

DRUG SHORTAGE CRISIS: LIVES ARE IN THE BALANCE

HEARING

BEFORE THE

SUBCOMMITTEE ON HEALTH CARE, DISTRICT OF
COLUMBIA, CENSUS AND THE NATIONAL ARCHIVES

OF THE

COMMITTEE ON OVERSIGHT
AND GOVERNMENT REFORM

HOUSE OF REPRESENTATIVES

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DRUG SHORTAGE CRISIS: LIVES ARE IN THE BALANCE

WEDNESDAY, NOVEMBER 30, 2011

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH CARE, DISTRICT OF
COLUMBIA, CENSUS AND THE NATIONAL ARCHIVES,
COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:01 a.m., in room 2247, Rayburn House Office Building, Hon. Trey Gowdy (chairman of the subcommittee) presiding.

Present: Representatives Gowdy, Gosar, McHenry, Davis, Murphy, and Cummings.

Staff present: Brian Blase, professional staff member; Will L. Boyington and Noelle Turbitt, staff assistants; Molly Boyd, parliamentarian; Christopher Hixon, deputy chief counsel; Christine Martin, counsel; Jaron Bourke, minority director of administration; Yvette Cravins, minority counsel; Devon Hill, minority staff assistant; Jennifer Hoffman, minority press secretary; Chris Knauer, minority senior investigator; Leah Perry, minority chief oversight counsel; and Pam Dooley, minority GAO detailee.

Mr. GOWDY. I want to welcome everyone to our hearing, Drug Shortage Crisis: Lives Are In the Balance.

Mr. Davis will be with us shortly and I will recognize him for his opening statement at that time. I will now recognize myself for an opening statement and then the ranking member of the full committee, the gentleman from Maryland, Mr. Cummings.

The drug shortage crisis in America has all the makings of a national crisis. Doctors are frustrated; patients and loved ones are worried. Lives are truly in the balance. Drugs are being rationed. Doctors are forced to sometimes look for less efficacious drugs. Clinical trials are being disrupted and, perhaps unbelievably, doctors are sometimes asked to pick between patients as to who will receive a drug.

For all those reasons and more, it is vital Congress conduct oversight of the drug shortage to understand why the problem exists and what can be done to remedy it. In order to find solutions, we must have a clear understanding as to why the drug shortages exist in the first instance.

Over the last decade, there were around 70 new drug shortages identified each year between 2003 and 2006. And then the number of drugs in shortage began to dramatically increase. In both 2010 and 2011, there have been over 200 new drug shortages identified. Typically, these drugs are used to treat cancer, heart disease, and

complicated infections. Dr. Michelle Hudspeth, testifying before us today, will discuss how these shortages affect the care plan she establishes for pediatric patients.

The shortage shortages will also affect clinical trials and whether or not the trials will actually go forward with participating patients. If there is a drug shortage that prevents participation, there will still be a cost associated with the trial. Considering the importance of drug trials for research, this is another reason identifying the cause or causes of the drug shortages is so very vital. If the money has been approved for trials, it is important to ensure the needed drugs are available.

Let me say nearly at the outset if there is anything for which there is no shortage of in this town, it is politics, and I suppose every issue can theoretically be turned into a political football if the notion strikes. One reason I enjoy this committee and the Members on it is that we are, from time to time, able to set aside politics and look for the root causes of an issue and have a good faith conversation about the remedy. And when it comes to sick patients, when it comes to children, and when it comes to research for the diseases that are or will impact very nearly every family here, my hope is that politics will go away, and we can earnestly and honestly identify the issues and suggest the remedies.

Several explanations for this crisis have been offered, but a recent report issued by the Department of Health and Human Services highlights pricing problems that limit the supply of these drugs. Part of this problem could be changes made to the Medicare Modernization Act in 2007 regarding the reimbursement of injectable drugs. One of the provisions of this law sought to increase price transparency and reduce the profit that providers make from delivering intravenous drugs in their offices.

In *The New York Times* recently, Dr. Ezekiel Emanuel, Oncologist and Professor of Health Policy at the University of Pennsylvania, discussed the issue thusly: "In the first two or three years after a cancer drug goes generic, its price can drop by as much as 90 percent as manufacturers compete for market share. But if a shortage develops, the drug's price should be able to increase again to attract more manufacturers. Because the 2003 act effectively limits drug price increases, it prevents this from happening. The low profit margins mean that manufacturers face a hard choice: lose money producing a life-saving drug or switch limited production capacity to a more lucrative drug."

Another potential cause of the increasing number of shortages could be the expansion of the 340(b) program. The 340(b) rebate program is a pricing program that requires drug companies to provide rebates to hospitals and clinics serving indigent communities. Although the 340(b) program is essential for providers of indigent care, the 340(b) program could be affecting the ability of manufacturers and suppliers to provide required drugs because the rebates may reduce the price of drugs to well below the cost it takes to manufacture them.

There have been proposals which would require drug manufacturers to alert the FDA of manufacturing problems or the discontinuation of a drug. Although this has superficial appeal, perhaps, simply knowing that a shortage is coming does little to cor-

rect the situation. Merely having more time to worry about whether the drug your doctor wants to prescribe for you may or may not be available provides little comfort. Thus, it is important to dig deeper into the actual causes of these shortages. Again, quoting Dr. Emanuel, “The FDA isn’t able to force manufacturers to produce a drug. And learning about impending shortages, with little authority to alleviate them is of limited benefit. Indeed, early warning could exacerbate the problem. The moment oncologists or cancer centers hear there is going to be a shortage of a critical drug, their response could well be to start hoarding.”

In talking with folks like Dr. Hudspeth, and let me say at the outset she is from South Carolina, but I do not represent the district where she lives or works. Two of my colleagues, Tim Scott and Jim Clyburn, have been very active in the Medical University at South Carolina and have done many wonderful things there, but I had the privilege of visiting the Medical University recently and I was struck by the passion with which Dr. Hudspeth laid out for me this crisis.

So I want to make sure that we have a full understanding of what the challenges are and that we can equip ourselves with the tools so perhaps we can do as the Good Book teaches and take care of the sick, the poor, and the children. I am concerned to hear that drug shortage is affecting the care and ultimately the health of patients, especially pediatric cancer patients.

If there is anything that can get the attention of every member of this committee, it is to hear stories of children with medical needs, and I have heard colleagues on both sides of this committee speak with great eloquence and passion about issues involving children and their health. So I look forward to having a clear understanding of the issues surrounding the drug shortages and what we can do to remedy it.

With that I would recognize the gentleman from Illinois, the ranking member of the subcommittee, Mr. Davis.

[The prepared statement of Hon. Trey Gowdy follows:]

Mr. Gowdy's opening statement

The drug shortage has become a national crisis. Patients are scared. Doctors are frustrated. Lives are in the balance. Many drugs are being rationed, and clinical trials are being disrupted. Congress must exercise its oversight role to understand how this occurs, why there seems to be increasing frequency, and what the solutions are.

At the beginning of the last decade, the number of new drug shortages identified each year was declining. There were approximately 70 new drug shortages identified each year between 2003 and 2006. But then the number of drugs in shortage began to dramatically increase. In both 2010 and 2011, there have been over 200 new drug shortages identified.

Based on data collected, there are similarities among the drugs in shortage. Approximately 80 percent of the drugs in shortage are injectable medications. The majority of the drugs in shortage are generics and many have come off patent in the past few years. Most significantly many of these identified drugs are used to treat cancer, heart disease, and complicated infections.

Several explanations for this crisis have been offered, but a recent report issued by the Department of Health and Human Services highlights pricing problems that limit the supply of these drugs. Part of this problem could be changes made by the Medicare Modernization Act in 2007 regarding the reimbursement of injectable drugs. One of the provisions of this law sought to increase price transparency and reduce the profit that providers made from delivering intravenous drugs in their offices.

In the *New York Times*, Dr. Ezekial Emanuel, oncologist, former Obama White House advisor, and professor of health policy at the University of Pennsylvania, discussed the unintended consequence of the MMA. Quote: "In the first two or three years after a cancer drug goes generic, its price can drop by as much as 90 percent as manufacturers compete for market share. But if a shortage develops, the drug's price should be able to increase again to attract more manufacturers. Because the 2003 act effectively limits drug price increases, it prevents this from happening. The low profit margins mean that manufacturers face a hard choice: lose money producing a lifesaving drug or switch limited production capacity to a more lucrative drug." Unquote.

Another potential cause of the increasing number of shortages could be the expansion of the 340B program in the President's health care law. The 340B rebate program is a pricing program that requires drug companies to provide rebates to hospitals and clinics serving indigent communities. Although the 340B program is an essential tool for providers of indigent care, the 340B program could be affecting the ability of manufacturers and suppliers to provide required

drugs, because these rebates may reduce the price of the drugs to well below the cost it takes to manufacture the drugs.

Last month, President Obama issued an executive order requesting drug manufacturers alert the FDA of manufacturing problems or the discontinuation of a drug. Although this may be worthwhile on the surface, if the root of the drug shortage problem is a pricing problem, this executive order may actually make the situation worse. According to Dr. Emanuel, quote, “[T]he F.D.A. isn’t able to force manufacturers to produce a drug, and learning about impending shortages with little authority to alleviate them is of limited benefit. Indeed, early warning could exacerbate the problem: the moment oncologists or cancer centers hear there is going to be a shortage of a critical drug, their response could well be to start hoarding.” Unquote.

In talking with folks like Dr. Hudspeth from South Carolina, I am concerned to hear that this drug shortage is affecting the care and ultimately the health of patients. It is hard for me to hear stories of children with cancer not receiving the best possible care plan because of uncertainty surrounding the availability of the best drugs to treat their cancers. The more we understand the causes of the drug shortages, the better equipped we will be to find a solution.

I look forward to hearing the from the witnesses who bring a wide range of experience and expertise and perspective to this issue.

Mr. DAVIS. Thank you very much, Chairman Gowdy, for holding this hearing. I want to thank all of the witnesses who have come to share with us.

The drug shortage is a major concern to me, as it should be to all who serve in this body. I happen to represent a congressional district that has 21 hospitals, 4 large medical center complexes, a number of research institutes, and we are building a brand new Children's Hospital now. So there is nothing more important to us than the provision and delivery of health care.

Our constituents, mothers, fathers, and children, depend on these drugs to survive and flourish daily. This body has successfully increased access to health care for millions. It would be a cruel irony for Members to now sit on our hands as lifesaving drugs are becoming unavailable. We must take the necessary steps and exhaust all available avenues to alleviate these shortages. This hearing is a good initial first step.

It is important to hear from physicians about the barriers they face in providing care and treatment. These doctors can certainly testify and illustrate the impact drug shortages are having on their patients. Their stories and, in particular, the work-arounds in providing alternative medicines when shortages occur illustrate not only the difficulty this problem poses to patients, but also the cost involved to our health care industry. Their stories are similar to those that have been expressed by a host of health care providers interviewed in the course of a lengthy investigation Mr. Cummings launched into the issue of drug shortages and the impact they are having, and illuminating those who seek to profit from these shortages. Our ranking member had the foresight to open that investigation several months ago.

Given our expertise, Mr. Chairman, I hope that this hearing and subsequent ones are an opportunity for us to work together to solve this problem, and I believe that we can. As I prepared for the hearing today, I must say that I was disappointed and puzzled by the absence of the Food and Drug Administration. They are a critical piece of the puzzle. Their knowledge and insight would have been invaluable today. Further, if we truly seeking to delve into this issue, we must have all the relevant players at the table. The drug manufacturers, the distributors, and health care economists should all be here before us under oath.

Mr. Chairman, again, I thank you for this hearing, but this is a very complicated and complex issue and requires a broader panel of witnesses than what we have here today. Therefore, I am requesting that a followup hearing with the manufacturers of these drugs, and I think we should strike while the iron is hot, and I hope that we could schedule that hearing for maybe 2 weeks from now. I have a list of several drug manufactures that should be requested to testify about the drug shortages and, with your indulgence, I would like to share this list with you and your staff. And I would say let's get these manufacturers here so we can understand the nature of this problem and move toward solutions to it, and I hope that you could accommodate this request. And I would like to give you this list of manufacturers and ask that we seriously look at asking them to come before us.

So with that, Mr. Chairman, and I will say who they are. They are Bedford Laboratories, APP Pharmaceuticals, Hospira, Teva Pharmaceuticals, Sandoz, the Generic Pharmaceuticals Division of Novartis, Abbot, Takeda, Baxter Oncology, and Johnson & Johnson. And with that, Mr. Chairman, I thank you and yield back the balance of my time.

Mr. GOWDY. I thank the gentleman from Illinois and would let the gentleman from Illinois know what he may already know. If he doesn't, the Energy and Commerce Committee had a hearing in September on drug shortages with the FDA and drug manufacturers present. And the gentleman from Illinois' point is well taken with respect to single committee hearings and then letting issues drop, and I will commit to him that that will not be the case with this.

I would recognize the distinguished gentleman from Maryland, the ranking member of the full committee, Mr. Cummings.

Mr. CUMMINGS. Thank you very much, Chairman Gowdy and Ranking Member Davis. I want to thank you for holding today's hearing. Given the impact that the ongoing drug shortage is having on patients and health care providers, this is exactly the type of issue this committee should be examining.

In 2010, the FDA reported 178 drug shortages, and that number has increased in 2011. In October, President Obama issued an Executive order urging manufacturers to notify FDA of potential drug shortages so they could work with health care providers and patients to prevent or mitigate shortages before they become a crisis.

It is unclear exactly what is causing the drug shortages. Experts believe there may be a number of causes, ranging from inadequate financial incentives for manufacturers, problems with production lines, and challenges in obtaining needed supplies. I look forward to hearing the perspective of today's witnesses on these very significant issues.

Although today's hearing is a step in the right direction, unfortunately, we do not have the benefit of hearing testimony from any of the drug manufacturers, and I echo what Mr. Davis said: these folks are the ones that produce these critical drugs that are now in short supply. If we had them here, we could have asked what they believe are the causes of the crisis and we could have asked their opinion about specific factors that contribute to the insufficient supply of these drugs.

Mr. Chairman, I was very pleased to hear what you just said with regard to looking forward to future hearings where perhaps we could call some of those folks so we might do what you said even earlier, and that was that we would lay our political hats down at the door and attack this crisis with everything that we have, and on a bipartisan basis.

Finally, let me note that I began my own investigation this summer into a related issue, which is the sale of gray market drugs. When hospitals and other providers cannot obtain drugs on the shortage list from their authorized distributors, they sometimes turn to so-called gray market distributors. These companies mysteriously always seem to have the product available, but at wildly exorbitant prices. We are still in the initial stages of this investigation, so I will withhold comment for now, but I think we can all

agree that nobody should be allowed to profiteer at the expense of cancer victims or other patients who are in dire need of these life-saving medications.

So, Mr. Chairman, I hope that we will be able to address some of these issues at a later hearing as well. With that, I thank you for your indulgence and I yield back.

[The prepared statement of Hon. Elijah E. Cummings follows:]

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Opening Statement

Rep. Elijah E. Cummings, Ranking Member

Subcommittee on Health Care, District of Columbia, Census and the National Archives
Hearing on “Drug Shortage Crisis: Lives Are in the Balance”

November 30, 2011

Chairman Gowdy and Ranking Member Davis, thank you for holding today’s hearing. Given the impact that the ongoing drug shortage is having on patients and health care providers, this is exactly the type of issue this Committee should be examining.

In 2010, FDA reported 178 drug shortages, and that number has increased in 2011. In October, President Obama issued an Executive Order urging manufacturers to notify FDA of potential drug shortages so they could work with health care providers and patients to prevent or mitigate shortages before they become a crisis.

It is unclear exactly what is causing these drug shortages. Experts believe there may be a number of causes, ranging from inadequate financial incentives for manufacturers, problems with production lines, and challenges in obtaining needed supplies. I look forward to hearing the perspective of today’s witnesses on these issues.

Although today’s hearing is a step in the direction, unfortunately we do not have the benefit of hearing testimony from any of the drug manufacturers that produce these critical drugs that are now in short supply. If we had them here, we could have asked what they believe are the causes of this crisis, and we could have asked their opinion about the specific factors that contribute to the insufficient supply of these drugs.

Mr. Chairman, I certainly hope you will schedule another hearing in short order with the makers of some of these drugs. Our work will not be complete until we do.

Finally, let me note that I began my own investigation this summer into a related issue, which is the sale of “gray market” drugs. When hospitals and other providers cannot obtain drugs on the shortage list from their authorized distributors, they sometimes turn to so-called “gray market” distributors. These companies mysteriously always seem to have the product available, but at wildly exorbitant prices.

We are still in the initial stages of this investigation, so I will withhold comment, but I think we can all agree that nobody should be allowed to profiteer at the expense of cancer victims and other patients who are in dire need of these life-saving medications.

Mr. Chairman, I hope we will be able to address some of these issues at a later hearing as well. Thank you again.

Contact: Ashley Etienne, Communications Director, (202) 226-5181.

Mr. GOWDY. I thank the gentleman from Maryland.

We are pleased and delighted to have such a wonderful panel of experts.

There are other Members who may wish to submit their opening statements or other extraneous material for the record.

It is my pleasure now to introduce our panel. I will introduce you from my left to right. I will introduce you en banc and then you will individually give your opening statements. The lights in front of you, I hope they are visible, mean what they traditionally mean in society: green is go; yellow means speed up, try to get under the light as quick as you can; and red mean start putting on the brakes.

Dr. Michelle Hudspeth is the division director of pediatric hematology/oncology at the Medical University of South Carolina. And, as a point of personal privilege, the first person to bring the issue to my attention on a recent tour of MUSC. Dr. Walter Kalmans is vice president of New Ventures at White Glove Health; Mr. Ted Okon is executive director of the Community Oncology Alliance; Dr. Scott Gottlieb is resident fellow at American Enterprise Institute; Dr. Kasey Thompson is vice president of policy, planning and communications for the American Society of Health System Pharmacists.

Pursuant to committee rules, all witnesses will be sworn in before they testify, so I would respectfully ask you to stand and raise your right hands.

[Witnesses sworn.]

Mr. GOWDY. May the record reflect all witnesses answered in the affirmative.

You may be seated.

With that, I would recognize Dr. Hudspeth.

STATEMENTS OF MICHELLE HUDSPETH, M.D., DIVISION DIRECTOR OF PEDIATRIC HEMATOLOGY/ONCOLOGY, MEDICAL UNIVERSITY OF SOUTH CAROLINA; WALTER KALMANS, VICE PRESIDENT OF NEW VENTURES, WHITEGLOVE HEALTH; TED OKON, EXECUTIVE DIRECTOR, COMMUNITY ONCOLOGY ALLIANCE; SCOTT GOTTLIEB, M.D., RESIDENT FELLOW, AMERICAN ENTERPRISE INSTITUTE; AND KASEY K. THOMPSON, PHARM.D., VICE PRESIDENT, OFFICE OF POLICY, PLANNING AND COMMUNICATIONS, AMERICAN SOCIETY OF HEALTH-SYSTEM PHARMACISTS

STATEMENT OF MICHELLE HUDSPETH, M.D.

Dr. HUDSPETH. Chairman and members of the subcommittee, thank you for inviting me to testify today. I am the Chief of the division of pediatric hematology/oncology and the director of pediatric blood and marrow transplantation at the Medical University of South Carolina in Charleston, South Carolina. I care for close to 75 newly diagnosed cancer patients each year who are children, as well as 30 patients who undergo bone marrow transplant for the best chance of survival from childhood cancer.

The National Cancer Act in 1971 officially declared the war on cancer. Since that time, the overall survival rate of childhood cancer has dramatically improved from 10 percent to almost 80 per-

cent. However, the incidence of childhood cancer has continued to increase over the past 20 years, and cancer remains the leading cause of death from disease in children. In 23 days, we will mark the 40th anniversary of the National Cancer Act being signed into law. Today, unfortunately, we mark the largest number of chemotherapy drugs ever in shortage. The war on cancer has been reduced to a mere skirmish with no weapons and no clear battle plan.

Just a few days ago, I was with a family in crisis in our pediatric emergency room. I had to tell the parents of a 2-year-old little boy that he has high risk acute lymphoblastic leukemia. This type of leukemia is the most common childhood cancer. For his first month of treatment, he needs four drugs plus another two chemotherapy drugs injected into his spinal fluid. Five of these six drugs are in shortage. Each of these drugs in shortage is a generic drug. Mercifully, we have the drugs right now. I held his mother's hand and told her that we will do everything humanly possible to cure her son. He needs 3½ years of chemotherapy treatments. Will I be able to tell her the same thing next month, in 6 months, or even in a year?

The scope of the problem continues to intensify. Between 2005 and 2010, the number of prescription drug shortages nearly tripled in the United States. Currently, 21 chemotherapy drugs are in shortage, as well as 2 essential chemoprotectant drugs. The vast majority of drugs in shortage are generic and are used to treat curable childhood cancers. Clearly, the most critical problem is a child being denied curative cancer treatment because of a drug shortage.

Furthermore, the additional downstream effects of chemotherapy shortages have significant ramifications as well. Research cures cancer. The major advancements in pediatric cancer have occurred through the Clinical Trials Cooperative Group funded by the NCI. The majority of clinical trials incorporate elements of standard treatments into one or more treatment groups in the trial. Clinical trial enrollment is not currently allowed if you do not have access to the standard treatment.

As a result, clinical trial enrollment is declining. Not only does this undermine the advancement of cancer treatment, but it comes with a significant financial cost as well. Cooperative group clinical trials have regulatory costs that add up. Consequently, up to \$1.2 million could be spent in 1 year alone for pediatric cancer clinical trials that are not able to enroll a single patient.

A recent study published in the American Journal of Health-System Pharmacy reported the overall personnel costs associated with managing these drug shortages costs an estimate of \$216 million each year. Regrettably, most institutions have had to institute a review board, often with an ethics committee, to develop harrowing plans of how to ration chemotherapy drugs, most of which are generic drugs that have been available for 30 years or more. How do you decide who should be given a chance to live?

In an effort to maintain some semblance of adequate chemotherapy treatment, drug substitutions are being made with less familiar products. Additionally, pharmacies are stocking multiple concentrations of the same drug. This can easily lead to dosing errors, either underdosing or overdosing, when one concentration of

the drug is mixed as if it is the other concentration. Chemotherapy agents are high-alert drugs. They have a very narrow therapeutic index, meaning there is a very small difference in the amount that gives benefit and the amount that causes death. Over a year ago, a national survey by the Institute for Safe Medication Practices noted that 35 percent of respondents reported a near miss error due to drug shortages. Twenty-five percent reported actual errors that reached the patient. One-third of physicians reported an adverse patient outcome due to drug shortages.

As with any issue, there are multiple reasons for the current drug shortage. However, the timing is notable. In 2003, the Medicare Modernization Act was put into place. In 2004, the FDA reported 58 drug shortages; in 2011, the number skyrocketed to over 200. The intent of the MMA was to create more transparency in pricing. However, generic prices are driven down by market competition and the current model under the MMA makes it difficult for companies to raise prices more than 6 percent per year. Product margins have fallen significantly for many generic drugs, leaving companies with no incentive to continue manufacturing the drug or to increase production.

The current situation is nothing short of a massive national emergency. The burden is on us to resolve the crisis to protect our children. None of my patients' families ever thought they would be faced with a diagnosis of childhood cancer. Today alone, in the United States, the parents of 36 children will be told your child has cancer. Let's act to ensure these parents can also be told we have drugs available to cure your child.

Thank you.

[The prepared statement of Dr. Hudspeth follows:]

Testimony of Michelle Hudspeth, M.D.
Chief, Division of Pediatric Hematology/Oncology
Director, Pediatric Blood and Marrow Transplantation at the Medical University of South Carolina
House of Representatives Subcommittee on Health Care, District of Columbia, Census, and National Archives

Chairman and members of the Subcommittee:

Thank you for inviting me to testify today. I am the Chief of the division of pediatric hematology/oncology and the Director of pediatric blood and marrow transplantation for the Medical University of South Carolina in Charleston, SC. I care for close to 75 newly diagnosed children with cancer each year as well as almost 30 children each year from throughout the Southeast who require a bone marrow transplant for their best chance of survival from cancer.

The National Cancer Act (P.L.92-218) in 1971 officially declared the war on cancer. Since that time, the overall survival rate of childhood cancer has dramatically improved from 10% to almost 80%. However, the incidence of childhood cancer has continued to increase over the past 20 years, and cancer remains the leading cause of death by disease in children. In 23 days, we will mark the 40th anniversary of the National Cancer Act being signed into law. Today, unfortunately, we mark the largest number of chemotherapy drugs ever in shortage. The war on cancer has been reduced to a mere skirmish with no weapons and no clear battle plan.

Just a few days ago, I was with a family in crisis in our pediatric emergency room. I had to tell the parents of a 2 year old boy that their son has high risk acute lymphoblastic leukemia. This type of leukemia, known as ALL, is the most common childhood cancer. For his first month of treatment, he needs four chemotherapy drugs plus another two chemotherapy drugs to be injected into his spinal fluid. Five of these six drugs are in shortage. Each of these drugs in shortage is a generic drug. Mercifully, we have the drugs available right now. I held his mother's hand and told her that we will do everything humanly possible to cure her son. He needs three and a half years of chemotherapy treatments- will I be able to tell her the same thing a month from now? 6 months from now? In a year?

The scope of the problem continues to intensify. Between 2005 and 2010, the number of prescription drug shortages nearly tripled in the United States. Currently, 21 chemotherapy drugs are in shortage as well as 2 essential chemoprotectant drugs. The vast majority of drugs in shortage are generic drugs and are used to treat curable childhood cancers. Drugs such as cytarabine, which is essential to cure acute myelogenous leukemia (AML), have absolutely no substitution available. Clearly, the most critical problem is a child being denied curative chemotherapy treatment due to the drug shortages.

Furthermore, the additional downstream effects of chemotherapy shortages have significant ramifications as well. Research cures cancer. The major advancements in pediatric cancer, as well as adult cancer, have occurred through the Clinical Trials Cooperative Group program of the National Cancer Institute. The majority of clinical trials incorporate

elements of standard treatments into one or more treatment groups in the trial. Clinical trial enrollment is currently not allowed unless there is clear access to the chemotherapy drugs included in the trial. As a result, clinical trial enrollment is declining. Not only does this undermine the advancement of cancer treatment, but it comes with a significant financial cost to the taxpayer as well. Cooperative group clinical trials are estimated to have \$5-6,000 of regulatory costs per institution that are incurred even if a patient never enrolls on the clinical trial. For instance, the Children's Oncology Group (the Clinical Trial Cooperative Group for pediatric cancer) has 210 member institutions and roughly 100 active clinical trials each year. Consequently, up to 1.2 million dollars could be wasted each year alone for pediatric cancer clinical trials that are never able to enroll any patients due to chemotherapy drug shortages.

A recent study published in the *American Journal of Health-System Pharmacy* reported that the overall personnel costs associated with managing drug shortages costs health systems an estimate of \$216 million each year. The increased burden affects pharmacists, pharmacy technicians, physicians, nurses, and information technology personnel. Additional time and effort is spent educating staff about shortages and potential drug substitutions when they exist. Regrettably, most institutions have had to institute a review board, often with involvement of their institutional ethics committee, to develop harrowing plans of how to ration chemotherapy drugs- most of which are generic drugs that have been around for 30 years or more. How do you decide who should be given the chance to live?

In an effort to maintain some semblance of adequate chemotherapy treatment, drug substitutions are being made with less familiar products. Additionally, pharmacies are stocking multiple concentrations of the same drug. A cardinal rule of drug safety is to stock one concentration of any particular drug so that all staff is readily familiar with the preparation. Now, the focus is simply on having drug available and pharmacies have multiple concentrations of the same drug. This can rapidly lead to dosing errors- either underdosing or overdosing- when one concentration of the drug is mixed for the patient as if it is the other concentration of the drug. Chemotherapy agents are high-alert drugs. They have a narrow therapeutic index, meaning there is a small difference in the amount that causes the therapeutic benefit and the amount that causes death. Over a year ago, a national survey by the Institute for Safe Medication Practices noted that 35% of respondents had experienced a "near miss" error due to drug shortages and that 25% reported actual errors that reached the patient. One-third of physician responders reported an adverse patient outcome due to drug shortages.

As with any critical issue, there are multiple reasons for current drug shortage crisis. However, the timing of the current drug shortage is notable. In 2003, the Medicare Modernization Act (MMA) was put into place. In 2004, the FDA reported 58 drug shortages; in 2011, the number is over 200. The intent of the Medicare Modernization Act was to create more transparency in pricing. With the MMA, the reimbursement rate moved from a percentage of average wholesale price to average selling price, which includes all discounts, rebates etc in the sale. Generic prices are driven down by market competition and the current model under the MMA makes it difficult for companies to raise prices more than 6% per year. Product margins have fallen significantly for many generic drugs, leaving companies with little incentive to continue manufacturing the drug or to increase production.

In addition to addressing regulatory and notification issues regarding drug shortages, a key component of the solution is addressing the economic issues underlying the drug shortage crisis. Potential components of the economic solution include offering financial incentives to ensure a steady supply of product as well as increasing the Medicare reimbursement amount.

The current situation is nothing short of a massive national emergency. The burden is on us to resolve the crisis in order to protect our children. None of my patients's families ever thought they would be faced with a diagnosis of childhood cancer. Today alone, the parents of 36 children in the US will be told their child has cancer. Let's act to ensure that these parents can also be told there are chemotherapy drugs available to cure their child.

Mr. GOWDY. Thank you, Dr. Hudspeth.
Mr. Kalmans.

STATEMENT OF WALTER KALMANS

Mr. KALMANS. Chairman and members of the subcommittee, good morning. My name is Walter Kalmans, and I am currently employed as vice president of New Ventures at WhiteGlove Health, a venture-backed company in Austin, TX. This testimony is not related in any way to my current employer. Rather, it is based on work independently developed as a result of 20 years of experience working as a consultant and commercial operations executive in the pharmaceutical industry.

Of particular relevance to this hearing is experience gained while serving as vice president of business development for Oncology Therapeutics Network [OTN], from 2003 to 2008. OTN was the 2nd largest specialty drug distributor in the United States until its acquisition by McKesson Corp. in 2007. The popular press, as well as recently publications by ASPE, FDA, and IMS Health, do a good job characterizing the generic drug shortage and tend to cite manufacturing and supply chain issues as chief culprits. As citizens, we are led to believe that over time, industry will fix the problem by investing in additional capacity, improving quality control, and identifying more high-quality suppliers of raw materials.

However, there is much more to this issue. Why, all of a sudden, would the pharmaceutical industry, one of the most sophisticated industries on earth, be experiencing an unprecedented growth of shortages, and why, in particular, shortages of generic injectable drugs? Manufacturing and supply chain issues certainly play a role, but it is my opinion that the Medicare Modernization Act of 2003, MMA, is the core culprit as to why generic injectable drugs are in growing shortage.

To most Americans, MMA is known as the act that expanded the prescription drug coverage for Medicare patients; however, another part of this legislation drastically altered how Medicare reimburses community-based oncologists who administer drugs in their offices, under Medicare Part B, B as in boy. Oncologists are one of the few specialists who make a margin on buying a drug for price X and receive Medicare reimbursement of price X plus Y.

Prior to MMA, Medicare reimbursed community-based oncologists based on a price called AWP, average wholesale price. MMA introduced a new price called ASP, average selling price. Calculating ASP required significant pricing transparency from pharmaceutical manufacturers and resulted in lower Medicare reimbursement payments to community oncologists and, notably, a more rapid price decline for many generic injectable drugs.

In addition, because the legislation set Medicare reimbursement for Part B drugs at ASP plus 6 percent, it established thinly veiled price controls, making it unpalatable for a pharmaceutical manufacturer to raise price more than 6 percent a year. For example, if a manufacturer were to raise the price on a \$100 drug by more than 6 percent during a year, an oncologist would likely be faced with the scenario of buying the drug for \$106 and receiving Medicare reimbursement of \$104.

Now fast-forward to today. If you were a generic injectable manufacturer with finite capacity, would you focus your capacity on manufacturing generics for products that have just lost patent protection, reaping high profits for the next few quarters, or would you manufacture lower priced generics, drugs whose patents expired long ago? Under normal economic circumstances, if there are shortages, prices adjust upward to reach a new equilibrium until additional product comes online, basic supply and demand economics. However, because MMA limits price increases to 6 percent annually, prices do not reach an equilibrium; even worse, because the profit potential of these drugs is so low, new entrants decide to stand on the sidelines or focus on more profitable products.

In conclusion, it is my opinion that we will experience generic drug shortages until legislation is passed to change the way generic injectable drugs are reimbursed by Medicare. Like any piece of legislation, MMA provided many citizens with benefits, but also like any piece of legislation, it had flaws. Unfortunately, these flaws took several years to become exposed and, for a variety of reasons, it may take quite some time to fix them.

Thank you.

[The prepared statement of Mr. Kalmans follows:]

Testimony of Walter C. Kalmans
wkalmans@lontraventures.com

Good morning! My name is Walter Kalmans, and I am currently employed as Vice President of New Ventures at WhiteGlove Health, a venture-backed company in Austin, TX. This testimony is not related in any way to my current employer. Rather, it is based on work independently developed as a result of 20 years of experience working as a consultant and commercial operations executive in the pharmaceutical industry.

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In conclusion, it is my opinion that we will experience shortages of generic injectable drugs until legislation is passed to change the way generic injectable drugs are reimbursed by Medicare. Like any piece of legislation, MMA provided many citizens with benefits, but also like any piece of legislation, it had flaws. Unfortunately, these flaws took several years to be exposed and for a variety of reasons, it may take quite some time to fix them.

Thank you!

Mr. GOWDY. Thank you, Mr. Kalmans.
Mr. Okon.

STATEMENT OF TED OKON

Mr. OKON. Chairman Gowdy, Ranking Member Davis, and members of the committee, I thank you for the opportunity to share my views on the drug shortages crisis relating to cancer care.

I am not a medical oncologist but serve as executive director of the Community Oncology Alliance, a non-profit organization dedicated to community cancer care. In my position, I hear from cancer patients and their providers how treatment has to be delayed, changed, and in cases stopped because low-cost, but potentially life-saving, generic infusible drugs are not available. Unfortunately, escaping the crisis is next to impossible for me as my wife is an oncology nurse who voices the frustrations of all cancer care providers when she asks, how can this be happening in the United States?

The drug shortage situation is very complicated; however, the root cause is not. The problem is grounded in economics and goes back to the way that Medicare reimbursement for cancer care was changed in the Medicare Modernization Act of 2003. The reason for the change was well intended: better balance Medicare payment for drugs and services to market rates. However, the policy change, exacerbated by poor implementation, has had unintended consequences. The first consequence has been a consolidation of oncology providers, including clinic closings and mergers into large hospital systems. The second is a severe reduction in the number of manufacturers supplying low-cost, generic cancer drugs.

Let me briefly explain the evolution of drug shortages.

The MMA changed Medicare Part B drug reimbursement from average wholesale price set by the manufacturer to average sales price, a market-based price. Oncology clinics administering chemotherapy are reimbursed by Medicare at ASP plus 6, which is intended to cover drug cost, overhead, staff, and materials. In actuality, reimbursement is lower than ASP plus 6 due to manufacturer-to-distributor prompt pay discounts included in the ASP calculation. It is also important to understand there is a perpetual lag of 6 months in updating ASPs each quarter, which results in providers subsidizing Medicare for drug price increases.

There are two key points to note about ASP reimbursement.

First, the system substantially reduced Medicare provider payments for cancer drugs. However, CMS never balanced this shortfall by increasing payment for non-reimbursed, essential services such as treatment planning. Instead, CMS put into place two demonstration projects in 2005 and 2006 to provide stopgap funding for the shortfall in services payments. A study by Avalere Health found that by 2008 Medicare covered only 57 percent of the cost of just the services associated with chemotherapy infusion. The overall shortfall in Medicare reimbursement has forced community cancer clinics to close, 199 over a 3½ year period, and an increase in mergers of clinics into hospitals, 315 over the same time period.

Second, the AWP reimbursement system allowed generic manufacturers to compete on the margins they established by setting a drug's AWP and then selling the drug at a discounted price. The ASP system changed the generic manufacturers' means of com-

peting to solely on actual sales price. That and the 6-month lag in updating Medicare reimbursement has resulted in a system that is effectively price capped.

There has been a steady downward pricing pressure on most generics since 2005, the year ASP was first implemented. For some of the top cancer drugs in short supply the ASPs have dropped approximately 50 percent since 2005. You should also understand that ASP masks the true decline in prices for manufacturers because they do not reflect discounts and rebates exempt from the calculation of ASP.

Generic manufacturers have felt additional pricing pressure from an increasing volume of 340(b) discounts, which they are required to extend to 340(b)-eligible hospitals and other institutions treating a disproportionate share of low-income and uninsured patients. As more oncology practices under reimbursement pressures have been acquired by hospitals eligible for 340(b) pricing, the volume of these discounts have increased. Furthermore, Medicaid rebates exert further downward pricing pressure on manufacturers.

Although, on the surface, declining prices are a positive for both payers and patients, the problem is that many generics have reached severely low prices. Consider if manufacturing a \$1 sterile infusible cancer drug is economically viable in the long run. In a market that is highly regulated, both in terms of pricing and manufacturing, normal market forces are not in effect.

Faced with the prospect of diminishing returns from low-priced, discounted, and rebated drugs, the incentive to stay in the market is reduced. This has led to fewer manufacturers producing these products. As a result, any manufacturing, regulatory, or quality problem that shuts down a production line has significant impact on the supply of product.

In closing, I implore the Congress to work with the cancer community in fixing this crisis. Next month will mark the 40th anniversary of when our Nation declared war on cancer. We have evolved our cancer care delivery system into the best in the world, as documented by survival rates. Americans battling cancer today and for generations to come should have access to quality, accessible, and affordable cancer care. We stand ready to provide you with supporting data and to work on immediate solutions.

Thank you for listening.

[The prepared statement of Mr. Okon follows:]

Chairman Gowdy, Ranking Member Davis, and members of the committee — I thank you for the opportunity to share my views on the drug shortages crisis relating to cancer care.

I am not a medical oncologist but serve as the Executive Director of the Community Oncology Alliance (COA), a non-profit organization dedicated to community cancer care. In my position, I hear from cancer patients and their providers how treatment has to be delayed, changed, and in cases stopped because low-cost, but potentially life-saving generic infusible cancer drugs are not available. Escaping the crisis is next to impossible as my wife is an oncology nurse who voices the frustrations of all cancer care providers when she asks, “How can this be happening in the United States?”

The drug shortage situation is very complicated; however, the root cause is not. The problem is grounded in economics and goes back to the way that Medicare reimbursement for cancer care was changed in the Medicare Modernization Act of 2003 (MMA). The reason for the change was well intended — better balance Medicare payment for drugs and services to market rates. However, the policy change, exacerbated by poor implementation, has had unintended consequences. The first consequence has been a consolidation of oncology providers, including clinic closings and mergers into large hospital systems. The second is a severe reduction in the number of manufacturers supplying low-cost, generic cancer drugs.

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There are two key points to note about the ASP reimbursement system.

First, the system substantially reduced Medicare provider payments for cancer drugs. However, CMS (the Centers for Medicare & Medicaid Services) never balanced this shortfall by increasing payment for non-reimbursed, essential services such as treatment planning. Instead, CMS put in place two demonstration projects in 2005 and 2006 to provide stopgap funding for the shortfall in services payments. A study by Avalere Health found that by 2008 Medicare covered only 57% of the cost for just the services associated with chemotherapy infusion. The overall shortfall in Medicare reimbursement has forced community clinics to close — 199 over a 3½-year period — and an increase in mergers of clinics into hospitals — 315 over the same time period.

Second, the AWP-based reimbursement system allowed generic drug manufacturers to compete on the margins they established by setting a drug's AWP and then selling the drug at a discounted price. The ASP-based system changed the generic drug manufacturers' means of competing to solely on actual sales price. That and the 6-month lag in updating Medicare reimbursement rates has resulted in a system that is effectively price capped. There has been steady downward pricing pressure on most generics since 2005, the year ASP was first implemented. For some of the top cancer drugs in short supply the ASPs have dropped approximately 50% since 2005. You should also understand that ASP masks the true decline in prices for manufacturers because they do not reflect other discounts and rebates exempt from the calculation of ASP. Generic manufacturers have felt additional pricing pressure from an increasing volume of 340B discounts, which they are required to extend to 340B-eligible hospitals and other institutions treating a disproportionate share of low-income and uninsured patients. As more oncology practices under reimbursement pressures have been acquired by hospitals eligible for 340B pricing, the volume of these discounts have increased. Furthermore, Medicaid rebates exert further downward pricing pressure on manufacturers.

Although, on the surface, declining prices are a positive for payers and patients, the problem is that many generics have reached severely low prices. Consider if manufacturing a \$1 sterile infusible cancer drug is economically viable in the long run. In a market that is highly regulated, both in terms of pricing and manufacturing, normal market forces are not in effect. Faced with the prospect of diminishing returns from low-priced, discounted, and rebated drugs, the incentive to stay in the market is reduced. This has led to fewer manufacturers producing these products. As a result, any manufacturing, regulatory, or quality problem that shuts down a production line has a magnified impact on the supply of product.

In closing, I implore the Congress to work with the cancer community in fixing this growing crisis. Next month will mark the forty-year anniversary of when our nation declared war on cancer. We have evolved our cancer care delivery system into the best in the world, as documented by survival. Americans battling cancer today and for generations to come should have access to quality, accessible and affordable cancer care. We stand ready to provide you with supporting data and to work on immediate solutions.

Thank you for listening.

Mr. GOWDY. Thank you, Mr. Okon.
Dr. Gottlieb.

STATEMENT OF SCOTT GOTTLIEB, M.D.

Dr. GOTTLIEB. Mr. Chairman, Mr. Ranking Member, thank you for the opportunity to testify today before the committee. I am a practicing hospital-based physician and a resident fellow at the American Enterprise Institute. Previously, I served as Deputy Commissioner at the Food and Drug Administration and as a senior official at CMS during implementation of MMA.

The causes for these scarcities can be complex and multifactor. Each episode typically has unique characteristics that make it distinct from other drug shortages. There are, however, some common problems that are, to a varying degree, threaded through each of these episodes. I believe these common factors should be the focus of our attention.

I group these common factors into three categories. The first are regulatory challenges that have made the manufacturing of these products safer and more reliable, but also, in some cases, more challenging and expensive. The second are mechanisms that make the prices sticky, limiting profitability and precluding new investment in additional supply and better and more efficient manufacturing. And the third and final category is market structures that prevent firms from branding their products and reflecting by how they price them legitimate improvements in manufacturing that allow drugs to be produced more reliably and in scalable facilities.

The first challenge is the way the manufacturers of these drugs are being regulated. In recent years, the Food and Drug Administration has gotten tough on potentially dangerous snafus that have long plagued the production of some injectable generic drugs. These include problems with sterility and particulate matter getting into the solutions.

The FDA has real concerns, but if we want to maintain high standards, we need policy measures to accommodate the economic impacts. This begins with making sure regulations governing drug manufacturing, FDA's good manufacturing practices, are as efficient as possible. Manufacturers have long complained that these policies are outdated and at times inflexible.

Another regulatory issue that plays in these shortages relates to the backlog that FDA currently has for generic drug manufacturing supplements. The backlog in reviewing manufacturing supplements can add as much as a several-year delay to the approval of manufacturing changes. Because of remediation now taking place at many plants, FDA is about to get hit with a deluge of supplements related to the manufacture of these shortage drugs.

The increased regulatory scrutiny presents a more immediate challenge also because of the way these generic parenteral drugs are being reimbursed by Medicare and private payers. The current system prevents manufacturers from adjusting prices to reflect the higher cost of goods as a result of the manufacturing upgrades that they are required to undertake.

A 2003 law sets the price Medicare will pay for physician-administered drugs to the average sales price that is at least 6 months old at any given time. This means even if a generic raises its price

to reflect increased production cost, Medicare won't pay the new price for about 6 months later, so purchasers lose money on these drugs for months at a time.

In order to make long-term capital intensive investments needed to bring on new manufacturing capacity for these parenteral drugs, generic firms would need to know that they can take and sustain price increases over a reasonable period of time.

The bigger issue with the way Medicare reimburses these drugs, however, is the way it sets a single flat price for each broad category of medicines, rather than paying for these drugs individually. Medicare assigns a single billing code to each category of medicines.

Since FDA's enforcement of facilities is often uneven, one firm might be facing significantly higher manufacturing and regulatory costs while others are getting by with older and perhaps less safe facilities. Lumping all the drugs in the same billing code creates a race to the bottom on the costs of goods, with the price reflecting the lowest cost producer.

The result is that prices can't rise to reflect change in demand or the need for investments in manufacturing. Any capital requirements are hard to recoup given the way Medicare pays for these drugs. When higher costs of goods erode slim profit margins, more manufacturers are choosing to exit product lines entirely rather than invest to meet higher standards.

To fix these problems, we should lift existing price controls when it comes to critical injectable drugs that are generic.

These drugs should also get a holiday from other price control schemes that serve to distort market prices and reduce incentives to invest in new product, such as the 340(b) discount program.

Medicare can also allow these drugs to have individual billing codes rather than paying for each class of drug according to the same billing code. This would allow manufacturers to price their drugs individually, eliminating the race to the bottom on the cost of goods.

Finally, we should consider policy constructs that would give manufacturers a financial incentive to develop intellectual property that improve the manufacturing characteristics of generic medicines, even if these changes didn't change the clinical properties of the drug. Recent policies have systematically eroded the ability of firms to earn returns on these products and make investments. The only way to mitigate these shortages is to make it profitable for firms to invest in manufacturing that enables safe, stable, and more scalable supply.

Thank you.

[The prepared statement of Dr. Gottlieb follows:]

Introduction

Mr. Chairman Issa, Mr. Ranking Member Cummings; I want to thank you for the opportunity to testify today before the Committee on Oversight and Government Reform, Subcommittee on Healthcare, on the shortages of critical sterile injectable and infused drugs.

The problems have affected mostly older parenteral drugs that are sold as generic medicines. These drugs are typically sold at low prices for slim profit margins. The cost of manufacturing them often comprises a sizable proportion of the overall price of the finished drug. More than 200 sterile injectable drugs are on the current shortage list kept by the American Society of Health-System Pharmacists.ⁱ ⁱⁱ

While other countries are also experiencing drug shortages,ⁱⁱⁱ in the U.S. the critical medicines that are in scarce supply, and the protracted nature of the underlying problems, make our situation uniquely challenging. The shortages have caused patients to miss or delay chemotherapy or to get inferior antibiotics, anesthetics and intravenous nutrition. Shortages of drugs have triggered clinical mistakes and bad outcomes in situations where patients received medicines that prescribers weren't accustomed to using.^{iv} Hospitals are being forced to ration key medicines and patients forced to sit on waiting lists for vital drugs.^v

Some blame these shortages on the "manipulation" of drug middlemen. These "gray market" distributors have become an unofficial alternative market for drugs -- operating outside the usual distribution networks. This shadow market has exploded in recent years, with vendors charging markups of up to up to 3000% for some cancer drugs.^{vi} These vendors stockpile supplies to be redistributed later at high prices, once shortages arise.

While unpleasant, the existence of this gray market is not the trigger of shortages but one of its consequences.^{vii} Neither is the lack of qualified manufacturers for these generic sterile injectable drugs itself a primary cause for the shortages.^{viii} Here again, the lack of qualified manufacturers is another symptom of the underlying problems. After all, branded drugs typically have only a single manufacturer, and aren't facing the same production problems. Under the right circumstances, a handful of adept companies can supply these markets.

In our search for the cause of the shortages, and the pursuit of solutions, we need to be careful not to confuse the consequences of the problems for its root causes.

The reality is that the causes for these scarcities can be complex and multifactor. Each episode typically has unique characteristics that make it distinct from other drug shortages. This makes finding policy solutions challenging. There are, however, some common problems that are -- to varying degrees -- threaded through each of these episodes. I believe these common factors should be the focus of our attention. They provide the most logical place for policymakers to start addressing the root causes of these drug shortages.

I group these common factors into three categories:

The first are regulatory challenges that have made the manufacturing of these products safer and more reliable, but also in some cases more challenging and expensive.

The second are mechanisms that make prices sticky, limiting profitability and precluding new investment in additional supply and better and more efficient manufacturing.^{ix}

The third and final category is market structures that prevent firms from branding their products, and reflecting by how they price them, legitimate improvements in manufacturing that allow drugs to be produced more reliably and in scalable facilities.

Regulation of Drug Manufacturing

The first challenge is the way the manufactures of these drugs are being regulated. In recent years, the Food and Drug Administration (FDA) has gotten tougher on potentially dangerous snafus that have long plagued the production of some injectable generic drugs. These include problems with sterility, and particulate matter getting into the solutions.

Consider these statistics: In the early part of the last decade, FDA prompted the recall of about 45 injectable drugs a year. Annually, about five of these recalls related to particulate getting into the formulations. This included things such as metal shavings from corrosion or abrasion in the manufacturing process, glass from delamination, or crystals of drug substance. In the last few years about 100 injectable products each year have been recalled. Between 20 and 30 of these recalls were the results of particulate found in the solutions.^x

Even if the incidence of these problems is on the rise, it's likely that better oversight is also prompting more recalls. FDA is catching more of these problems, triggering more recalls.

Take the example of more glass lamellae being found in solution. Through 2010, firms typically recalled no more than a single product for this kind of deficiency. By the end of the second quarter in 2011, there had been 21 products recalled for glass lamellae being found in drug solutions. This surge in recalls was primarily due to a single decision by a number of different firms to simultaneously switch to packaging their drugs in lower-cost vials that degraded under certain conditions. But the episode speaks to a lot of the problems plaguing the market for sterile injectable drugs. That these problems were spotted quickly suggests that FDA's detection methods have improved. In a previous era, this might have evaded scrutiny longer. That the firms switched to these cheaper vials suggests that there is a lot of pressure to lower the costs of these goods, creating the opportunity for new risks.

Now just because some manufacturers have long produced to lower standards doesn't mean FDA should continue to ignore legitimate problems. The FDA has real concerns about the integrity of how some of these drugs are manufactured. Contribution to the finished solution from equipment, process, components, and packaging should never be considered acceptable. In the past, FDA may have lacked resources to apply strict standards to manufacturers (especially those products made at foreign sites).^{xi} But the fact is that there has been a fairly rapid tightening of the regulatory scrutiny of these products over a short period of time. To the degree that the market for these products was already populated with older-line, less nimble, less well-capitalized manufacturers; that increased regulation has caught them off guard. Low margin producers can't easily meet higher standards.^{xii}

The regulatory scrutiny isn't the cause of shortages, but another of the multiple factors that have contributed to the conditions challenging these drug makers.^{xiii} With its vigilance

heightened, the FDA has required manufacturers to undergo major plant renovations, suspend facilities or stop shipping goods from suspect production lines. The FDA and the manufacturers often don't understand the drug-production processes well enough to detect the root cause of problems. Instead of calling for targeted fixes of troubled plants, the agency has often required manufacturers to undertake costly, general upgrades to facilities. As a result, in 2010, product quality issues -- and the subsequent regulatory actions taken by FDA to address these problems -- were involved in 42% of the drug shortages.^{xv}

The regulatory oversight of manufacturing processes shouldn't be scaled back just because it's chasing some substandard manufacturers out of the market. But we need to take measure of the impact these standards have on the cost of manufacturing the drugs. If we want to maintain high standards, we need policy measures to accommodate the economic impacts.

This begins with making sure the regulations governing drug manufacturing, FDA's Good Manufacturing Practices (GMPs), are as efficient as possible. Manufacturers have long complained that these policies are outdated, and at times inflexible. The general refrain is that it's too hard for producers to upgrade manufacturing facilities without drawing inordinate scrutiny from regulators. This has resulted, at times, in outmoded production methods persisting because product developers concluded -- rightly or wrongly -- that it was too hard to get approval to incorporate better manufacturing technologies into plants.

FDA has undertaken a broad effort to implement new GMPs. But it made mostly modest changes. Drug companies have cited examples where the FDA requirements were so out of date that they maintained two facilities -- a modern plant next to an older facility, one making drugs for the European Union and rest of the world, and the older plant to meet FDA's out-of-date requirements. While branded drug companies can afford to do that, or to invest in the long process to stand up new facilities while still maintaining their older plants, the manufacturers of lower margin generic parenteral drugs often cannot. Generic manufacturers estimate that it can take as long as seven years, from start to finish, to stand up a new manufacturing facility for sterile injectable drugs. The divergent, and sometimes outdated specifications required by FDA is one reason why we see a number of drug makers manufacturing their generic parenteral products only for sale outside the U.S.

Policy makers have suggested that one way to alleviate the U.S. shortages is to import drugs manufactured for other markets. Rather, I believe the question we should be asking is why the companies making these drugs aren't choosing, on their own volition, to market these drugs inside the U.S. in the first place. Pricing is certainly one factor. Companies can often charge more for the generic parenteral drugs when they sell these medicines in Europe. But regulation is also a factor. In some cases, the newer facilities that these drugs are being manufactured in haven't met FDA clearance. Bringing our regulatory standards up to date, making it easier for manufacturers to adapt plants with new technologies, and harmonizing GMP requirements across different established markets like Europe would better enable manufacturers to enter the U.S. with reliable supplies. All of these elements should continue to be part of FDA's efforts to modernize its approach to GMPs and address the shortages.

Another regulatory issue at play in these shortages relate to the backlog that FDA currently has for generic drug manufacturing supplements. The FDA expedites the review of supplements related to shortage drugs, so the backlog doesn't directly affect these products.

But the agency's expedited review often kicks in only once drugs approach shortage status. For the rest of the almost 3,000 supplements that are on backlog, these applications can sit for months and sometimes years owing to a lack of resources to enable their timely review.

While I have no direct knowledge of the flow of FDA's queues, it seems almost inevitable that some of these backlogged manufacturing supplements (requests of FDA to allow a company to either improve existing facilities or stand up new plants) sat in this backlog while the drug approached the precipice of the shortage list. In other words, FDA's prioritization of supplements only kicks in once a drug is judged to be at or near shortage. What about drugs that approached shortage long after new facilities couldn't be stood up? The correlation between the regulatory action and the shortage may not be obvious, but we should explore whether some of the drugs on the shortage list had supplements that were at one time delayed because the resources didn't exist at FDA to enable their timely review.

The backlog in reviewing manufacturing supplements can add as much as a several year delay to approval of those manufacturing changes. Often these supplements are requests to expand or modernize manufacturing facilities. The delay in reviewing these supplements can have significant economic implications. For example, to submit these applications, companies may also have to manufacture three commercial batches with the new manufacturing process while still running the old manufacturing and only selling the old batches. The backlogs are now so long the new batches may become worthless by the time the new manufacturing facility is approved. The financial burden to the generic drug manufacturers of having to waste these first-run batches is a huge disincentive to modernize.

FDA's position has been that without additional resources, they cannot hire a sufficient number of chemist-reviewers to solve the problem. Resources are certainly a large part of the issue. To these ends, the proposal for a Generic Drug User Fee program should provide the agency with the additional money that's needed to tackle this backlog.^{xx} Congress should look to build into this legislation specific constructs that allow FDA to prioritize resources to the review of supplements related to the manufacture of generic sterile injectable drugs -- not only those drugs that are currently in shortage but all of the generic parenteral drugs. That way we will not only tackle current shortages but also better avoid future ones.

Regulation of Drug Pricing

The greater regulatory scrutiny presents a more immediate challenge also because of the way these generic parenteral drugs are reimbursed by Medicare and many private payers. The current system prevents manufacturers from adjusting prices to reflect higher cost of goods as a result of the manufacturing upgrades that they are required to undertake.

A 2003 law sets the price Medicare will pay for physician administered drugs to an "average sales price" that is at least six months old at any given time. This flawed concept means even if a generic firm raises its price to reflect increased production costs, Medicare won't immediately pay the new price until approximately six months later. As a result, purchasers (mostly hospitals and in some cases individual physicians) lose money on these drugs for months at a time since the price they pay for the drug could be significantly higher than the historical price that Medicare reimburses for the medicine. Since many of the manufacturers producing these parenteral drugs do so in order to win group purchasing contracts with

larger institutions like hospitals, and already view these drugs as “loss leaders” that allow them to get more lucrative contracts for other medicines, they’re reluctant to raise prices to match rising production costs if it means leaving customers in a financial pinch. The easier path for these manufacturers is to cease production of these individual medicines.^{xvi} Because the margins in this space (and profits from incremental sales) are slim, and there are few penalties for shirking contracts, there’s little incentive for maintaining redundant capacity.

In order to make the long-term, capital intensive investments needed to bring on new manufacturing capacity for these parenteral drugs, generic firms would need to know that they can take, and sustain, price increases over a reasonable period of time. It should come as no surprise that a recent analysis by the Department of Health and Human Services found that among the group of drugs that eventually experience a shortage, average prices decreased in every year leading up to a shortage. The mean price decrease over these periods leading up to the shortages averaged of as much as 27%. By comparison, the average prices of drugs that were never in shortage over this period, in most cases, rose slightly.^{xvii}

The bigger issue with the way Medicare reimburses these drugs, however, is the way it sets a single, flat price for each broad category of medicine rather than paying for these drugs individually. Medicare assigns a single “billing code” to each category of medicines. The agency then establishes a single rate that it will reimburse for each code. That rate reflects the average price of all of the drugs in a particular category of medicines. That means that even if a drug has multiple manufacturers, some better than others, all of the drugs in a particular category will be paid the same average rate. In other words, the drugs are treated like commodities by CMS. The reimbursement level is the same for every drug in a billing code regardless of whether a particular manufacturer has been subject to more stringent regulatory oversight in recent years or has invested in upgrading its manufacturing processes.

Since FDA’s enforcement of these facilities is often uneven at any given time, one particular manufacturer might be facing significantly higher manufacturing and regulatory costs while other drug producers in the same category are still getting by with older, cheaper, and perhaps less safe facilities. By lumping all of the drugs into the same billing code, it creates a race to the bottom on the cost of goods, with the price paid for the entire category influenced by the lowest cost producer. This race to the bottom on manufacturing costs can work reasonably well in producing significant savings when it comes to products that are easy and cheap to manufacture, like small molecule drugs (pills). But it creates significant risks in markets like sterile injectable drugs, where the manufacturing is not a trivial affair and a constant drive to lower costs can mean necessary manufacturing safeguards are being forgone. Certainly this race to the bottom creates significant disincentives to making any manufacturing upgrades that would end up raising the cost of goods.

The result of these policies is that generic prices can’t rise to reflect changing demand or the need for bigger investments in manufacturing. Branded parenteral drugs have faced similar production and regulatory issues. These drugs are also paid for under the same flawed “ASP” scheme. But the branded drugs have larger profit margins to offset the cost of plant upgrades. The generic parenteral drugs are already being sold at slim profit margins, and sometimes for a loss. Any capital requirements for investments in new manufacturing equipment and production facilities are hard to recoup given the way Medicare pays for these drugs. When the slim profit margins of the generic drugs become eroded by the cost of

upgraded production facilities, more and more manufacturers are choosing to exit product lines entirely rather than invest money to meet steadily higher standards.

Some have suggested that the ASP construct is behind these shortages through its impact on clinical prescribing.^{xviii} According to this argument, doctors receive a financial incentive to prescribe the highest priced drugs because of the 6% spread that they earn for administration of agents. As a result, it is argued, when higher-priced versions of drugs come along, they switch away from cheaper generics.

But this argument, even if true, is a non sequitur. It still doesn't explain why the generic markets can't be adequately supplied. Even if demand diminishes as a result of branded competition for a generic medicine, the fact is that the current manufactures are still not keeping up with the now reduced demand. Under this argument, the price is used to help explain the demand. But it doesn't take any measure of the supply side of the equation. Even if demand for these drugs diminishes over time, if the market was healthy, if prices could adjust for supply, and if profits could be earned, there would be manufacturers willing to step in to supply the need for these generic medicines, even at newly reduced levels.

Proposals for Reform

To fix the problems with inadequate supply for generic sterile injectables, we should lift existing price controls when it comes to critical injectable drugs that are generic, and take steps to provide manufacturers with incentives for making improvements in the manufacture of these drugs that can lead to a more stable supply and more scalable production facilities.

First, Medicare should ditch the flawed "average sales price" when it comes to generic sterile injectable drugs and reimburse manufacturers according to the price paid by wholesalers on the open market. This wholesale acquisition cost (WAC) is already collected and reported to Medicare. Reimbursing the parenteral drugs according to WAC would allow generic firms to more quickly adjust charges to match rising production costs and meet demand.

These drugs should also get a holiday from other Medicaid price-control schemes that serve to distort market prices and reduce profitability and incentives to invest in new production. These include constructs such as Medicaid Best Price rules, the 340B drug discount program, and other mandatory rebating schemes.

Medicare can also allow these drugs to have individual billing codes, rather than paying for each class of drug according to the same billing code. This would allow manufactures to price their drugs individually. It would help to eliminate the race to the bottom on pricing and, in turn, cost of goods. If manufacturers made legitimate improvements in their manufacturing to enable more stable supply, they could try to represent these improvements in contracting discussions to secure better pricing. Some purchasers might well be willing to pay for supply that's produced from more up-to-date and reliable facilities. Providers are becoming increasingly conscious of how and where drugs are manufactured. Allowing drugs to have individual codes would let manufacturers price products to reflect these attributes.

Finally, we should consider policy constructs that would give manufacturers a financial incentive to develop intellectual property that improved the manufacturing characteristics of

generic medicines even if these changes it didn't change the clinical properties of a drug. We could establish criteria for which manufacturing improvements are believed to allow for more reliable, stable, and scalable supply. FDA already evaluates manufacturing sites for these qualities and can help establish the criteria. In turn, manufacturers can be allowed to make limited claims in labeling attesting to upgrades that meet these criteria. These would include improvements in manufacturing that are believed to reduce the chance for error or lead to a process that can be more quickly scaled up in a time of shortage. Once producers that invested in these new processes get a green light to make certain claims on their labels that reflect these improvements, it would, in turn, trigger specific incentives – perhaps guaranteed purchase by government programs or preferential pricing under Medicare. This would provide a direct incentive for investing in the kind of manufacturing improvements that can help ensure a more scalable, and less trouble-prone supply of a product.

Conclusion

The problems fueling the recent shortages of sterile injectable drugs do not lend themselves to easy solutions because these episodes aren't typically driven by a single, common cause. Each shortage has unique features. In addition to the factors cited in this testimony, byzantine contracting arrangements, inefficient sourcing arrangements, a reluctance of hospitals to buy products 'off contract,'^{xxx} problems with the sourcing of raw materials^{xx}, and a myriad of other factors all play a role in select shortage cases. There are, however, some flawed policy threads woven through all of these episodes. To the degree that some of these common issues stem from the way the price and manufacture of these drugs is regulated by government agencies, this presents policy makers obvious levers to start repairing this particular market. Before we start manipulating factors not in the control of government agencies, we should address factors that are in the direct purview of this committee.

I know one of the proposals before this committee is a system for early notification to FDA of impending shortages. I don't believe that relying on early notification of impending shortages is going to resolve these problems. In fact, I fear such a policy construct could make matters worse, by institutionalizing these shortages. Current proposals call for early notification from pharmaceutical companies when a factor arises that may result in a shortage. These factors may include changes made to raw material supplies, adjustments to manufacturer production capabilities and certain business decisions such as mergers, withdrawals or changes in output. In the end, the net effect of this legislation may simply be to provide an additional disincentive to firms who want to take one of these actions, even though these may be precisely the steps necessary to help ensure better long term supply.

The only way to improve the availability of these products is to make it profitable for firms to invest in the manufacturing that enables stable, safe, and more scalable supply. Policies enacted over the last few decades have systematically eroded the ability of manufacturers to earn returns on these products and make these investments. We need to reform the policies governing these markets if we're going to lure investment back into these important areas.

ⁱ Food and Drug Administration. Current drug shortages (<http://www.fda.gov/drugs/drugsafety/drugshortages/ucm050792.htm>)

- ⁱⁱ Kaakeh R, Sweet BV, Reilly C, et al. Impact of drug shortages on U.S. health systems. *Am J Health Syst Pharm* 2011;68:1811-9.
- ⁱⁱⁱ UK Lawmakers to Probe Medicine Shortages. Reuters, November 21, 2011.
- ^{iv} Provisional observations on drug product shortages: Effects, causes, and potential solutions. Summary of a stakeholder's meeting on drug shortages convened by the American Medical Association and the American Society of Health-System Pharmacists. *American Journal of Health-System Pharmacists* 2002;59:173-182.
- ^v Kaakeh R, Sweet BV, Reilly C, Bush C, DeLoach S, Higgins B, Clark AM, Stevenson J. Impact of drug shortages on U.S. health systems. *American Journal of Health-System Pharmacy*. 2011;68:e13-e21. http://www.ajhp.org/site/DrugShortages.pdf?fm_preview=1
- ^{vi} Mandy L. Gatesman and Thomas J. Smith. The Shortage of Essential Chemotherapy Drugs in the United States. *New England Journal of Medicine* 2011;365:18
- ^{vii} The report from ASPE states: "These gray market distributions appear to be a result of a drug shortage, not a cause, but the potential for hoarding and strategic behavior in the gray market is a concern with respect to future policy actions."
- ^{viii} According to the ASPE analysis, most of the production of a given drug is by three or fewer manufacturers in this space. Analysis of a sample of 33 generic sterile injectable oncology drugs shows that of 33 drugs, for 28 at least 90 percent of total unit sales in 2010 was by 3 or fewer manufacturers.
- ^{ix} The Health and Human Services Office of Assistant Secretary for Planning and Evaluation also found that supply and demand do not respond much to short-term changes in price. Rather than seeing a price increase when a disruption occurs, the drug instead goes into shortage. ASPE Issue Brief, "Economic Analysis of the Causes of Drug Shortages," October 2011.
- ^x Data presented by Steven Lynn, Chief, Recalls and Shortages, FDA/CDER Office of Compliance, Division of Manufacturing and Product Quality. Recalls, presentation to CASA, May 20, 2011, Baltimore, MD.
- ^{xi} FDA Faces Challenges Overseeing the Foreign Drug Manufacturing Supply Chain. Statement of Marcia Crosse Director, Health Care, GAO. September 14, 2011. Available at www.gao.gov/new.items/d11936t.pdf
- ^{xii} Corresponding to this increased regulatory scrutiny, the number of shortages has also increased almost proportionally. In 2005 and 2006 about 25 sterile injectable drugs were said to be in shortage by FDA. By 2009 that number had increased to about 75, matching the rise in the number of enforcement actions FDA took. By 2010 the number of parenteral drug shortages was put at more than 125 by FDA.
- ^{xiii} To Prevent Drug Shortages, Don't Look to Inspections, FDA Says. *The Pink Sheet Daily*, August 22, 2011
- ^{xiv} The ASPE report finds that problems in manufacturing are linked to 54% of shortages of sterile injectable drugs. The report finds that some of the largest manufacturers of sterile injectable drugs have had serious quality problems leading to temporary voluntary closure or renovations of major production facilities. This means that quality problems that affect an entire plant may result in shortages for many drugs.
- ^{xv} Congress has set the floor for FDA's Office of Generic Drugs funding at \$52.947 million in fiscal 2012, almost 5% less than the minimum of \$55.5 million it directed FDA to spend on OGD in fiscal 2011. FDA proposed a budget of \$88.8 million for OGD in fiscal 2012. But \$40 million of that was to have come from \$40 million in generic drug user fees that are not yet authorized.
- ^{xvi} Scott Gottlieb. Solving the growing drug shortages. *The Wall Street Journal*, November 07, 2011. A21 available at <http://www.aei.org/article/health/healthcare-reform/solving-the-growing-drug-shortages/>
- ^{xvii} ASPE Issue Brief, "Economic Analysis of the Causes of Drug Shortages," October 2011. For the 44 sterile injectable oncology drugs in shortage since 2008, these drugs experienced an average price decline of 26.5% between 2006 and 2008; 6.3% between 2008 and 2011; and 27.4% between 2006 and 2011. By contrast, the 28 generic injectable oncology products not in shortage since 2008 experienced small price increases over all these time periods.
- ^{xviii} Mandy L. Gatesman and Thomas J. Smith. The Shortage of Essential Chemotherapy Drugs in the United States. *New England Journal of Medicine* 2011;365:18
- ^{xix} Wynn Bailey. Globalization of the Life Sciences Supply Chain. *Contract Pharma*, January/February 2011. (available at www.contractpharma.com)
- ^{xx} More than 80% of the raw materials used in pharmaceuticals come from outside the United States.

Mr. GOWDY. Thank you, Dr. Gottlieb.
Dr. Thompson.

STATEMENT OF KASEY K. THOMPSON, PHARM.D.

Dr. THOMPSON. Good morning and thank you, Chairman Gowdy, Ranking Member Davis, and distinguished members of the subcommittee for holding this hearing. My name is Kasey Thompson and I am vice president of policy, planning and communications for the American Society of Health System Pharmacists. I am here today to talk about the problem of drug shortages and the impact shortages are having on the ability of health care providers to care for our patients.

For the last 10 years, ASHP, in collaboration with the University of Utah Drug Information Program, has been tracking and studying drug shortages and making that information available free to the public on our Web site. Since that time we have seen the number of shortages increase, almost tripling since 2006. As a result, hospital pharmacists and other health care providers have had to go to heroic lengths to find needed medications, spending time tracking down the product rather than caring for patients. In some cases we are told why there is a shortage. For example, there may be a quality issue with the production of the product. In other cases we simply have no idea.

Our analysis of shortages over the last 10 years has shown that most drug shortages are the result of quality issues in the manufacturing process. However, we recognize that there is no one cause to this problem, nor is there one solution. For example, it has been suggested that Medicare reimbursement policies may be partially to blame for drug shortages. While we believe this is an area that should be explored further, we do not currently have the data to confirm that this is in fact the case. We do know that drug shortages are not confined to oncology medications.

Other significant shortages affect anesthesia, pain management, nutrition support medications as well. These other drug classes have experienced increases since 2006, in addition to oncology drugs. This suggests multiple reasons for drug shortages, both quality assurance and economic. We are pleased, however, to see that other facets of drug shortages, including economic factors, are being considered, but would warn against rushing to any conclusions, given the limited data at this time. It will be important to learn from other stakeholders in the supply chain, including pharmaceutical manufacturers, in order to fully assess the causes and solutions to this public health crisis.

Fortunately, the Food and Drug Administration has been able to take steps to address drug shortages when they had access to certain information from drug manufacturers. For example, in 2010, 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 101 shortages averted for 2011.

For this reason, ASHP supports bipartisan legislation in both the House and Senate that would require manufacturers to confidentially notify the agency when they experience production problems or discontinue a product. We know that confidential notification by

drug manufacturers to the FDA is not a complete solution, nor does it prevent drug shortages from occurring, but it is a proven solution based on FDA's experience that can be implemented immediately while we look to examine other potential causes of drug shortages, including economic factors.

Hospital and health system pharmacists have been collaborating with other clinicians and members of the supply chain to work with FDA to address the problem. For example, we believe FDA should have the necessary resources to speed up the regulatory process to help resolve drug shortages. Other alternatives include improved communication between FDA field personnel in the drug shortages program to assess the risk of public harm when potential enforcement action may worsen a drug shortage; exploring incentives for manufacturers to continue or reenter the market; a generic user fee program to speed approvals; and, last, ensuring the agency has the funding it needs to carry out its mission.

In conclusion, drug shortages continue to be a very serious public health threat not just for oncology drugs, but also for pain medications, anesthesia drugs, and nutrition products. While some causes are known, others are not as clear. ASHP supports more examination of these other factors to help identify causes of drug shortages currently plaguing our health care system.

Again, thank you, Mr. Chairman, Mr. Ranking Member, and all members of the committee, for this opportunity to provide input on this urgent public health crisis.

[The prepared statement of Dr. Thompson follows:]

Good morning and thank you Chairman Gowdy, Ranking Member Davis, and distinguished Members of the Subcommittee, for holding this hearing. My name is Kasey Thompson and I am Vice President of Policy, Planning and Communications for the American Society of Health-System Pharmacists (ASHP). I am here today to talk about the problem of drug shortages and the impact shortages are having on the ability of healthcare providers to care for our patients.

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In conclusion, drug shortages continue to be a very serious public health threat, not just for oncologics, but also for pain medications, anesthesia drugs, and nutritional products. While some causes are known, others are not quite as clear. ASHP supports more examination of these other factors to help identify additional causes of drug shortages currently plaguing our health care system. Again, thank you

Mr. Chairman, ranking member, and all members of the committee for the opportunity to provide input on this urgent public health crisis

Shortages of prescription drugs in the United States have gained increasing attention in recent years due to the scope and severity of the drugs in short supply. The majority of these shortages occur in drugs that are generic injectables, often administered in a hospital or clinic setting. The shortages have been occurring for anti-cancer drugs, anesthetics, pain, and nutritional drugs, all of which play crucial roles in the care of patients. The result of drug shortages is that caregivers must scramble to find the drug, or use an alternative if one is available. Many caregivers have expressed concern that even if a therapeutic alternative exists, it is likely an older drug which may have more severe side effects or negatively interact with other medications the patient is taking. Further, drug shortages have caused widespread fear among caregivers who are deeply concerned that care could be delayed, rationed, or is provided in a suboptimal manner to stretch doses and preserve scarce supplies.

According to a study conducted in partnership between ASHP and the University of Michigan Health System, labor costs associated with managing drug shortages have an estimated annual impact of \$ 216 million nationally, and more than 90% of respondents agreed that drug shortages were associated with an increased burden and increased costs today compared to two years ago.

Causes of drug shortages are many and complex. Manufacturing issues that lead to drug shortages include product quality issues that result in production halts or recalls, product discontinuations, and unavailability of active pharmaceutical ingredients (APIs) or other raw materials. Secondary shortages—or shortages that occur based on shifts in market demand caused by an initial shortage of another drug—are also common. Other contributing causes to drug shortages include quality issues that arise from the ever-increasing reliance on foreign ingredient and manufacturing sources and a lack of FDA resources to expedite approval of supplemental new drug applications and conduct foreign inspections. While not a cause of drug shortages, just-in-time inventory practices by product distributors and

practice sites have removed the buffer previously provided by larger inventories and resulted in an immediate impact of drug shortages on patient care.

While information on the root cause of each drug shortage is not always publicly available, the cause of many shortages can be traced back to aspects of the manufacturing process. These manufacturing issues are compounded by substantial industry consolidation over the last few years that has resulted in fewer manufacturers producing critical drugs. When one manufacturer experiences a production interruption, other companies must ramp up production of their product to meet market needs. This increased production is sometimes, but not always, possible. In the case of sole-source drugs, this situation almost instantly results in a shortage situation.

ASHP continues to work with FDA, other health care provider groups and members of the supply chain to address the issue. However, we also believe Congress can help us as well. ASHP supports bipartisan legislation (S. 296, H.R. 2245) that would require drug manufacturers to notify the Agency when they experience an interruption in the production of a drug product potentially resulting in a shortage situation. According to FDA, in 2010 the Agency was able to avoid 38 drug shortages when they were made aware of production interruptions ahead of time, and so far this year, 101 shortages were avoided. However, we believe other steps can be taken as well, for example, require confidential notification of the disruption in supply of single source active pharmaceutical ingredients (API), require manufacturers to develop continuity of supply plans, establish incentives for manufacturers to remain or re-enter the market, and urge FDA to develop expedited approval pathways for pre-1938 (unapproved) drugs. Finally, ASHP believes that FDA must have adequate resources devoted to alleviating and preventing drug shortages.

Notification System

Under current law, manufacturers are not required to report to FDA when they experience an interruption in the production of their products, unless that drug is deemed medically necessary by the agency. The same holds true for manufacturer plans to discontinue a product. Even in cases where the drug is deemed medically necessary and reporting is required, FDA has no enforcement mechanism to penalize a drug maker for failing to report these problems. This information could be extremely useful to FDA in the case of drugs with multiple suppliers where the agency could urge alternate suppliers to step up production of a product to offset the decrease in supply due to the interruption or discontinuation of the initial product. In some instances, FDA is not told there is a problem, or the nature of the problem. This information could be useful in determining the duration and severity of the interruption and may allow the agency to implement countermeasures to help ensure supply.

The importance of notification is highlighted by quality concerns associated with the increased globalization of pharmaceutical manufacturing. A number of drug shortages can be traced back to quality concerns with foreign-produced APIs. An extreme example was the heparin contamination that occurred in 2007, which resulted in a recall, and a subsequent product shortage that was immediate and continued for an extended duration of time. While FDA has increased foreign inspections, it still lacks the resources necessary to fully address this issue. Therefore, drug shortages precipitated by recalls caused by substandard APIs will continue and likely increase.

Legislation (S. 296/H.R. 2245) in Congress would mandate that companies confidentially notify FDA of the interruption in production of any product six months in advance, or as soon as possible in the event of an unplanned stoppage. Manufacturers that fail to report this information would be subject to civil monetary penalties. This early warning system would allow the agency to communicate more effectively

with manufacturers and others in the supply chain to plan for pending supply interruption. The early warning system should be the cornerstone of congressional action to address drug shortages.

Confidential Notification for Single-Source API

In addition, information that can make drugs vulnerable to shortages, such as a single API source, is also frequently unknown beyond the manufacturer. This information is, and should be considered proprietary, but this lack of transparency hinders the development of contingency plans for vulnerable drugs. A requirement that manufacturers confidentially notify FDA when there is a single source of API may help the Agency work with manufacturers to identify backup sources should supply issues arise.

Continuity of Supply Plans

Related to the reporting or an early warning system, FDA could work with manufacturers to develop continuity of supply plans. The current lack of transparency acts as a significant barrier to this type of collaboration. With increased information exchange, contingency plans could be developed that include countermeasures such as manufacturing redundancies or backup supplies; more effective communication among FDA, manufacturers and others in the supply chain; and finally, development of plans that utilize production capabilities of other manufacturers either here in the United States or abroad to ensure availability of a drug in short supply.

In 2010, FDA worked with APP Pharmaceuticals to help alleviate a shortage of propofol, a widely used anesthetic preferred by anesthesiologists because of its excellent safety profile compared to other available drugs. By enabling the company to work with its German counterpart to import the drug, FDA was able to substantially improve product availability after the shortage occurred. Using this example, if an acceptable foreign alternative could be identified before a shortage occurs through establishment of

continuity of supply plans for vulnerable drugs, then importation could be expedited and the negative impact of a specific shortage on patient care could be minimized or averted. Importation represents an extreme example of contingency planning. In its simplest form, manufacturing strategies that include collaborating with other manufacturers, establishing back-up suppliers of raw materials and APIs, and creating alternative production capabilities that can be used as countermeasures would be a significant step forward to combating drug shortages. Contingency planning by companies producing drugs critical to patient care must be a standard of practice. S. 296/H.R. 2245 support the development of contingency plans for drugs that are vulnerable to shortages.

Incentives

Further, shortages are occurring overwhelmingly among generic injectable drugs, where production processes tend to be more complex than their solid dosage counterparts. Low margins for these expired patent products coupled with complex manufacturing processes may lead some manufacturers to abandon production of these drugs altogether in favor of products with higher profit margins, thus reducing the number of potential suppliers of products critical to patient care. A way to offset this problem may be to explore incentives to encourage manufacturers to either stay in the market or enter the market with a new product line. More study needs to be conducted to validate the need for incentives. In addition, other stakeholders in the supply chain need to provide input on the economic factors that influence production capability.

Require development of an expedited approval pathway for pre-1938 drugs.

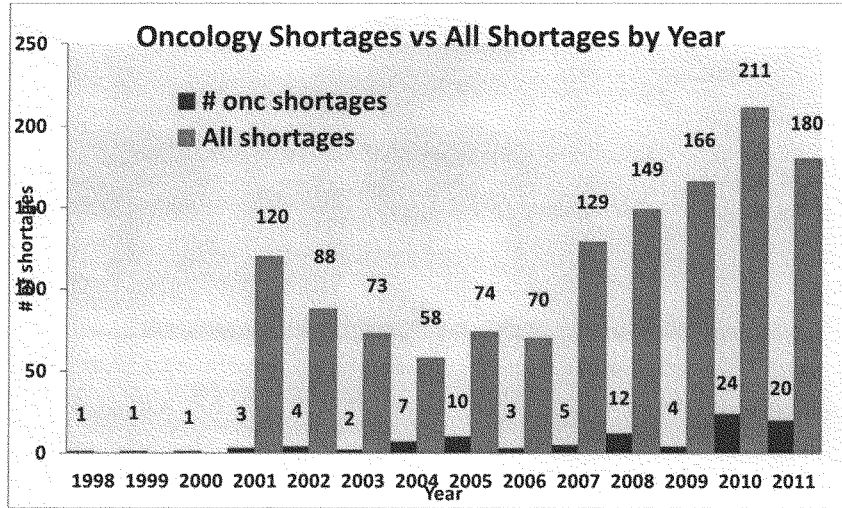
FDA must find a way to abbreviate and prioritize approval processes for existing therapies that are unapproved, but widely used and essential for patient care. For these drugs, the agency should work with manufacturers to fast track their approval for the U.S. market, especially in cases where the

potential exists for those drugs to fall in short supply. Barriers to manufacturing and marketing these drugs must be minimized in order to foster production and availability of these drugs.

Conclusion

Unfortunately, there is no single solution that can prevent the occurrence of all drug shortages. The complexity of manufacturing processes, the requirement for safe and high-quality products, and globalization of the pharmaceutical supply chain all contribute to fluctuating product supplies that may never be entirely eliminated. However, there are critical steps that Congress, FDA and other stakeholders can implement to ensure that patient care remains available, safe, and effective. While the adjustments and compromises required from all stakeholders are difficult, the need for change is critical. First and foremost is the need for increased communication and transparency.

ASHP, along with several other stakeholder groups has been working collaboratively with Congress and supply chain stakeholders to develop solutions to the drug shortage problem. As indicated before, there is bipartisan legislation in both houses of Congress. Passage of legislation that provides additional authority to FDA is a step in the right direction. In the long term, FDA will require additional resources to best address this and other issues that impact the quality and safety of drugs.



Mr. GOWDY. Thank you, Dr. Thompson.

I will recognize myself for questioning.

Dr. Hudspeth, what percentage of drugs used to treat childhood cancer are generic?

Dr. HUDSPETH. Over 90 percent of the drugs that we use to treat and cure childhood cancer are generics. And I understand we have to be good stewards, just like you all, of the budget, and I can imagine your concerns. We are talking about our concern about prices and increasing costs. But you have to understand if you look at generic injectable cancer drugs, they represent only 2 percent of the entire budget spent each year on cancer chemotherapy drugs. So even by improving this, you are only looking at a very small overall increase. They make up 0.5 percent of the total cost for cancer care each year.

I have a young man who is an honors college student whose leukemia has relapsed. He needs a drug to start tomorrow. But we have an adult in our institution who is also due to start a regimen that needs the same drug. I don't know who we are going to be able to treat tomorrow. And that is real. That is me getting off the plane yesterday calling, emailing back with my home institution. So this is real.

Mr. GOWDY. Are there particular types of incentives that would encourage manufacturers to enter the market and stay in the market?

Dr. HUDSPETH. There have to be incentives, I believe, for production capacity. If you notice, the drugs primarily in shortage are injectable drugs. They are typically more complex to produce than a pill and typically, in a company, they have to dedicate an entire production line to, say, that one drug. So there are some real things about injectables that are different.

So I think there has to, at the end of the day, be some form of incentive for the companies to be able to run 24/7 production lines. Have a contingency plan. That is a current problem, they really do not have contingency plans, and there are some measures in H.R. 2245 that do recommend that the FDA require contingency plans for single makers of critical drugs.

Mr. GOWDY. Dr. Hudspeth, you were good enough this morning, and again in response to a question, to mention the untenable choice that a physician would have to pick among patients. Without violating the confidences of any of your patients, has the drug shortage caused you to change the way you practice medicine in any other regards?

Dr. HUDSPETH. Yes. We have had to start chemotherapy regimens sooner than normal. Typically, we require that a patient recover from their prior chemotherapy regimen to a certain level to be safe enough to start the next cycle. We start a patient sooner than normal just out of fear that if we wait another week there simply won't be drugs available. And this has come up. Cytarabine has been a drug that is mentioned a lot in the press. There is absolutely no substitution for Cytarabine. It is in every single regimen in order to cure AML.

The other issue is medical errors. When the pharmacists—a cardinal rule of pharmacy safety is you stock one concentration of a drug. That way everybody that makes that drug day in and day

out, they understand this is what we are working with. Well, now people are scrambling. We are just happy to have the drug. So you have five different concentrations. People are unfamiliar. You are going to absolutely increase the amount of errors.

Mr. GOWDY. If the pricing problems are not remedied, what do you see the future of drug crises being? Drug shortages. Will they be exacerbated?

Dr. HUDSPETH. Absolutely. Right now it feels like practicing medicine in a Third World country. I never dreamed of a day where I would have to spend hours on end that I should be at the bedside talking to the families or with the kids, but now I am on the phone with our pharmacists and the other oncologists trying to figure out alternative treatment plans and who gets what. It is taking up time that could be used in so many other ways. And at the end of the day, if it is your family member being treated for cancer, do you want me worrying about if we have drug or not, or do you want me thinking about taking care of you?

The other drug shortages that are mentioned are antibiotics, antivirals, nutrition solutions. Well, my patients all need those too, right? So one of the consequences of chemotherapy is you can't eat and you get a heck of a lot of infections. So we have had significant issues, too, where we simply haven't even had the support of care drugs to treat them, to support them through the therapy when we do have the therapy.

Mr. GOWDY. I want to ask a question, and I will give the other four gentlemen a chance to answer with respect to negatively impacting clinical trials. I only have 30 seconds, so if you could give a quick response if this is an area that you feel comfortable talking about. Dr. Hudspeth already told us in the actual practice, with respect to research, the drug shortage, how is it impacting clinical trials?

Mr. OKON. Mr. Chairman, I can just say that, hearing from oncologists all across the country, it is a real problem because the problem is the trials in many cases, and I understand in talking to some of the manufacturers trials have actually had to be stopped because of the unavailability of a particular drug.

Mr. GOWDY. My time is up. I would now recognize the gentleman from Illinois, the ranking member of the subcommittee, Mr. Davis.

Mr. DAVIS. Thank you, Mr. Chairman. With your indulgence, I know that the ranking member of the full committee has another assignment that he needs to be engaged in. I would like to switch places with him.

Mr. GOWDY. Of course. The ranking member of the full committee, Mr. Cummings.

Mr. CUMMINGS. Thank you very much. I want to thank the gentleman for yielding.

As most of you know, since this summer I have been looking into the role of so-called gray market during drug shortages. My investigation has focused on determining where some of the companies obtain drugs in critically short supply and how much they mark up the drugs that they sell to hospitals and other health care facilities.

My staff has heard from countless health care providers about the constant unsolicited offers for drugs on the shortage list, but at prices that are nothing short of price gouging. For example, one

company offered to sell a cancer drug for over \$990 per vial, more than 80 times the price a hospital normally pays for it. I recognize the incredible predicament that this puts our health care providers in. I do not envy their choices of either delaying or denying treatment until drugs become available from a reputable distributor or paying huge markups on the drugs.

Dr. Hudspeth, by the way, I really appreciate your passion; I feel it. When your hospital no longer has a needed drug available, what steps does your hospital undertake to obtain a needed drug? I am very familiar with chemotherapy. It is done in cycles. So I guess you might have enough to start a cycle but not enough to finish a cycle, so I guess you don't start it, is that how that works?

Dr. HUDSPETH. That is correct. And basically part of our committee meetings each week is looking at who, throughout the institution, is due for what and how much that will entail and how much supply is on hand. Our institution does not deal with the gray market. We have certainly been approached. Our policy is we do not deal with them. And I am continually indebted to the wonderful pharmacists at our institution that have spent an amazing amount of time speaking with manufacturers, trying to get drug. It has really been an all-out effort.

Mr. CUMMINGS. Do you think there are a lot of other health care facilities in, say, South Carolina that refuse to deal with the gray market folks?

Dr. HUDSPETH. It is hard to say. I could see how the pressures could get to you. It is very easy to say, sure, we don't want to deal with the gray market, but at the end of day, when you know there is a patient on the other end, you can see where that temptation could come along. So I don't know of any instances for sure, but I know that the threat is out there.

Mr. CUMMINGS. To all of our witnesses, can you explain to me how it would be potentially harmful for a patient to be given a drug that has changed hands many times?

Mr. OKON. I can just say, Mr. Cummings, that the amazing thing about the distribution system, it is very regulated and you understand the pedigree of the drug, which is very important. So the problem is when you have some distributor that you don't know at all that basically sends a fax, I hear from practices all the time that they get faxes about drugs, they get emails about drugs, and you don't understand the pedigree of that, again, I am not an oncologist, but I think the problem is administering that drug, which I don't think my wife would be in favor of, as an oncology nurse, administering that drug without a set pedigree is very dangerous because you are talking about extremely, extremely potentially toxic medication.

Mr. CUMMINGS. I was just thinking, going back to you, Dr. Hudspeth, if you have somebody with cancer and they face life or death, and the patient knows, people begin to research.

Dr. HUDSPETH. Absolutely.

Mr. CUMMINGS. Have you ever come into a situation where somebody says, wait a minute, doc, we know you don't have the drug, but we have done some discovery here and learned that XYZ Gray Market Co. has it. We don't care what it costs, we will pay. Do you run into those kinds of situations?

Dr. HUDSPETH. It is getting to that point, and 85 percent of the children I take care of are Medicaid funded. I am a native South Carolinian, but we are a poor State, and part of my passion is that these kids have to have treatment no matter what background or circumstances they come from.

So what I am afraid of is you are going to set a hierarchy of treatment. If you have the money to obtain some drug, travel to Canada, you can get treatment, but the folks who don't have the finances to do that are left behind. And who is that going to be? It is going to be the kids.

Mr. CUMMINGS. Dr. Thompson, are your members concerned with the safety of such drugs that circulate in the gray market?

Dr. THOMPSON. Yes, sir, they are, and this has been a phenomena that they have dealt with for a very long time. The notion of receiving faxes came up and this does happen. When there is a shortage, our members get contacted with offers to provide these drugs at exorbitant prices.

But it is really not the price issue so much. Not that that is not a factor. It is the safety issue. When everybody knows that there is a profound shortage of a drug, they are asking the question, Where did these distributors get the product? Is it safe? How was it stored? What is the pedigree? So it raises real concerns.

Many pharmacy departments in hospitals will not buy from the secondary market at all. But, as others have mentioned, sometimes there is no other option.

Mr. CUMMINGS. Thank you, Mr. Chairman.

Mr. GOWDY. I thank the gentleman from Illinois.

The Chair would now recognize the gentleman from Arizona, the vice chairman of the subcommittee, Dr. Gosar.

Mr. GOSAR. As a health care professional, I look at symptoms, and I don't treat symptoms, I am looking at what the disease process is. So I want to ask you yes or no down the road, is the gray market a symptom or is it the disease?

Dr. HUDSPETH. It is a symptom.

Mr. KALMANS. It is a symptom.

Mr. OKON. Symptom.

Dr. GOTTLIEB. It is a consequence, it is a symptom.

Dr. THOMPSON. Symptom.

Mr. GOSAR. Thank you. So what we really need to do is concentrate back on the cure back to the disease process. So it seems to me like we have something going wrong here and we need to get back down to it.

There are some clear problems in the way that we are addressing the drugs themselves. Very quickly, can you give me an idea on how we can do this? Because it seems like arbitrarily isn't allowing bureaucrats to set, it seems anywhere the Federal Government is involved we have problems, and when we have somebody outside the business of medicine dictating to medicine, we tend to get bigger problems.

So, real quickly, is there a way that you can see that we can simplify this and let the markets work, but also have some control, very simple, but also allow the patients to have skin in the game? Doctor, what do you think?

Dr. HUDSPETH. I think there is going to have to be an allowance for the market to work, for the prices to reach market value. There are clearly still some drugs that would benefit from regulation that will allow us to treat the greatest number of patients overall. So it may not be that we abandon some of the tenets of the MMA altogether, but I think it is clear that in the generic injectable industry it is a very different beast, so probably there need to be allowances made differently for these types of drugs.

So is it that we grant exclusivity, even though it is a generic drug, for a certain period of time? Do we offer financial incentives for the production? So is it maybe focusing on incentives for production and good manufacturing process, which helps everything, perhaps maybe even over just the price of the drug itself? And that may be able to be better controlled when focusing on overall incentives to the company.

Mr. KALMANS. There are several different kinds of solutions to look at. I will give an example of one. We know there is a rapid price decline when drugs go generic, and right now they are limited from price increases to a maximum of 6 percent based on the ASP legislation. One idea might be to look at changing for drugs that have been generic for a couple of years, changing the ASP to be ASP plus 20, to allow prices to have greater fluctuation to make sure that the profits can continue to be earned and generics are priced at a market price that is palatable.

Mr. GOSAR. I know we are going to put up a slide before Mr. Okon does, but this actually shows just one drug, Carboplatin, that you can see how much it has decreased. So this gives you an example of one idea.

Mr. Okon.

Mr. OKON. I think, Dr. Gosar, that what has to happen is I think on the manufacturing side there has to be some clear incentives, whether we look at tax credits or something else that basically incents not only manufacturer coming into the market, a manufacturer staying in the market over a period of time. And I think that it is very clear on the reimbursement side we need to do something differently and we need to do something immediately with these drugs.

You have to realize that some of these drugs are what we talk about as being even underwater, that their cost is higher than the reimbursement for Medicare right now. And because Medicare and cancer care basically accounts for 50 percent of the cost, it has an inordinate influence on private payers as well, too.

So this is having a consolidation factor. We are seeing consolidation on the provider side; we are seeing consolidation on the manufacturing side. So I think we need to do something. And one of the things is when a new product comes into market and there is not an established ASP, it is basically WAC plus 3, wholesale acquisition cost plus 3. Maybe we need to do something like that in terms of on an immediate basis.

But I have to say this. Whatever we do, we have to put the politics aside right away. We have to get in a room and come up with some solutions because this is really a crisis.

Mr. GOSAR. Dr. Gottlieb.

Dr. GOTTLIEB. Yes, I think we need to go to a different pricing scheme, and I advocate my written testimony, looking at the wholesale acquisition cost, which might allow producers to take and sustain price increases that would allow them investment facilities. I think the regulation of the facilities needs to be uniform so you don't have the cost of goods going up for one manufacturer but not up for others. I think there are schemes we can think of that would allow some limited rebranding of these products so that manufacturers could make representations about the manufacturing quality that might allow them to either sustain higher prices in the market or get automatic government purchasing for programs like VA or others.

The other thing that I think this committee might think about is the fact that there is a significant portion of the manufacturing capacity that is offline right now, that has been taken offline by the Food and Drug Administration. If you look at just the first five companies that the ranking member mentioned, APP, Bedford, Hospira, Teva, Sandoz, that is probably 80 percent of the parenteral market, and you might have upwards of almost 20 percent of the manufacturing capacity of those companies offline right now, if I am just thinking of a couple of those companies. Those manufacturing facilities are going to be coming back online, and as they do they are going to hit FDA with literally hundreds, if not thousands, of supplements, and the question is is the regulatory agency prepared to approve those and evaluate them in an efficient fashion.

Dr. THOMPSON. Mr. Davis mentioned involving manufacturers in this process. My organization has been researching drug shortages for 10 years now, and one thing we do is we conduct a root cause analysis and we ask every stakeholder in the supply chain what is causing this, what would help, what is the issue. Getting insights from pharmaceutical manufacturers is a challenge in terms of what are the issues, what would the incentives be, and we would really like to get some answers to those questions from the manufacturers' standpoint.

What specific incentives could be provided to you by the Federal Government to help you stay in this business, get in this business, ramp up supply. I would strongly encourage this committee and others to have a discussion with pharmaceutical manufacturers and see if you can get some better sense from their perspective what the incentives would be that would help them be in these businesses that are so critical to our patients.

[The prepared statement of Hon. Paul A. Gosar follows:]

Congressman Paul Gosar

Oversight Subcommittee on Health Care, District of Columbia, Census and National Archives

November 30, 2011

“Drug Shortage Crisis: Lives are in the Balance”

Opening Statement TO BE SUBMITTED FOR THE RECORD

Chairman Gowdy and Ranking Member Davis, on behalf of medical providers in rural Arizona, I thank you for calling this subcommittee together for this crucial hearing today. I also thank the witnesses for taking the time away from their careers in medicine, patient advocacy, and policy research to share their perspective on the issue of prescription drug shortages in our country. I do not think it is an exaggeration to say that lives are in the balance and we must band together to find common sense bipartisan solutions to the problem.

Hospitals and medical providers across my district have shared disturbing stories about how lack of access to anesthesia, pain medication, and even chemotherapy and other cancer drugs cannot be obtained consistently and are frequently subject to shortages or back orders. According to a study by the American Hospital Association (AHA), these shortages are having a real life impact on sick patients every single day. While dedicated providers are valiantly trying to make up the difference when critical drugs go missing, the AHA survey indicates that 82% of hospitals have had to delay treatment on account of drug shortages. 78% have actually had to ration drugs – or be forced to consider the possibility of turning away patients. As a medical provider myself, I know that the responsibility to care for patients is a sacred one that doctors and nurses do not take lightly – but if we cannot come together to address this drug shortage problem, we are facing even more serious lack of access to care. I cannot stress enough how critical it is, especially for rural areas like the ones I represent, to address this.

While scenarios of doctors sitting around a conference room, forced to decide which patients will receive critical treatment that day and which ones will have to wait is shocking enough, the drug shortage problem also has financial implications for hospitals which are already struggling to day by day to meet their bottom line and keep their doors open. An emerging regional hospital in my district has shared with me their consistent difficulty in obtaining, for example, anti seizure medications, epinephrine which is often used in the case of cardiac arrest, and a variety of pain medications desperately needed to recover from surgery or to administer palliative care to terminally ill patients.

Despite the clear implications to daily patient care, these drug shortages are financially burdensome on the hospital. At times, these drugs are only obtainable in large doses, leaving extra medication that cannot be used on another patient and ultimately must be discarded. In addition, the man hours needed to hunt down drugs under shortage are extensive; staff resources are being used on fixing this problem when pharmacy management is already demanding enough. The financial instability this drug shortage crisis has caused is simply one more burden these hospitals should not be forced to bear.

I am concerned about the apparent effects that price controls under the Medicare Modernization Act of 2003 have had on the availability of generic, inject able drugs -- in fact this portion of the legislation seems to have had unintended consequences leading to today's crisis, which is often the case with central government planning. While this policy has caused manufacturers to leave the generic inject able market in droves, I am also concerned that the FDA's current regulatory regime may be erecting barriers to solving the problem. When market supply dips, a manufacturer seeking to enter the market and produce the needed drug is greeted with a pile of paperwork and list of inspections from the FDA before the drugs can hit the market. No one disputes the need for safety and consistency in our drugs, but surely more can be done to allow responsible drug manufacturers to fill crucial gaps in our drug supply.

I look forward to hearing more from the witnesses on how to address this crucial need in our health care system.

Mr. GOWDY. I thank the gentleman from Arizona.

The Chair would now recognize the gentleman from Illinois, Mr. Davis.

Mr. DAVIS. Thank you very much, Mr. Chairman. And again I want to thank you for your indulgence relative to Mr. Cummings' need.

As a member that represents over a dozen safety net hospitals in the 340(b) drug discount program, I am extremely concerned about the unsubstantiated suggestions linking 340(b) and drug shortages. It is hard to believe that this small, but critically important program is of the magnitude to affect the drug market in this way.

Dr. Thompson, can you cite any specific evidence that the drug shortage is significantly affected by the 340(b) program?

Dr. THOMPSON. Sir, in our research we have seen no evidence to support that claim and I personally don't find it to be highly likely. The 340(b) program is a very small program, it makes up about 2 percent of the national drug market, so it just doesn't seem that likely.

Mr. DAVIS. Let me ask if any of the other witnesses have any evidence that you have come into contact with or unearthed that would suggest any difference.

Dr. GOTTLIEB. Manufacturers feel otherwise. I mean, the 340(b) program has been significantly expanded and drugs are started to get diverted into that program and sold at a much lower cost, and to the extent that the program that you now see arbitrated in the marketplace, where hospitals are literally buying out community oncologists and other providers to try to capture the drug revenue and move it toward the hospital environment, where they could earn the money on the spread for what they are buying the drugs for versus what they are billing Medicare for, you are seeing a growing proportion of the overall drug utilization start to shift to that program. I think it creates a lot of uncertainty in the marketplace and just more impediments to people making investment decisions.

I sympathize with the idea that we need to subsidize these hospitals. I have worked at some of these hospitals that are beneficiaries of this program. I wish we could find ways from a policy construct to subsidize them directly, rather than doing it indirectly by this sort of arbitrage on the drug revenue.

Mr. OKON. I think, Mr. Davis, first of all, the 340(b) program, the intent of it is a wonderful program. What it is meant to do and taking care of indigent patients and patients who can't afford care is absolutely right-minded. I think we just have to keep in mind, though, that ASP, because 340(b) discounts and Medicaid rebates as well, too, are not included in the calculation of average sales price, that when we look at ASPs going down, that is not reflective of what the manufacturers are actually paying.

So in no way, shape, or form, knocking either, obviously, 340(b) or Medicaid, but I think we have to be aware that there are other pressures downwards on the manufacturer to give up-front discounts and rebates that we just have to be aware of are actually increasing. If you look at the number of DSH hospitals that are qualified for 340(b), it has expanded from about 519 in 2004 or

2005 to the estimate is close to 3,700 next year. So we just have to be aware of the impact that these discount and rebate programs are also having on ASP. That is my point.

Dr. HUDSPETH. I think it is important to note, though, for children's hospitals, essentially everyone is going to be part of a DSH program. Children's hospitals historically always serve a tremendous portion of patients who are funded by the Government, so it is important to realize the impact on kids. I agree with the representative from the HSP. As I was reviewing it, I see the rule of twos, 2 percent. It only concludes 2 percent of all drugs. The other thing is that if you look over the past 2 years, any of the drugs that have been on shortage, none of those have been on the so-called penny pricing list for the 340(b) program.

Mr. DAVIS. Thank you all.

Dr. Hudspeth, let me ask you, you mentioned earlier that your institution does not deal with gray markets.

Dr. HUDSPETH. That is correct.

Mr. DAVIS. Could you tell us why and what dangers there might be inherent in that kind of transaction?

Dr. HUDSPETH. Absolutely. It has been well outlined by the other folks that you simply don't know what you are getting. You really have no idea how to really know, has the drug been stored properly, has it expired, does it really contain what you think it contains? And with that type of uncertainty, patients undergoing chemotherapy treatments are fragile; we push them to the limit. Then if you then expose them to something that may be a completely different drug altogether, and maybe it is not even drug at all, there could be real inherent dangers in that. You simply don't know what you are getting.

Mr. DAVIS. So the risks simply are not worth the costs.

Dr. HUDSPETH. Absolutely.

Mr. DAVIS. Thank you very much, Mr. Chairman.

Mr. GOWDY. I thank the gentleman from Illinois.

The Chair will now recognize the gentleman from Connecticut, Mr. Murphy.

Mr. MURPHY. Thank you, Mr. Chair, and thank you very much for this incredibly important hearing.

According to probably the most comprehensive FDA study that we have, the leading cause of these drug shortages are quality problems during manufacturing. I think the study showed that about 54 percent of the shortages studied were due to manufacturing problems.

I will pose the question to you, Dr. Thompson. You mentioned that there is a multitude of causes here, but while we spend most of the time here talking about pricing, the data at least coming out of the FDA suggests that the biggest problem is manufacturing. The information that you have collected thus far, does that back up the idea that the biggest cause here is manufacturing problems?

Dr. THOMPSON. Yes, sir, the 54 percent number is the one that you know has been backed up by the research we have done over the years on the issue.

Mr. MURPHY. That study goes on to further say that outside of that 54 percent that is due to product quality and manufacturing issues, 21 percent is due to delays in capacity issues, 11 percent

is due to discontinuations, 5 percent are due to raw material issues, 4 percent are increased demand because of another shortage, etc.

None of the reasons that the FDA cites are due to pricing issues, and certainly none of them are related to 340(b), so maybe, Mr. Okon, I will ask you the question, and I would be glad to hear comments from others. Is this study wrong? And if it is not, how do you square the focus that we have heard on this panel on pricing when the FDA suggests that it is much more due to underlying manufacturing issues?

Mr. OKON. No, I think that is absolutely right. But I think what you have to understand, Mr. Murphy, is that what we have done is we have consolidated the manufacturing market. So we have looked at, and actually I have a couple of charts looking at ANDAs. That is an abbreviated new drug application that a manufacturer of a generic has to file. It is an abbreviated process.

If you look at those numbers of new ANDAs, I think we put up Carboplatin before, I can show you that 17 have been filed for most form strains. There are only three or four manufacturers in the market now. So you can look at double digit number of ANDAs have been filed, but if you look at the number of available manufacturers now for any type of product, it is usually one, two, or three.

So what happens is that, as a result of that, any manufacturing glitch, any quality glitch, anything that the FDA said, which is absolutely right, it is happening on a much smaller base. And what happens, typically, is you take the whole production line, other products off cycle. So that is our problem. The problem is that it is economic and it is not using reimbursement as an excuse. It was driven by that, that is the root cause, but because we have consolidated the manufacturing market down now, any kind of a glitch, regulatory, quality, supply glitch, is going to be magnified.

Dr. GOTTLIEB. The other issue is, it is true that the agency has gotten more vigilant in recent years around the manufacturing of parenteral, the injected products, particularly looking at foreign sites. After years of criticism that it wasn't doing enough to look at the overseas manufacturing facilities, it has gotten more aggressive, so it has stepped it, it has brought regulatory actions against a lot of the manufacturers in this space, and that has prompted them to have to take remediation that has increased the manufacturing cost, increased the cost of goods. I think the pricing issue comes into play when they can't take price increases to reflect their higher cost of goods. So rather than continue to market the products at a loss, more manufacturers are choosing to get out of certain lines of business.

Mr. MURPHY. So let's take the pricing issue, because there has been an incredible benefit of generic drugs coming onto the market and the very justifiable incredible decrease in cost that comes along with it. So if you believe that pricing is the cause here, how do you adjust upwards for shortage areas without adjusting upwards for drugs that aren't shortage drugs? And then, secondarily, how do you do that in a way that doesn't create an incentive for shortages? How do you create an incentive to make the stuff that you really

need without creating a reason for people to declare a shortage in order to get a little extra benefit?

Mr. KALMANS. A couple of comments. One is the FDA paper I think is accurate, but the FDA regulates manufacturing, so the FDA is commenting on its mandate, not commenting on pricing because it is outside of their mandate. I would like that noted.

Second, if you look at the data, the drugs that are in shortage tend to be the lower priced generic drugs, not the higher priced generic drugs. They aren't manufacturing shortages cited for many high priced generic drugs, just the low priced ones. So I think that is evidence that points in the direction that pricing is a factor.

Third, I mentioned earlier and I will mention briefly again, I think that after a drug has gone generic and you have taken a price decline over a period of time, there needs to be a rebalancing so that drugs, rather than having the bottom fall out, are able to move back up. So I think after the drug has been generic for 12 to 24 months, then there needs to be something put in legislatively to allow that price to float more freely.

Mr. MURPHY. Thank you very much.

Thank you, Mr. Chairman.

Mr. GOWDY. I thank the gentleman.

Given the wonderful resources we have and the five witnesses, we are going to have a second round of questioning. It will be quicker, if your schedules can accommodate it. If they cannot, we understand, but this is a rare opportunity for us to talk to people who are experts in the field. So, with that, I would recognize the gentleman from Arizona, Dr. Gosar, if he has any followup questions.

Mr. GOSAR. I do.

Dr. Hudspeth, you really brought this to a tee, that there is this oncology, these drugs that are a problem right now. But there are also anesthetics and antibiotics. So this is a multifaceted problem. And it seems to me that we have a number of problems. It was just alluded to here that instead of having a wider variety of manufacturers, we are down to several, two or three. So when there is a glitch we have a problem.

Number two is we have problems with the FDA. And I want to get back to you, Dr. Gottlieb, in making the FDA being a little bit more nimble. You know, instead of being antiquated to shut everything down, they are starting to work with industry. But it seems like it is the rules regulations that have really—and we need them, don't get me wrong. We need them, okay? But we need to have a constant vigilance about applicability and how things fluctuate and work. Nothing follows an equation all the way across the board, just like every cancer patient isn't treated the same way.

So to me it seems like the system itself is all out of whack. And not just reimbursement rates are not the key here. And I am tired, I like going for the surgery, okay? Go right to the point. We have to do something different than what we are doing. It is not working. It is definitely not working and we need to revamp this.

And we need to openly talk about the business of medicine, frankly. I am great at this because I am a dentist, okay? I am one of those people who can talk to you. There is nothing wrong about

making a profit. You have to make a profit in keeping your doors open. It, frankly, has to come about.

So when I see these, there is another part of this equation that bothers me. When you are having to huddle around deciding who gets what, there is a liability issue, is there not, doctor?

Dr. HUDSPETH. Absolutely. We sit around and say, Do we need to call the hospital risk management? Should we have ethics committee here? How do you begin to make these decisions? Absolutely.

Mr. GOSAR. Dr. Gottlieb, I want to go back to you and your background, particularly with the FDA. I know that when we see a glitch in manufacturing, the FDA tends to be very recalcitrant in shutting everything down, instead of being more interactive and maybe looking at one part of that. How do you see the FDA changing a little bit that could help this scenario? Not just with the cancer drugs, but all the way across the drug shortages.

Dr. GOTTLIEB. Right. Well, I think that the agency has and had legitimate concerns around a lot of the remediation that its forced and some of the capacity that is frankly offline right now is a result of the FDA actions. Contribution from manufacturing process should never get into the sterile injectable drug, and that was a lot of the problem with some of the things that they shut down.

Thinking of a couple things that the agency could do, the agency, right now, prioritizes the supplements for drugs when they approach shortage status or when they are in shortage. I think it could prioritize all the supplements, the manufacturing supplements, for all the sterile injectable drugs, because what could happen is a supplement can sit in the queue now and 2 years from now that drug will be in shortage.

But I believe some of the drugs that are currently in shortage might, one of the contravening factors is because supplements might not have been reviewed in a timely fashion 1 or 2 years ago; and to do that the agency is going to need to put more chemist reviewers on these supplements. I think as part of the generic drug user fee program that is being considered by this Congress, you could prioritize resources directly for all the sterile injectable drugs, and not just segregate them once they get into shortage.

I think you can think about changing the regulations to make it easier to make manufacturing changes and improvements and undergo remedial steps without having to file supplements every time. It is a very cumbersome process.

And then the other problem here is that the agency, and the manufacturers, for that matter, don't understand the root causes of a lot of these problems, so what happens is entire factories get shut down, entire product lines get refurbished. And I think there needs to be more work done to try to understand how some of these problems arise in the first place. There is just not a lot of intelligence either on the regulatory side or on the manufacturing side, for that matter.

Mr. GOSAR. Dr. Hudspeth, you know, I am from Arizona, rural Arizona, and it is a little bit different when it is coming from hospitals in rural America, because we are at another disadvantage, much more than the metropolitan. Now we are talking about surgeries that are being rescheduled, putting people on a prioritization

based upon the drugs that we have available for anesthesia. Do you even see that from the standpoint, from outlying areas as a problem?

Dr. HUDSPETH. Absolutely. We have actually shipped drug to another children's hospital in our State because they didn't have any Cytarabine for a little boy with AML. So we try to band together and help other folks when we have the capacity to do that. But we are hearing widespread shortages at many, many other children's hospitals.

Mr. GOSAR. So I guess what my whole point is we are seeing a symptom again. This may be just a small choreographed part of drugs, but there is more coming, and that is the biggest problem.

Dr. HUDSPETH. Exactly. There is no reason to think this is going to get any better any time soon.

Mr. GOSAR. Thank you.

Mr. GOWDY. I thank the gentleman from Arizona.

The Chair will now recognize the gentleman from Illinois, Mr. Davis.

Mr. DAVIS. Thank you, Mr. Chairman.

Mr. Okon, you assert in your statement that Medicare is the root cause of the drug shortage which have affected oncology drugs. However, a recent Health and Human Services study entitled, The Economic Analysis of the Causes of Drug Shortages, noted that 54 percent of the shortages are caused by production and quality problems. What is the basis of your assertion?

Mr. OKON. Well, I think the FDA study, as I told Mr. Murphy, is absolutely, positively spot on, Mr. Davis, in terms of it being right now due to a lot of manufacturing quality and problems, but again what has happened here is that when we changed reimbursement, and the change was really well intended, part of it was the fallback of the falling of the execution on CMS's part, but the nature of ASP and the price regulated nature around that, we just have to realize what it has done is we shrunk the manufacturing base.

So when you look, Mr. Davis, at how many manufacturers were in the product, and remember these products were on the market well before MMA, so when you shrunk that down, what happen is you shrink that base. Now, when you have a manufacturing problem you have a regulatory problem, you have a quality problem, even a supply problem. You have so few manufacturers that you have a huge problem associated, and that is why I think we are getting so profound in terms of the number of shortages, because our manufacturing base has shrunk down. And I applaud you and I think you should get the manufacturers in on the generic side, and we all need to come around and talk and put politics aside and just solve the crisis.

Mr. DAVIS. Are you saying that HHS is a little behind?

Mr. OKON. Well, Mr. Davis, I probably am saying HHS is a little behind. Actually, if you look at the HHS report, what was kind of interesting about that is they started talking about the economics and then they kind of stopped. So I am wondering if somebody edited that portion of the report out. But I think that it is a problem.

Mr. DAVIS. Dr. Thompson, how would you respond to that?

Dr. THOMPSON. Clearly, the FDA data is accurate and we do think the economic factors need to be looked at. One thing that we have learned over a decade of looking at shortages is that there is no single root cause of these shortages; they are in the tens and twenties and it runs the gamut of things.

We have been very supportive of the concept of looking at the range of potential economic factors that have happened, that are being suggested, and we have tried to sort of get insights from manufacturers, wholesalers, GTOs and others that really are the critical part of that supply chain around what some of those may be to help solve the problem, but I think a more substantial conversation with these various groups needs to happen so we better understand what the economic drivers are.

Mr. DAVIS. Let me ask if any of you are saying that our regulatory activity really needs to be stepped up and become perhaps a bit more direct.

Mr. KALMANS. I like the idea of directness. One of the things that I think is possible here is, when you are citing manufacturing issues, these issues aren't apparently related to high-cost generic drugs. They are having no problem making enough Gemcitabine and Docetaxel; it is the ones that are low-cost. Same manufacturing plant. So manufacturing issues could just be defined as capacity constraints. So I think it is a question of how you define things as a regulator.

Mr. OKON. And I just want to add to Dr. Kalmans' remarks is you have to understand some of these generics we are literally talking about a dollar, under a dollar to manufacture a sterile injectable. So it is not like stamping out a generic tablet; it is a very intricate process.

Mr. DAVIS. Well, the next time I am talking with any of them, I am going to suggest that maybe, rather than dancing, that they need to come out and say here is what we need to do and let's do it.

Thank you, gentlemen, very much, and thank you, Dr. Hudspeth.

Mr. GOWDY. I thank the gentleman from Illinois.

If we were looking at this like a trial, I would say you have proven beyond a reasonable doubt that there is a drug shortage. You have proven beyond a reasonable doubt that it is a crisis. You have proven by clear and convincing evidence that there are a number of causes.

So I want to do this. Dr. Hudspeth, I asked you this morning and I am going to ask you to do it again. I want you to assume that you made the grades I made in college, and not the ones you made, and that you weren't in medical school, but that you found yourself in a legislative body. What is next? There is no need to continue to have hearings on whether or not it is an issue. You can beat a dead horse. It doesn't hurt the horse, but it doesn't do any good. So what is next? Who should we be asking questions of and what questions would you ask if you were sitting here?

Dr. HUDSPETH. Sure. I think there has to be a strategy group that looks at pricing and pricing options. And I am not an economist, so that is going to require all those folks to be involved. Looking at pricing strategies and how you deal with that.

But then the second fold of that, yes, we are going to need to give incentives; yes, we are going to need to make it profitable to make generics. But they can't cry wolf over and over again, okay? So they cannot have continued manufacturing problems. So there is going to have to be some sort of three strikes you are out policy. Incentives and those things are only so good as long as you can prove that you can keep up with GMP.

And then I think the second thing is contingency planning. That is what we all have to do. In school you have to have a fire escape plan. And here we have lifesaving drugs with no contingency plan and a single manufacturer, and I think some solid planning for A through Z, what you do when you go offline, how do we fill that in.

Mr. GOWDY. Mr. Kalmans.

Mr. KALMANS. Well, there has been stockpiling of medicines for defense in the past. It could be an idea to look at providing incentives to stockpile a generic injectable drug stockpile. Just coming up with ideas, potential solutions. That is one area I would look at. But this is an issue that is going to stick around. It will grow for a period of time. I think it may, over time, which we don't have, by the way. We don't have the benefit of time.

But over time there has been an unprecedented number of branded drugs that have gone off patent. Those actually will, there are not as many drugs coming off patent in the future in the generic injectable space, so I think the capacity will come back into line. But, unfortunately, the bottom line is we don't have the benefit of time, so the sooner we figure out a solution together, the better off we all are.

Mr. GOWDY. Mr. Okon.

Mr. OKON. Mr. Chairman, I think we have to draw a line down the paper and I think that what we have to do is put in place a solution that basically provides the proper incentives on the manufacturing side, realizing that this is a regulated market. It is regulated both in terms of price, it is regulated in terms of manufacturing. We have to accept that. So I think we have to put the incentives on the manufacturing side and I think we basically have to do something on the reimbursement piece.

The other side of the paper is more immediate, because even when we do that it is not going to take care of Dr. Hudspeth's patient that basically she has to find a drug. I think this is a crisis, it is a national crisis, and we need to come together, put all politics aside and say, how can we get these drugs safely distributed through the proper channels? How can we get them immediately so that we can basically get the drugs in the patients' hands that need them?

And I think that with all what we have to do and I think we should do on the legislation side to put the proper incentives in place and basically take care of both the manufacturer and the provider side, I think we have to do something more immediate and I think it has to be drastic.

Mr. GOWDY. Dr. Gottlieb.

Dr. GOTTLIEB. Well, unfortunately, I think it is going to get worse before it gets better. There are things we can do both immediate and long-term. Immediate, I would urge the committee to

send a letter to the top five manufacturers and ask them how much of their manufacturing capacity is currently offline because it is undergoing remediation, and make sure that, as that manufacturing capacity gets remediated in consultation with the FDA, it is done in as efficient a fashion as possible with the regulatory authorities.

The reality is we have more manufacturing in this country, but the industry is consolidated so more of that manufacturing capacity is sort of consolidated at a handful of very large facilities. So when you take Teva's Irvine facility offline or Hospira's facility offline, you have just taken out 15 percent of the entire market.

Longer term, I think we need to find ways to allow these prices to float to justify long-term investments. It could take as long as 7 years to stand up a new manufacturing facility for parenteral drugs, so the companies need to know that they can take and sustain price increases for some of these drugs if they are going to make those long-term investments. And that would be sort of a long-term policy.

Mr. GOWDY. Dr. Thompson.

Dr. THOMPSON. Step one, pass the current legislation that is pending in Congress, that is S. 296 and H.R. 2245. Reporting, confidential reporting to the FDA isn't going to solve drug shortages, but there is evidence to say that in 101 cases the FDA has been able to prevent a shortage when a manufacturer confidentially reported to them, and that is what this legislation does.

Now, there are 240 shortages on the list now, so you can imagine that if reporting occurred across the spectrum, that that number would be higher than 101. So I would say step one, pass that legislation now that requires confidential reporting. And it is confidential reporting to the FDA, it is not public reporting.

And then the second would be to explore all these other factors. I think that there is a little more time to do those sorts of things. Not a lot of time, but look at the economic factors. Really have a deep discussion with the manufacturers and other members of the supply chain and get a very thorough understanding of really what these drivers are, and then go to that next step. But I think the legislation that is pending Congress now needs to move.

Mr. GOWDY. Well, on behalf of all of us, thank you for loaning us your expertise, your time. Fascinating is not the right word. I don't know what the right word is, but I thank you, Dr. Hudspeth, for bringing it to my attention and for the other witnesses for loaning us your acumen and expertise.

The committee stands adjourned.

[Whereupon, at 11:27 a.m., the subcommittee was adjourned.]

[Additional information submitted for the hearing record follows:]



**Susan G. Komen for the Cure®
Statement for the Committee on Oversight and Government Reform
Subcommittee on Healthcare**

**“Drug Shortage Crisis: Lives are in the Balance”
November 30, 2011**

Thank you Chairman Gowdy, Ranking Member Davis, and distinguished Members of the Subcommittee, for holding a hearing to highlight the critical problem of drug shortages and to receive input from health care and policy experts on ways to address this crisis.

On behalf of breast cancer survivors, their loved ones, and those who will fight the disease in the future, Susan G. Komen for the Cure® (Komen) appreciates this opportunity to comment on this important issue. Komen is the largest grassroots network of breast cancer survivors and advocates. At the heart of Komen’s mission is saving lives, empowering people, ensuring quality care, and energizing science to find the cures. Since 1982, Komen has played a critical role in every major advance in the fight against breast cancer. With 230,480 new cases of invasive breast cancer expected to occur this year alone, we have grave concerns that, if left unaddressed, the drug shortages crisis will continue to deepen and eventually have a serious impact on women who are currently being treated for breast cancer and those who will be treated in the future.

As most experts agree, drug shortages are a complex problem with no single, distinct root cause. While we work toward a comprehensive solution, Komen would like to express the breast cancer patient perspective and the essential elements of a solution that would address the needs of this population.

The economic forces and regulatory issues that have led to the number of shortage drugs tripling annually since 2005 can only be addressed with a multi-faceted solution. As we actively seek legislative proposals and regulatory solutions to ensure access to lifesaving medicines while safeguarding their quality and safety, Komen urges legislators, drug manufacturers, and regulators to continue to keep the needs and interests of the patients who depend on these drugs as the focal point of any solution. After all, while many health care sector stakeholders are impacted, it is the patients who are most at risk when they are left unable to finish a treatment cycle, or are prescribed a drug regimen that was not their physicians' first choice for their unique needs. In some cases, the shortages are leading to dosing errors with grave consequences for patients. Additionally, both the government and patients must shoulder the cost of more expensive alternatives and the labor and time it takes to identify substitute treatments, if they do exist.

We urge Congress to explore a productive combination of regulatory reform, possible incentives, and other measures, such as developing mechanisms to identify and maintain excess inventory of medically necessary drugs and their Active Pharmaceutical Ingredients (APIs) in the event of a shortage. Other regulatory proposals to consider include: streamlining Current Good Manufacturing Practices (CGMP) regulations, which are often viewed as burdensome, outdated, and as a contributing factor in making sterile injectibles so difficult to produce; allocating the resources needed to efficiently inspect the facilities of APIs for shortage drugs and applying regulatory discretion when possible to efficiently resolve manufacturing problems; and expediting the FDA approval process, in certain circumstances, for manufacturers of generic sterile injectibles and other drugs frequently susceptible to shortages. Any regulatory reform must be implemented in a manner that ensures high quality through oversight, while also mitigating the impact of any enhanced regulation.

Finding a comprehensive proposal may require exploring new regulatory and tax incentives to develop greater manufacturing capacity and to encourage existing manufacturers to continue to produce the low cost, vital drugs that are vulnerable to shortages. A comprehensive review of the Average Sales Price (ASP) reimbursement formula should also be undertaken. The ASP is updated only every six months, allowing for minimal opportunities to adjust pricing, and

hindering flexibility to respond to the market changes and to support production of shortage-prone drugs. Addressing the drug shortage problem also may involve potential changes in the way that drugs are reimbursed by Medicare and private payers, in order to remedy possible deterrents to suppliers that may prevent them from adding capacity and increasing production of these drugs. Yet, this must be done with extreme caution in order to ensure quality and safety of these critical medicines and to prevent shifting the problem rather than solving it. Executive agencies, Congress, and industry will have to work together to achieve the delicate balances needed to ensure that new policies do not result in unforeseen adverse consequences.

It is widely acknowledged that the gray market is a symptom rather than a cause of drug shortages, but it exacerbates the problem. The safety concerns associated with turning to the gray market as an alternate source for drugs must be recognized. Congress should consider enacting laws to severely penalize price gouging by individual actors and companies. Existing laws designed to prevent abuses should be aggressively enforced and prioritized. Finally, a mechanism to report information about suspected hoarding, price gouging and counterfeit drug should be developed to facilitate investigation by law enforcement authorities.

While a comprehensive solution is being developed, communication surrounding existing or emerging drug shortages is critical. The necessary communication includes, but also goes beyond, what is included in current legislative proposals that require FDA notification by manufacturers of shortage drugs. Notification should also include the responsibility to communicate with supply chain partners, physicians and other health care professionals who prescribe and administer drugs vulnerable to shortages, and clinical trial investigators, to the fullest extent allowed by confidentiality requirements.

Fifteen of the twenty-two cancer agents on the drug shortage list are needed for clinical research purposes. The significance of the impact on cancer research is due to the fact that cancer clinical trials rarely use placebos, and instead, test the standard of care treatment against or alongside the new treatment being investigated. As a result, groundbreaking clinical trials of cancer drugs are delayed or even halted by shortages that impact the standard of care cancer agents. This wastes research dollars, the time and resources directed toward the trials, and the personal investment

made by investigators and participating patients who have courageously agreed to enroll in these trials. Treatment delays and obstacles to research efforts being translated into approved anti-cancer drugs affect patients' chances of survival.

It is also critical that physicians are promptly notified of all actual and likely shortages, so that they can fulfill their professional obligation to discuss the implications of shortages on treatment regimens and to advise patients of treatment options and risks. If the preferred treatment protocol needs to be adjusted because of a possible or existing shortage, patients should be informed of any possible ramifications of interruptions or delays and the consequences and side effects associated with substitute treatments. They should also be given the choice to inquire about and discuss other options. After all, we must keep in mind, that while the whole health care system is impacted, it is these patients' lives that are in the balance.

Thank you for this opportunity to submit this statement on an issue of such vital importance to cancer patients and those who love them. On behalf of Susan G. Komen for the Cure, I appreciate the efforts Congress is making to identify and implement a comprehensive solution to resolve a crisis that is jeopardizing access to treatments that save lives.

If you have any questions or would like any additional information, please do not hesitate to contact me or Karen Handel, Senior Vice President, Public Policy, Komen Advocacy Alliance, at 202.654.6536 or khandel@komen.org.

Sincerely,



Elizabeth Thompson
President
Susan G. Komen for the Cure®