarily use injectable drug forms for treatment. Data collected by the FDA Drug Shortage Program shows that, of 110 shortages that occurred in 2008, 39 involved sterile injectables (35%). In 2009, the proportion rose to 73 of 157 drug shortages (46%).

The shortages are most acute in the availability of cancer drugs, forcing oncologists to suspend treatment or resort to unproven chemotherapy combinations. Treatment of pediatric cancer can become more difficult due to delays in obtaining drugs. These complications of treatment may compromise patient outcomes and can impact survival. Clinical trials are also affected by the unavailability of cancer drugs which might be part of the “control” regimen or part of the experimental regimen. If a key component of either regimen is unavailable, patients cannot proceed to be treated in the trial. Not only is patient care compromised but meaningful outcomes and data post trial are unreliable.

(For additional information and a full list of drug shortages, see the [FDA](#) and the [American Society of Health-System Pharmacists \(ASHP\)](#) web sites.)

## What is Being Done?

CHCA and Premier have been working diligently to assist CHCA Owner Hospitals in mitigating shortage issues by:

- Working to ensure product alternatives are available and on-contract;
- Working with suppliers regarding product allocations;
- Regularly updating members regarding drug shortage statuses; and
- Premier PDIN newsletter provides drug shortage updates directly from FDA and [ASHP Drug Shortage](#) web sites.

CHCA is proactively working to keep products in short supply available through relationships with various vendors. However, when vendors drop out of the market completely or delete the product from their portfolio of products this complicates supply and increases the price from the remaining vendors.

In 2009, Premier launched a Failure to Supply program which helps alliance hospital members optimize recovery for drug shortage costs. This program is representing more than 1,100 members and has netted more than \$3.5 million in costs recovered for failure to supply in its first year.

The American Society of Clinical Oncology (ACOS), American Society of Anesthesiologists, American Society of Health-System Pharmacists and ISMP have recently become very involved in this issue. Last November, the group convened an important summit to address the problem. They developed "an assertive action plan to reflect the recommendations and intent of stakeholders to work together to stop patient harm and disruptions in patient care caused by drug shortages." Also in attendance were manufacturers, wholesalers, distributors, group purchasers and the [Food and Drug Administration](#) and other regulators. In January, the group released recommendations for preventing drug shortages including: improving communication across the supply chain, removing barriers to suppliers and the FDA to minimize the impact of drug shortages, and clarifying the regulatory definition of "medically necessary," which could prompt earlier reporting of impending shortages to the FDA. They will provide detailed public policy and other recommendations in the next few months. They will also prioritize interventions believed to have the most impact.

"At the summit we tried to determine why this was happening and realized it is not just profit-driven; there are some real business decisions that come into play—manufacturing problems and legislation and oversight limits by the FDA. The outcome of the summit was acknowledging we could all work together toward a resolution," explained Michael Link, M.D., MPH, Pediatric Oncologist at Lucile Packard Children's Hospital and Stanford and ASCO President-Elect.

In addition to acquiring access to products and distributing information to CHCA Owner Hospitals, CHCA and Premier are also identifying and participating in opportunities to lobby Congress for relief from the current drug shortage crisis. We are also in communication and collaboration with our counterparts at HIGPA and National Association of Children's Hospitals and Related Institutions in their advocacy efforts.

Recent legislation has been introduced to address drug shortages. The Preserving Access to Life Saving Medications Act (S. 296) proposed by Sens. Amy Klobuchar (D-Minn.) and Robert Casey (D-Pa.), is an [important first step](#) towards preventing the patient harm that often occurs when a medication is in short supply. The bill would require manufacturers to provide the FDA with early notice of impending shortages, and to expedite importation of substitutes when necessary. The Obama administration is also launching a federal research institute to speed development of new drugs, though this will not address shortages of existing compounds.

“We had planned to form subgroups from the summit of stakeholders to discuss legislation,” Dr. Link commented. “We were pleasantly surprised by the speed at which legislation was introduced and the language in the proposal is almost identical to our summit recommendations. But, we certainly would like the opportunity to review and make sure we understand the ramifications of this proposed bill.”

## **What You Can Do?**

### **1. Institutional Approach**

Your hospital should have a crisis plan in place that includes identifying drug shortages proactively along with therapeutic alternatives, prioritizing patients and limiting use, conducting failure analysis to avoid look-like errors, establishing a drug shortage network (CHCA can help), implementing an organizational policy on alternate suppliers and monitoring shortage-related adverse events.

The medical staff should be included in the process and have an active role in dealing with the shortages. Develop a preemptive plan particularly for the use of antibiotics. Try to get medical staff to understand the problem and be willing to allow prioritization of patients who need drugs most. This may not be the physicians’ first choice but should be considered for patients with no other alternative. The goal is to maintain cohesiveness among the medical staff about drug availability.

Raise awareness of drug shortages and increase communication about the issue at all levels within your hospital.

You may want to consider establishing collaborative and reciprocal relationships with other institutions including local adult hospitals to share supplies and resources for alternative therapies.

Dr. Link added an important hospital strategy—reassuring the patients. “The majority of patients will not be affected by a drug shortage. As a bigger consumer, our children’s hospitals can get better access than small practices. For the general pediatric patient population there are really effective workaround drugs, unlike oncology, where there are fewer drugs and alternatives available and therefore shortages can affect patient outcomes and care. Patients are hearing about this through the media and those most concerned may try to hoard the drug or worry whether the drug will be there for their next treatment. Encourage them to talk with their own physicians directly to see if they are affected, or if there are effective substitute drugs for their treatment.”

### **2. Utilize Existing Relationships and Alliances**

CHCA and Premier will continue to assist Owner Hospitals by providing current shortage information, leveraging manufacturer relationships to secure products, and communicating with the pharmacy directors and Pharmacy Buyers Forum.

In addition to your CHCA and Premier clout, leverage your own vendor and manufacturing relationships. You may want to reach out to other children’s hospitals in your state or region to arrange a reciprocal sharing program or even adult hospitals in your community.

“We almost completely ran out of neostigmine to stock our 60+ anesthesia trays. We exhausted all of our options—Cardinal, American Reagent direct, Baxter direct and even personal contacts at AmerisourceBergen—to no avail. Through his contacts, Ben Lizak at CHCA was able to place an order the same day to obtain an emergency supply until our next anticipated release date.” – Aaron Sinner, Pharm. D., Pharmacy Operations Manager, Phoenix Children’s Hospital.

Contact me ([johnvaneekhout@chca.com](mailto:johnvaneekhout@chca.com)) or Ben Lizak ([ben.lizak@chca.com](mailto:ben.lizak@chca.com)) with an urgent drug shortage issue and we will do our very best to help you attain the necessary drugs without disruption of care.

### **3. Support Legislation and Advocacy**

Add your voice in support of resolving the drug shortage issues and the safety, access and quality of care, and financial burden felt by children's Hospitals. Engage your government relations and public advocacy professionals on this issue. Ensure the FDA has the tools it needs to help minimize the impact of drug shortages on patient care by urging your senators to cosponsor the Preserving Access to Life Saving Medications Act (S. 296). Contact your senators and let them know about the impact of drug shortages on the patients you serve.

"CHCA and children's hospitals can also support additional legislative efforts to give authority to the FDA to respond more quickly particularly with indication and labeling drugs for usage," said Link. "In addition, support efforts to review efficacy of expired drugs and their potential so that expiration dates may be extended safely as well as work with payers to understand and accept temporary substitution regimens and not stick the patients with the price."

### **4. Don't Buy from Gray Marketers**

Gray marketers are charging hospital 10 to 20 times contract price for these short supply products. More importantly, quality cannot be assured since you don't know how they gained access to the product. The drugs could be counterfeit and since pedigrees aren't officially documented and tracked, you assume a huge liability risk when dealing with these distributors. Recognized distributors have a documented chain of custody.

### **Working Together**

The drug shortage issue is not going to be quickly or easily resolved. It may get more intense with supplies increasingly dwindling before resolution occurs. If we can get some discussion beyond the FDA and the regulatory realm, which can be very black and white, we can begin to resolve these issues. Without robust dialogue and proactive plans of action, denial of treatment or an increase in adverse events may be inevitable and devastating to your patients and their families as well as your staff.

We hope you will talk with your pharmacy directors and leadership teams and plan your course of action to resolve these issues. CHCA and your children's hospital colleagues are available to help you navigate this issue.