THE CANCER LETTER

Vol. 37 No. 38
Oct. 14, 2011

PO Box 9905 Washington DC 20016 Telephone 202-362-1809

Guideline Aftermath

Reaction to PSA Guideline Seems Muffled Compared To 2009 Mammography Guideline

By Paul Goldberg

The U.S. Preventive Services Task Force last week published a draft guideline, downgrading prostate-specific antigen-based screening from "I," insufficient evidence, to "D," a recommendation against.

Several groups that advocate screening men for prostate cancer responded by arguing that the draft recommendations of the independent board would harm men, and urged the government to err on the side of relying on the controversial test until better alternatives come along.

However, the intensity of political reaction didn't match the outcry over the 2009 USPSTF guideline that sought to relax the recommendation for annual mammography among women between the ages of 40 and 50.

Political pressure, name-calling and accusations over mammography grew so strong that two days after the recommendation was published, HHS Secretary Kathleen Sebelius distanced the Obama administration from the non-partisan group of public health experts who comprise the USPSTF.

(Continued to page 2)

The Gray Market

Hey Doc, Wanna Score Some Leucovorin? Drugs Available at 80 Times the Standard Price

By Lucas Thomas

Few people claim to understand the reasons for the long-running shortage of cancer drugs. But one thing is certain: hospitals and physician practices across America regularly receive offers for drugs in short supply

These offers are unsolicited, and usually they don't include the details—such as the price or provenance of the drugs. The markup can end up being 80 times higher than the usual contract price.

According to a recent survey by Premier Healthcare Alliance, an organization that has analyzed the "gray market" in generic drugs, the advertisements urge potential buyers to act immediately: "We only have 20 of this drug left and quantities are going fast."

A congressional committee recently launched an investigation into this generic drugs gray market and sent letters to a handful of known vendors. The topic of gray market practices was also addressed at a recent House hearing.

"Where and how gray-market vendors are getting these drugs, no one knows," said Mike Alkire, CEO of Premier, at a hearing of the Subcommittee on Health of the House Committee on Energy and Commerce on Sept. 23.

(Continued to page 4)

Guideline Downgrade May Not Change Screening Practices

(Continued from page 1)

The panel doesn't set policy, Sebelius said at the time, and policy would remain unchanged (The Cancer Letter, Nov. 20, 2009).

The reaction to the prostate cancer guideline may be relatively muffled in part because prostate cancer isn't as prominent in the U.S. popular culture as breast cancer. Blue, the color chosen by prostate groups, doesn't begin to approach the oomph of pink, the color of breast cancer.

The PSA recommendation triggered words of protest from urologists, funders of prostate cancer research, and patient groups that generally advocate screening.

At least in the immediate future, believers in screening will likely be able to just keep screening. Long-term implications are also unclear.

The PSA blood test is cheap, and is often offered at no charge by organizations that later capture revenues from the cascade of follow-up services. The only thing that may change is demand, as men at average risk of developing prostate cancer opt out of screening.

While the breast cancer recommendation left some room for interpretation, the prostate cancer recommendation is clear:

"The common perception that PSA-based early detection of prostate cancer prolongs lives is not supported by the scientific evidence. The findings of the two largest trials highlight the uncertainty that remains about the precise effect that screening may have, and demonstrate that if any benefit does exist, it is very small after 10 years.

"The European trial found a statistically insignificant 0.06 percent absolute reduction in prostate cancer deaths for men aged 50 to 74 years, while the U.S. trial found a statistically insignificant 0.03 percent absolute increase in prostate cancer deaths. A meta-analysis of all published trials found no statistically significant reduction in prostate cancer deaths.

"At the same time, over-diagnosis and over-treatment of prostatic tumors that will not progress to cause illness or death are frequent consequences of PSA-based screening. Although about 90 percent of men are currently treated for PSA-detected prostate cancer in the United States—usually with surgery or radiotherapy—the vast majority of men who are treated do not have prostate cancer death prevented or lives extended from that treatment, but are subjected to significant harms.

"The USPSTF concludes that there is moderate certainty that the harms of PSA-based screening for prostate cancer outweigh the benefits."

The full text of the guideline is posted at http://www.uspreventiveservicestaskforce.org/tfcomment.htm.

A comprehensive review of evidence is posted at http://www.annals.org/content/early/2011/10/07/0003-4819-155-11-201112060-00375.1?aimhp

Using a new bureaucratic procedure, USPSTF will take a month to review public comments on the proposal, respond to comments from the public, and issue a final screening guideline.

USPSTF Downgrade Tougher Than ACS Guideline

The proposed USPSTF guideline now contains a stronger recommendation than the guideline of the American Cancer Society.

"We are still studying their paper," said Otis Brawley, ACS chief medical and scientific officer. "We plan on issuing a comment, and we are examining our recommendation to patients."

The ACS guideline recommends against mass screening and discourages participation in screening health fairs.

The American Urological Association said the USPSTF recommendation "will ultimately do more harm than good to the many men at risk for prostate cancer both here in the United States and around the world."

"The AUA's current clinical recommendations support the use of the PSA test, and it is our feeling that, when interpreted appropriately, the PSA test provides

THE CANCER LETTER

® The Cancer Letter is a registered trademark.

Editor & Publisher: Paul Goldberg
Copy Editor: Conor Hale
Intern: Lucas Thomas

Editorial, Subscriptions and Customer Service:
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
General Information: www.cancerletter.com

Subscription $395 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

important information in the diagnosis, pre-treatment staging or risk assessment and monitoring of prostate cancer patients," AUA President Sushil Lacy said in a statement.

AUA said it is preparing a guideline on prostate cancer, and have convened a committee that would review tests and diagnostics that are scheduled to be introduced on the market.

"Until there is a better widespread test for this potentially devastating disease, the USPSTF—by disparaging the test—is doing a great disservice to the men worldwide who may benefit from the PSA test," Lacy said.

The Prostate Cancer Foundation, a group founded by the financier Michael Milken, said that it supports continuation of PSA screening of informed patients "until new American Urological Association clinical guidelines on PSA screening are issued and disseminated."

Meanwhile, reimbursement for screening should continue, the foundation said.

"The USPSTF has heightened awareness with new data of the issue of severe complications and patient suffering from the over-diagnosis and overtreatment of indolent prostate cancers. In addition to the emotional and physical suffering experienced by men and their families, a recent cost-effectiveness analysis of PSA screening estimated that the cost of diagnosis and treatment is over $5,227,306 per patient to prevent one U.S. prostate cancer death," the foundation statement continues.

"The USPSTF's position provides a teachable and actionable moment for the medical community to improve targeting of PSA screening in patients, reduce over-testing and improve processes of patient education on the risks of overtreatment from PSA screening.

"In the abstract, task force recommendations can create patient confusion and may result in unquantifiable numbers of men who will get a delayed diagnosis of a lethal and curable cancer."

Zero—The Project to End Prostate Cancer, an advocacy group that operates screening vans, posted the texts of the letters to legislators on their website.

"This is a disservice to men—particularly men who are at highest risk of dying from prostate cancer," Zero said of the recommendation. "Please send a letter to your Representative and Senators today to bring their attention to this very harmful action and ask for their support to raise awareness about the importance of early detection and education about prostate cancer."

Gingrich Turns to an Expert: Von Eschenbach

One of more puzzling statements about the guideline was made by presidential hopeful Newt Gingrich during the Republican Primary debate Oct. 11.

Asked about wasteful spending on Medicare, Gingrich said: "I am really glad you asked that, because I was just swapping e-mails today with Andy von Eschenbach, who was the head of the National Cancer Institute, the head of the Food and Drug Administration.

"But before that, he was the provost at MD Anderson, the largest cancer treatment center in the world.

"And he wrote me to point out that the most recent U.S. government intervention on whether or not to have prostate testing is basically going to kill people. So, if you ask me, do I want some Washington bureaucrat to create a class action decision which affects every American's last two years of life, not ever.

"I think it is a disaster. I think, candidly, Governor Palin got attacked unfairly for describing what would, in effect, be death panels.

"And what Von Eschenbach will tell you if you call him is, the decision to suggest that we not test men with PSA will mean that a number of people who do not have—who are susceptible to a very rapid prostate cancer will die unnecessarily.

"And there was not a single urologist, not a single specialist on the board that looked at it. So, I am opposed to class intervention for these things."

The absence of subspecialties on USPSTF is neither a mistake nor a clever political manipulation. Rather, it's part of the design of the task force. The group is an independent panel of non-federal experts in prevention and evidence-based medicine and is composed of mainly primary care providers. Its members are internists, pediatricians, family physicians, gynecologists/obstetricians, nurses, and health behavior specialists.

Specialists, who have a greater financial and academic stake in screening procedures, testify before the task force as it decides on its screening recommendations. Under new procedures, specialists and others will be allowed to comment after the draft recommendations are published by USPSTF.

After lobbying by the AUA in 2000, Medicare started to pay for screening and digital rectal examination. The Medicare Part B program pays for one PSA test a year for patients who show no signs or symptoms of prostate cancer. The policy is described at http://bit.ly/paOEeN.

Medicare's description of coverage is posted at: http://1.usa.gov/nQhDbN.

The Affordable Care Act extends full coverage for preventive services if they are recommended with a grade of A or B by USPSTF. Even before the downgrade from I to D, PSA didn't qualify for coverage. Of course the real issue is not the cost of the test—it's the cost of the follow up—and it's unclear how this will be regulated.

The issue is even more complicated because 28 states mandate insurance coverage for PSA screening. The list of states that have these laws is posted at: http://www.ncsl.org/default.aspx?tabid=13988.

Disclosure: ACS Chief Medical and Scientific Offcer Otis Brawley and The Cancer Letter Editor and Publisher Paul Goldberg are co-authors of the upcoming book How We Do Harm: A Doctor Breaks Ranks On Being Sick In America, to be published by St. Martin's Press in February 2012.

The Gray Market

Congress Probes Drug Shortage, Data Requested From Vendors

(Continued from page 1)

The gray market is legal. The vendors are licensed. However, the provenance of the drugs is untraceable. According to FDA officials, these drugs can have unlabelled ingredients, and often change hands several times before reaching a doctor and, ultimately, the patient. Imported drugs are similarly unmonitored.

In April 2011, Premier asked its members to report unauthorized offers to sell drugs affected by the shortage.

Premier gathered the following offers over two weeks:

• 1,745 offers were collected from 42 acute care hospitals,

• 636 examples with both national drug codes and prices offered,

• 310 different generic drugs that could be matched to Premier contract price,

• Offers came from 18 different gray market vendors.

All the drugs offered were back-ordered by the manufacturer or were no longer available. The average markup, compared to a typical contract price, was 650 percent.

The top ten highest markups include the following drugs:

• Labetalol—4,533 percent
• Cytarabine—3,980 percent
• Dexamethasone injection—3,857 percent
• Leucovorin—3,170 percent
• Propofol—3,161 percent
• Papavarine—2,979 percent
• Protamine—2,752 percent
• Levophed—2,642 percent
• Sodium Chloride Concentrate—2,350 percent
• Furosemide Injection—1,721 percent

"It's been disheartening to learn that the so called gray market would take advantage of such a dire situation to engage in price gouging at the expense of those desperate enough to pay," said Rep. Frank Pallone (D-N.J.) at the Energy and Commerce hearing.

The gray market stems from a shortage that has been growing in severity over the past five years, which now threatens the future of cancer clinical trials.

Even with the markup, these drugs can be cheap compared to newer-generation drugs. Yet they are still an essential element of oncology practice, and are frequently used in combination with new drugs.

"The underlying issue here is—why does this happen?" NCI Director Harold Varmus said to the National Cancer Advisory Board Sept. 13. "What is the marketplace doing?

"We are never short of Avastin, but we are short of Ara-C." (A story about the extent of the drug shortage and its history appears on p. 6).

The shortage has left some doctors and hospitals with no way to acquire generics.

As generic drugs change hands on the gray market, the level of care for patients is essentially disregarded, said federal officials. It is common for these drugs to be improperly stored or subjected to adverse temperatures. By the time the drug reaches the patient, the potency may have been compromised.

"To have this dimension complicating an already complicated situation is very disturbing," said Howard Koh, HHS assistant secretary for health, at the House hearing.

The only solution to eliminating the gray market may have to come from eliminating the conditions that have created the drug shortage in the first place. Mystery surrounding the gray market works it difficult to regulate, or even introduce practical legislation that could control untraced and even counterfeit drugs.

"There's just too much money on the table for the counterfeiters in terms of the U.S. pharmaceutical marketplace," Rep. Jim Matheson (D-Utah) said at the hearing Sept. 23.

Separately, the gray market is being investigated

by the House Committee on Oversight and Government Reform, led by ranking member Rep. Elijah Cummings (D-Md.).

On Oct. 5, Cummings sent letters to five gray market vendors, requesting documents about their products.

The letters requested "the identity of all companies and individuals from which your company purchased [respective drug], the date of each purchase, the quantity of each purchase, and the price paid for each purchase; the identity of all companies and individuals to which your company sold [respective drug], the date of each sale, the quantity of each sale, and the price paid in each sale; your company's handling, storage, and recordkeeping procedures for this drug; your company's gross revenues, net profits, and the compensation of company executives; your company's costs for labor, equipment, and other costs for handling, storage, and delivery."

Cummings said he launched the investigation after receiving a letter from Brenda Frese, the head women's basketball coach at the University of Maryland, whose son was diagnosed with leukemia and treated with cytarabine, a drug in short supply.

Letters were sent to:

• Allied Medical Supply Inc., which offers cytarabine at over $990 per vial, more than 80 times a typical contract price—about $12 per vial. According to the committee, the corporate address for this company appears to be the same as the address for Minnuto Publishing LLC, which sells the "Passive Income For Life" system, allowing users to "create a steady stream of passive income every single month for the rest of your life with no money down apartment buildings."

• Superior Medical Supply Inc., which offers paclitaxel for over $500 per vial—more than seven times the typical contract price, or approximately $65 per vial. The California attorney general filed a case alleging that the company "purchased, traded, sold or transferred dangerous drugs they knew, or reasonably should have known were misbranded," and that the company "disseminated false, misleading or deceptive statements, claims or images via the internet, to induce the rendering of professional services or furnishing of products."

• Premium Health Services Inc., for offering leucovorin for over $270 per vial— more than 50 times the typical contract price of approximately $5 per vial.

• PRN Pharmaceuticals, for offering fluorouracil at over $350 per vial, more than 23 times a typical contract price of approximately $15 per vial.

• Reliance Wholesale Inc., for offering magnesium sulfate—used to control life-threatening seizures in pregnant women and to treat magnesium deficiency in patients who receive intravenous feeding—for over $400 for 25 vials, more than 40 times the typical contract price of approximately $9 for the same amount.

The letters can be found at: http://democrats.oversight.house.gov/index.php?option=com_content&view=article&id=5445&Itemid=107

When reached by The Cancer Letter, Allied released the following statement:

"Recent media attention on prescription drug shortages highlights the vital role that Allied Medical Supply and other companies play to ensure that hospitals and patients have the medicines they need when they need them. Published surveys, highlighted in the media, grossly misrepresent Allied's business model.

"Allied Medical Supply responds to daily requests from our hospital customers for medicines they need immediately for their patients. Our company purchases treatment of life threatening conditions, are not always being provided by in a timely manner to our customers by suppliers because of a variety of network distribution issues.

"The amount of the Leukemia drug Cytarabine that we sourced and delivered to our hospital customers is less than one percent of the total need for the drug. But it is medicine that they needed immediately for their patients.

"Allied Medical Supply welcomes a review of the secondary wholesale distribution industry and will cooperate fully with the inquiry initiated by the Congressional Committee on Oversight and Government Reform."

Efforts by The Cancer Letter to reach the other four companies were unsuccessful.

So far, only Premium Health Services and PRN Pharmaceuticals have agreed to cooperate with Cummings' investigation, committee sources said.

"Price gouging for drugs that treat cancer in children is simply unconscionable," Cummings said in a statement. "We want to know where these companies are getting these drugs, and how much they are making in profits. Obtaining this information will help us develop concrete solutions."

As part of the investigation, Cummings also announced the creation of an online tipline for anyone with information about price gouging and speculation in drugs that are in critically short supply.

The tipline is available at: http://democrats.oversight.house.gov/

Six Years Into Drug Shortage, Causes Remain A Mystery

By Lucas Thomas

Since 2005, the U.S. has been experiencing an escalating shortage of generic drugs.

In 2010, 178 drugs were listed by FDA as in short supply. This is three times the number of drugs listed in 2005, when FDA first started to track the problem.

Of those drugs, 93 percent are deemed "medically necessary" by HHS.

Most of the drugs (132 of 178) in shortage are sterile injectables. The problem is not limited to any specific type of drug. The diminishing supply of cancer drugs, anesthetics, antibiotics and emergency medicine drugs shows that this issue spans the entire industry—yet FDA has little authority to take preventive action.

In most cases, the shortage of bulk ingredients is not the main cause. This affects only 10 percent of drugs, said FDA officials. No shortage of generic drugs exists outside of the country. Branded drugs, which are not affected by price controls in the U.S. market unlike generics, are in plentiful supply.

But the causes of the problem still remain unclear, and so far no one has proposed a comprehensive strategy for fixing the problem. Last month, FDA held a workshop on the shortages, and next week the agency is expected to issue a report.

Also last month, the board of the American Society of Clinical Oncology heard a proposal to fund a non-profit drug company that would market generics (The Cancer Letter, Sept. 9). Sources said the proposal has been referred to a committee.

HHS officials attribute the shortage to a synergy of problems: industry consolidation, shortage of raw materials, changes in inventory and distribution practices, quality and manufacturing problems, discontinuation of a drug for financial reasons, and unanticipated increases in demand.

Manufacturing issues and consolidation in the generic drug industry are the principal causes of the shortages, said Howard Koh, HHS assistant secretary for health, and Sandra Kweder, deputy director of the FDA Office of New Drugs.

The two officials testified before the the Subcommittee on Health of the House Committee on Energy and Commerce Sept. 23.

Kweder said that the most pressing issue "by far and away has something to do with manufacturing and product quality"—problems that stem from outdated facilities. The drugs simply do not meet industry standards, and, as a consequence, production decreases.

The typical timeframe for developing new manufacturing facilities and seeking FDA approval for a new active pharmaceutical ingredient is between two and three years.

The concern among the subcommittee members was that this timeframe stalls efforts needed to connect patients with their treatments. Kweder testified that in the event of a shortage, this process can be expedited to "a matter of months."

"These are areas where we are trying to show as much regulatory flexibility as possible to accelerate approvals when necessary," Koh said. "Whenever there is an issue related to a supplier where it requires FDA to approve a new supplier or even a new facility, we turn those around very quickly; in a matter of weeks to months, these are not business as usual where there's a long wait time," Kweder added. "We understand patients are at the end of this line."

Consolidation in the Industry

"We view industry consolidation as one of the driving root causes here," Koh said at the hearing. "As you can imagine, if your denominator of available manufacturers shrinks—and then any one of them has a manufacturing problem or delay—it really puts the onus on the others. And if the others don't happen to produce that product, and if this particular company is the sole-source producer, you have the ramifications we are seeing right now."

Koh said that in order to ensure that consolidation does not lead to further shortages, maximum communication between FDA and drug manufacturers is required, adding, "We have had excellent dialogue to date."

There are parallels to be drawn between consolidation and financial decisions to discontinue the production of a drug, FDA officials said.

Since the majority of these drugs are generic, they typically carry a small profit margin. This decreases the incentive for manufacturers to produce drugs that do not yield as much profit as name brand drugs—which is when industry consolidation usually occurs.

"There is an issue with respect to business forces here, and the profit margin is understood to be quite low for many of these individual products," Koh testified.

In most markets, the concept of supply and demand would correct this problem, allowing companies to charge more for drugs that are in short supply. However, the power of the market forces is muffled in the generics

market, Koh said.

"These agreements are made often through long-term contracts, and so this whole process involves multiple stakeholders, especially and including the pharmacy benefit managers and purchasing organizations, so it complicates this environment, and does not make relevant the standard supply and demand economic principles we see in other businesses," Koh said.

Cancer patients have been particularly harmed by this shortage, losing access to treatments—some of which are exclusive on the market. The following is a list of oncology drugs in short supply: bleomycin, busulfan, carboplatin, cisplatin, cytarabine, dacarbazine, denileukin diftitox, dexamethasone, doxorubicin, etoposide, fludarabine, 5-FU, granisetron, idarubicin, irinotecan, leucovorin, mechlorethamine, mesna, mitomycin, ondansetron, paclitaxel and vincristine.

There is no alternative to some of these drugs—such as cytarabine, which treats certain types of leukemia and lymphoma. Some of these drugs are available at high markup on the gray market—at prices upwards of 3,000 to 4,000 percent higher than the typical contract price.

Kweder and Koh pointed out examples of FDA action, such as in the case of cytarabine, where they worked with manufacturers to prevent a more significant shortages from occurring.

When the predominant manufacturer of cytarabine was experiencing production delays,

FDA contacted lower-volume manufacturers and worked with them to increase production. This action was cited as an example of the usefulness of early warning notification.

Shortages have directly impacted NCI clinical trials.

"This impact is not only immediate for the patients in our clinics today, but also affects the future care of cancer patients because the next generation of cancer therapy is driven by today's clinical trials," said Robert DiPaola, director of the Cancer Institute of New Jersey, at the Energy and Commerce hearing.

DiPaola cited clinical trials have been halted due to shortages of of paclitaxel and doxorubicin. He added that half of clinical trials conducted by members of the Coalition of Cancer Cooperative Groups require drugs in short supply.

As a result, drugs need to be substituted in order to continue the trial.

Industry insiders propose purchasing drugs abroad as an alternative to shopping in the gray market.

However this could be risky too, FDA officials warned.

Agency regulations on safety, efficacy and purity do not apply outside the U.S. "The importation process is done very carefully and selectively," Koh said.

Members of the subcommittee questioned the agency's level of confidence in foreign drugs.

Rep. Bill Cassidy (R-La.) posed the question to FDA's Kweder: "Is there a worldwide supply of drugs that are currently in shortage here—it's just that we are not trusting the manufacturing process by which they are produced, and therefore are not allowing their importation?"

Kweder said it's not an issue if it is necessary to import the drug in question.

"If there is a foreign source, we are usually able to work through and get it approved," Kweder said. "There have certainly been circumstances where there have been important problems that would prevent that, but in most cases if going to a foreign source is necessary, we are able to work through that."

FDA Actions

FDA officials say that there is no policy in place that requires manufacturers to notify the agency of an impending shortage, unless the company is the sole provider of a certain drug.

Also, FDA can't require a company to increase production during a shortage, and it can't impose an allocation plan.

To combat these limitations, Reps. Diana DeGette (D-Colo.) and Tom Rooney (R-Fla.) introduced the Preserving Access to Life Saving Medication Act (H.R. 2245 and S.296). This bill would give FDA authority to make changes to the current system, by requiring drug companies to issue notifications of anticipated shortages.

But even early notification can have a downside. While early notification can spur a proactive approach to drug shortages, the emergence of the gray market during this crisis has bred a cynical outlook. There is concern among sponsors of the bill that early warning could lead to hoarding of a particular drug.

"We take that potential for making things worse very, very, seriously," Kweder said. Therefore, FDA is cautious as to when they should make that information public on websites and other outlets. "Early notification to FDA is a very useful tool, we see that as different than early publication," Kweder said.

Kevin Coglan, corporate director of pharmacy at Rush University Medical Center, agreed with Kweder while testifying in front of the congressional commitee of behalf of the American Society of Health. "Public

benefit of an early warning system far outweighs the risk of hoarding," he said.

The Sept. 23 congressional hearing is archived at: http://energycommerce.house.gov/hearings/hearingdetail.aspx?NewsID=8926.

What Can Practitioners Do

Recently, the Journal of the National Comprehensive Cancer Network published a step-by-step guide to handling the shortage.

The approach, by Philip Johnson, a pharmacist, appeared in the August issue of the journal. Johnson's recommendations appear below:

• Stay informed by monitoring the FDA website (www.fda.gov/Drugs/DrugSafety/DrugShortages) and other professional sites such as the American Society of Health System Pharmacists (www.ashp.org/DrugShortages/Current/) to determine the drugs that will affect your practice. The FDA has an e-mail alert service that is recommended.

• When an actual or projected drug shortage becomes known, initiate your strategy. This can include proactive purchasing (no hoarding please), changing the order point and order quantity, sharing inventory between affiliates, developing and approving substitution policies, and implementing well-reasoned rationing policies that include patient and payor education.

• Establish who in your organization is accountable for managing the shortage and providing updates to all stakeholders through regular meetings, an intranet site, memos, or other communications systems. Some institutions maintain a virtual status board listing the drug, inventory available, number of potential patient treatments available, and current number of patients under treatment. Your GPO can help forecast future product availability.

• Work with your GPO and wholesale distributor to secure (as best you can) adequate supply. Establish as many supply options as possible, even if they are non-traditional sources. If you purchase through a distributor that you are not familiar with, take measures to ensure the integrity of their product and their business ethics, by checking their business history through your GPO or state Attorneys General.

Ask the distributor to provide evidence of a drug pedigree that certifies every step and possession of the drug from the manufacturer to final provider. Report unusual circumstances or unfair business practices to the Federal Trade Commission (www.ftc.gov/ftc/contact.shtm) and your state Attorneys General, or the National Association of Attorneys General (www.naag.org/).

Finally, for product integrity issues, contact the FDA Office of Criminal Investigations (www.fda.gov/ICECI/CriminalInvestigations/default.htm) and the National Association of Boards of Pharmacy (www.nabp.net/).

• Call the manufacturer to determine if an emergency supply is available for critical patients and the criteria required for release.

• Check on the supply of drugs likely to be substituted for the unavailable drug, because that may also soon be in short supply.

• Establish drug substitution rules and rationing criteria for your institution or practice through authorized bodies such as the Pharmacy and Therapeutics Committee. Build these rules into your drug formularies, ordering pathways, and protocols.

• Provide clinical needs and impact assessment information to the FDA to help them determine the seriousness of the shortage and if they can facilitate expedited review of a new product or manufacturing process that will offset the shortage, or approve the importation of the drug.

• Document the cost of each drug shortage—both the variance in cost among drug products and the professional time and patient impact—and include this in your institution's budget analysis. This cost should also be considered in the operational or facility costs reported by your facility for CMS payments. Note that sometimes the manufacturer will negotiate "consideration to offset additional costs" for a product they could not provide.

• Collaborate with your information technology (IT) department to ensure they understand the importance and urgency of IT system changes that are required. Create a list of all IT systems that manage medication information, including the contact person and data fields that must be changed. The list should include systems related to 1) computerized prescriber order entry; 2) care sets and protocols; 3) pharmacy, nursing, surgery, radiology, and investigational drug systems; 4) formularies or catalogs associated with smart technology devices used for inventory, production, dispensing, or drug administration; and 5) patient billing.

• Document the impact of the drug shortage on patient care outcomes, addressing all relevant issues objectively and with solid evidence. Growing public and legislative concern must be addressed through education and accurate information as we seek to enlist understanding and support.

• When the situation is resolved, clearly

communicate the impact and what the "new normal" is. Will drug usage patterns change back? Will IT technology be "re-set"? Will inventory be changed? What was the budget impact? Documenting the cost of returning to normal is also important, so sufficient resources can be planned for future occurrences.

In Brief

Ralph Steinman Wins Nobel Prize Three Days After His Death

RALPH STEINMAN was named one of three recipients of the **Nobel Prize in Medicine**, three days after he died of pancreatic cancer. He was 68.

Steinman, director of the Laboratory of Cellular Physiology and Immunology at Rockefeller University and senior physician at the university hospital, was recognized for his research into dendritic cells, and their use in the immune system, a class of cells that he and biologist Zanvil Cohn discovered in 1973.

He shares the Nobel prize with **Bruce Beutler**, of UT Southwestern Medical Center and Scripps Research Center in San Diego, and **Jules Hoffman**, former research director of the National Center for Scientific Research in Strasbourg, France and was president of the French National Academy of Sciences. Beutler and Hoffman, sharing the other half of the prize, worked on the biological sensors of innate immunity.

The Nobel committee has rules against awarding the prize posthumously, but recognized this as an exception. The committee was unaware of Steinman's passing three days before the announcement of the 2011 prize winners. They decided that Steinman should still be recognized, as the committee's decision was made "in good faith."

Steinman was diagnosed with pancreatic cancer four years ago. Part of his immunotherapy treatment utilized his own research into dendritic cells.

As quoted in The New York Times, his daughter, Leslie, said: "He was very enthusiastic about the possiblities of immunotherapy. As soon as he was diagnosed, he said, 'I'm going to get right on this with some things I've been working on.'"

MARGARET FOTI will receive the **Research!America** Raymond and Beverly Sackler Award for Sustained National Leadership.

Foti, CEO of the American Association for Cancer Resarch, will be recognized for her leadership in AACR's role in science and public policy.

Research!America will also present its Advocacy Awards for advancing research. The honorees are: Scott Johnson, president and founder of the Myelin Repair Foundation; Donald Lindberg, director of the National Library of Medicine; CNN's chief medical correspondent Sanjay Gupta; and the Food Allergy Initiative.

Foti was recognized for her work in the production of AACR's Cancer Progress Report 2011, which highlighted the progress made in cancer research over the past 40 years.

The awards event will take place March 14, 2012, at the Andrew W. Mellon Auditorium in Washington, D.C.

FRED HUTCHINSON Cancer Research Center and the **Uganda Cancer Institute** have broken ground for the construction of the first collaborative, comprehensive cancer center in sub-Saharan Africa.

Ugandan Vice President **Edward Ssekandi** was joined at the groundbreaking ceremony by NCI Director Harold Varmus, Ugandan Minister of Health Christine Ondoa and other government officials and health experts.

The new clinic and training institute will host studies on the links between infectious diseases, such as HIV and Epstein-Barr virus, and cancers such as Kaposi sarcoma and Burkitt lymphoma, the most common life-threatening cancer among Ugandan children.

Nearly 25 percent of cancers cases worldwide are infection related, and 50 percent of these cancer deaths occur in sub-Saharan Africa, said **Corey Casper**, an associate member of the Hutchinson Center's Vaccine and Infectious Disease Division and co-scientific director of the collaboration between the Hutchinson Center and the Uganda Cancer Institute.

The facility is funded in part by two grants totaling $1.4 million from the United States Agency for International Development and a $900,000 investment from the Hutchinson Center.

Follow The Cancer Letter on Twitter:
@TheCancerLetter