



**Testimony of the National Coalition for Cancer Research
United States Senate Committee on Finance Hearing:
“Drug Shortages: Why They Happen and What They Mean”
December 7, 2011**

Member Organizations

*American Association
for Cancer Research*

*American Cancer Society
Cancer Action Network*

*American Childhood
Cancer Organization*

*American College
of Radiology*

*American Society for
Therapeutic Radiology
and Oncology*

*American Society of
Clinical Oncology*

*American Society
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Kidney Cancer Association

*The Leukemia and
Lymphoma Society*

*The Lustgarten Foundation for
Pancreatic Cancer Research*

Melanoma Research Alliance

Oncology Nursing Society

*Pancreatic Cancer Action Network
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Prevent Cancer Foundation

Prostate Cancer Foundation

*The Society of
Gynecologic Oncologists*

*The V Foundation for
Cancer Research*

The National Coalition for Cancer Research (NCCR) commends the United States Senate Committee on Finance for holding this important hearing to address the severe drug shortage issue that is significantly impacting cancer research and care.

The National Coalition for Cancer Research is a nonprofit coalition of 24 national cancer research, cancer care and patient organizations representing cancer patients and survivors, children with cancer and their families, cancer researchers, nurses and physicians, and cancer hospitals, centers, clinics and specialized research institutions. The organization directs its efforts at making widely known the value of cancer research and the major contributions the National Cancer Program has made to the biomedical sciences and related fields, patient care, to the reduction of cancer incidence, morbidity and death, and issues faced by cancer survivors.

According to the University of Utah Drug Information Service, there were 211 reported drug shortages for calendar year 2010. As of November 30, 2011 there have been more than 250 reported drug shortages. If the current trend continues, it is estimated that up to 300 drugs will be, or have been, in short supply by the end of 2011, an increase of approximately one-third over the span of one year.

As an initial step in addressing the complex and multi-faceted issue of drug shortages, NCCR strongly supports the immediate passage of S. 296 or similar pending legislation in the House of Representatives (H.R. 2245), both entitled the “Preserving Access to Life Saving Medicines Act.” These bipartisan bills would require manufacturers to confidentially notify the US Food and Drug Administration of a discontinuance, interruption, or other adjustment of the manufacture of a drug that would likely result in a shortage of such a drug. Evidence shows that an advance notification system, and the resulting collaboration between FDA and manufacturers, can greatly assist in either mitigating or averting the impact of potential drug shortages. In 2010, for example, the FDA was able to prevent 38 shortages when drug manufacturers notified the agency when a product was discontinued or a manufacturing problem occurred. That number has increased to more than 100 shortages averted for 2011. Passage this year of the aforementioned legislation would be an important, immediate step to mitigate drug shortages.

Drug Shortages Impacting Cancer Clinical Trials

The shortage of some cancer drugs is not just affecting patients currently undergoing treatment, but it is also having a significant negative impact on current and future cancer clinical trials. Of the drugs on the most current shortage list, 22 are cancer agents. Approximately half of all active cooperative group cancer clinical trials have at least one drug on the shortages list.

This impact on cancer research is largely due to the fact that placebos (sugar pills) are rarely used in cancer clinical trials, and are never used alone if an acceptable treatment is available. Therefore, cancer clinical trials are traditionally designed to test the safety and efficacy of the standard of care against, or in combination with, a new treatment being investigated. When the drug that is the standard of care is in short supply or is no longer being manufactured, it severely compromises high priority clinical trials.

These shortages have resulted in important cancer clinical trials being delayed, suspended and/or halting the accrual of new patients into them. Halting a trial wastes the investment made in the treatment, data management and time investment by the patients and clinical scientists participating in the study and causes the loss of valuable information. In some cases, clinical trial sponsors have been placed in the difficult position of, when permitted, utilizing alternative regimens that are not part of the original protocol due to a shortage of the existing drug being used as part of the investigation. For some clinical trials, particularly those with FDA registration implications and requirements, substitutions of drugs used in the trial are not permitted.

Furthermore, as patients are recruited for clinical research trials with the intent to receive an investigational therapy, the treatment described in the consent form details both the benefits, side effects, and other standard of care treatment options. It is concerning that a patient who opts to receive an investigational treatment in combination with an existing drug, which is in short supply, could have instead elected to receive alternative, standard treatment – perhaps in a more timely way. Treatment delays of days to months are critical in the life of a cancer patient and could limit their chances for a cure or remission of their disease.

Another residual impact of drug shortages is the delay in obtaining the data necessary to bring new cancer therapeutics to patients. With more than 400 cancer agents in various stages of development, it is imperative that cancer clinical trials continue uninterrupted in order to obtain the necessary data to seek approval of new anti-cancer drugs as soon as possible.

Following are examples of the impact the current drug shortages are having on cancer clinical trials:

- The Coalition of Cancer Cooperative Group research sites report they are unable to enroll patients in certain clinical trials, even though the patients meet protocol eligibility requirements, due to the lack of an existing cancer drug being used in the clinical trial.
- Due to a shortage of the drug doxorubicin, two important clinical trials have been delayed. These clinical trials were designed to test this drug in combination with novel agents in patients with Advanced Recurrent Epithelial Ovarian Cancer and those with Hepatocellular Carcinoma of the liver, which is one of the most common tumors in the world and is a leading cause of cancer deaths.
- A shortage of the drug paclitaxel has resulted in delaying the enrollment of eligible lung cancer patients into clinical trials. Furthermore, the shortage of paclitaxel may result in current clinical trial participants being removed from the study.

- Daunorubicin is a chemotherapy treatment for children and adults with Acute Lymphoblastic Leukemia and Acute Myelogenous Leukemia. In one adult trial, a comprehensive cancer center in Alabama reported that, although a patient was eligible to participate in a study, they had no daunorubicin at the center. Drug substitutions are not allowed for this study, and therefore the center was unable to enroll the patient into the study.
- The Children's Oncology Group reports difficulties in obtaining daunorubicin for its pediatric Acute Lymphoblastic Leukemia studies. In one trial, a substitution is allowed by the National Cancer Institute when no drug is available; however, the substitution is more toxic, resulting in increased risk for patient harm and side effects.

These are but a few examples of how the shortages of existing cancer therapeutics are impacting cancer clinical trials. Additional examples from various parts of the country are provided in the attached supplemental information accompanying this testimony.

This unprecedented drug shortage situation comes at a time when tremendous advances are being made in the treatment of cancer.

- According to the American Cancer Society, the 5-year relative survival rate for all cancers diagnosed between 1999 and 2006 is 68%, up from 50% in 1975-1977.
- The National Cancer Institute estimates that approximately 11.7 million Americans with a history of cancer were alive in January 2007.
- The 5-year relative survival rate for female breast cancer patients has improved from 63% in the early 1960s to 90% today. The survival rate for women diagnosed with localized breast cancer (cancer that has not spread to lymph nodes or other locations outside the breast) is 98%.
- For all childhood cancers combined, the 5-year relative survival rate has improved markedly over the past 30 years, from less than 50% before the 1970s to 80% today.

A robust and sustained cancer clinical trial enterprise is essential if this positive trend in cancer survivorship is to continue, particularly given that there are some forms of cancer for which the 5-year survival rate is still below 50%. Addressing the drug shortage issue is a critical component to the continued advances in clinical cancer research and treatment.

We understand and appreciate the complexity of this issue. We are working with our colleagues in the biomedical research and provider communities to identify potential regulatory and legislative solutions to address this ever-growing problem. However, we cannot overemphasize the urgent need for continued bipartisan efforts to act thoughtfully and expeditiously in order to resolve this critical issue.

The National Coalition for Cancer Research looks forward to working with the members of the United States Senate and House of Representatives, the Department of Health and Human Services, the Food and Drug Administration and the biomedical research community to address this urgent matter.

We thank you for the opportunity to provide this testimony for your consideration.

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Following are additional examples of cancer research studies which have been impacted by drug shortages:

- One large phase III trial compares outcomes for **lung cancer patients** given an accepted standard treatment (either carboplatin and paclitaxel or carboplatin, paclitaxel, and bevacizumab) and patients given the same treatment plus an additional drug – cetuximab. A research site in **Lexington, KY** reports not being able to offer participation in this clinical trial because the center cannot guarantee availability of paclitaxel to these patients.
- No daunorubicin in supply at a research site in **Birmingham, Alabama** led to physicians being unable to enroll a patient with **Acute Myeloid Leukemia** in a cooperative group protocol, and there was no substitution allowed.
- Standard initial treatment for **children with Acute Myeloid Leukemia**, which has a survival rate of between 50-60%, involves the drug daunorubicin, which is in short supply.
- A cancer center in **Boston, MA** almost missed an opportunity for one of its patients to participate on the trial due to the shortage of daunorubicin. Fortunately, the patient was randomized to the clofarabine arm of the trial. If the patient had been randomized to the daunorubicin arm, the center may not have been able to keep the patient on study due to the daunorubicin shortage. Until the drug shortage is resolved, the center may not be able to continue to accrue patients onto this trial.
- The same center reports that lack of availability of paclitaxel, one of the drugs used in a clinical trial, has been affected by this drug shortage and substitution for paclitaxel is not allowed for this study. If the paclitaxel supply is expected within three weeks from the planned date of treatment, treatment can be delayed for those three weeks by the participating clinical trial sites. After a three-week delay, participating clinical trial sites are asked to remove patients from the study. **Until the shortage of paclitaxel is resolved, the center may not be able to accrue patients to this trial because of uncertainty over drug supply.**
- Shortage of daunorubicin for a cooperative group are impacting a study testing a new therapy for patients (ages 18-60) with newly diagnosed **Acute Myeloid Leukemia**, as reported by a research site in **Pittsburgh, PA**, where drug the has not been available since June 1, 2011.

- A cancer center in **St. Louis, MO** reports that a clinical trial for breast cancer that has had scientific approval for over two months, but **has not begun because the clinical trial involves a study drug in combination with doxorubicin**. Due to the shortage of doxorubicin, the investigator is rewriting the trial protocol to change the doxorubicin to another drug. This will delay final approval and activation of the study, which delays this treatment option for its patients.
- Due to the national shortage and allocation of doxorubicin, a cancer center in **Tampa, FL** has had to limit accrual to a study involving patients with Advanced Recurrent Epithelial Ovarian Cancer. It has also been extremely difficult to obtain sufficient supplies of doxorubicin for patients that were previously enrolled in the trial prior to the shortage. One of its active patients is currently on the “waiting list” to receive an allocation of the drug.
- The **Albuquerque, NM**, cancer center recently **lost 21 breast cancer patients to accrual** to a cooperative group trial due to the lack of doxorubicin. The trial is exploring improved treatment methods for women with breast cancer who have a high risk of recurrence. This same research site was unable to enroll an additional **19 patients to other trials for breast, melanoma or ovarian cancer** primarily due to the doxorubicin and doxorubicin shortages.
- A research site in **Lombard, IL** reported shortages of 5FU and Taxol. The site had **three patients with stage 3 colon cancer** eligible for a cooperative group study, who were not able to go on protocol due to the shortage of 5FU. In another study involving 5FU a center in **St. Louis, MO** reported a 5FU shortage that impacted one of its active colon trials. The investigator is working on adding language allowing capecitabine to be substituted for 5FU.
- Shortages of Taxol reported by a research site in **Wheeling, WV**, had led to loss of patient accrual to a cooperative group study for **patients with inoperable non-small cell lung cancer**, stage III. The site seeks to ensure that supply will be available prior to placing patients on study, and the pharmacy at the site is advising that it cannot guarantee supply.
- The same location in **Wheeling, WV** reported shortage of Taxol had led to loss of patient accrual in a cooperative group study testing a second line treatment for **patients with metastatic esophageal or GE (gastro-esophageal) junction cancer**. Adenocarcinoma of the esophagus and the gastro-esophageal junction is reportedly one of the fastest rising malignancies.
- Without Taxol, 5FU, or Leucovorin, **many patients have been unable to participate in trials** at a research site in **Columbus, OH**. Access to drug varies with hospitals in this community network, but priority in the shortage is given to the adjuvant patient population. The site is now getting Taxol in but it is not promised to study patients at this time nor can the site assure its physicians that if they start treating a patient that there will be enough of the drug for the entire treatment plan.