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WOMEN AND CANCER: WHERE ARE WE IN PREVENTION, EARLY DETECTION AND TREATMENT OF GYNECOLOGIC CANCERS?

HEARING

BEFORE THE

SUBCOMMITTEE ON CRIMINAL JUSTICE, DRUG POLICY, AND HUMAN RESOURCES

OF THE

COMMITTEE ON GOVERNMENT REFORM

HOUSE OF REPRESENTATIVES

ONE HUNDRED NINTH CONGRESS

FIRST SESSION

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WOMEN AND CANCER: WHERE ARE WE IN PREVENTION, EARLY DETECTION AND TREATMENT OF GYNECOLOGIC CANCERS?

WEDNESDAY, SEPTEMBER 7, 2005

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON CRIMINAL JUSTICE, DRUG POLICY,
AND HUMAN RESOURCES,
COMMITTEE ON GOVERNMENT REFORM,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:45 a.m., in room 2154, Rayburn House Office Building, Hon. Mark E. Souder (chairman of the subcommittee) presiding.

Present: Representatives Souder, Burton, Cannon, Issa, Foxx, Waxman, Cummings, Watson, Sanchez, Ruppersberger, and Norton.

Staff present: Marc Wheat, staff director and chief counsel; Michelle Powers, counsel; Malia Holst, clerk; Kristin Amerling, minority general counsel; Tony Haywood and Naomi Seller, minority counsels; Richard Butcher, minority professional staff member; Earley Green, minority chief clerk; Cecelia Morton, minority office manager; and Christopher Davis, minority investigator.

Mr. SOUDER. The subcommittee will come to order.

Good morning and thank you all for being here.

Today's hearing will examine the Federal efforts targeting gynecologic cancers, specifically where we are in the areas of education, research, prevention, and treatment. The hearing will also provide an opportunity for medical and research specialists, patients, and family members to discuss the relevant issues involved in gynecologic cancers and where more work is needed.

This month marks Gynecologic Cancer Awareness Month, as well as National Ovarian Cancer Awareness Month. According to the American Cancer Society, over 79,000 women are diagnosed every year with cancers affecting the reproductive organs. If diagnosed in the early stages, the survivability rate is as high as 95 percent. Nonetheless, this year alone, more than 27,000 women will die from gynecologic cancer.

Any woman is at risk for developing a gynecologic cancer.

The most deadly gynecologic malignancy is ovarian cancer. Patients with ovarian cancer often report that they had symptoms for months before diagnosis, but early signs of this cancer are frequently mistaken for more common digestive disorders. As a result, most ovarian cancer cases are diagnosed at an advanced stage, where the chances of survival drop to only 20 percent. This year,

out of the more than 22,000 new diagnoses of ovarian cancer, more than 16,000 women will die from the disease.

The most common gynecologic cancer is uterine cancer, which will afflict more than 40,000 women this year and kill over 7,000 women. While there have been advances in therapy for uterine cancer, including the innovative new surgical treatments, women are largely unaware of the risk factors contributing to this disease, which include obesity, hypertension, diabetes, and inappropriate estrogen use. However, if a women is diagnosed early, surgical therapy is usually adequate for a cure.

Where there is effective screening, there has been a significant reduction in deaths from certain gynecological cancers; over the last 50 years, routine use of the pap test to screen for cervical cancer has reduced deaths from that disease by 74 percent. However, there are no widely accepted and effective screening tests for other gynecologic cancers. This leaves women vulnerable to late diagnosis, and lower chances of recovery.

Even with effective screening, the American Cancer Society estimates that cervical cancer will kill more than 3,700 women this year. The primary cause of virtually all cervical cancers is human papillomavirus [HPV], which is transmitted through sexual contact. More women will die from this disease than from AIDS, among non-injection drug users. Although Federal agencies are working on vaccines developed to prevent HPV infection, current proposed vaccines do not address all strains of HPV.

Moreover, the FDA has yet to comply with Public Law 106–554, signed by President Clinton in 2000, requiring that condoms be accurately labeled to reflect the fact that condoms do not protect women from HPV infections. The Gynecologic Cancer Foundation's 2005 State of the State Report on Gynecologic Cancers notes that both women and men do not fully understand the association between HPV infection and its severe health consequences.

It is inexcusable that Federal agencies have yet to comply with a law passed more than 5 years ago and, in the meantime, thousands of women continue to die from this preventable disease. The cost to comply with the law requiring accurate condom labeling is quite low. The benefit is measured in terms of women's lives. There is simply no justification for the FDA and the White House Office of Management and Budget dragging their feet on this critical public health matter.

I am surprised that the FDA's testimony today makes no reference to their progress in complying with this law since the FDA last appeared before this subcommittee on this very issue on March 11, 2004. Perhaps the FDA witness is not prepared to address this matter this morning, but I would ask that FDA provide a full explanation on this matter in 5 days, and we will be happy to forward FDA's response to all subcommittee members. I hope the other agencies represented here today will address these issues in oral testimony.

There is an evident need to raise awareness among patient and medical communities about all aspects of gynecologic cancers, including prevention, symptoms, screening, and treatment. A recent poll commissioned by the Gynecologic Cancer Foundation found that the majority of women believe that they are at risk for devel-

oping gynecologic cancers, and fear them even more than lung cancer, which is the leading cause of cancer deaths among women. More than a third of women say they have little knowledge about gynecologic cancers, and in fact, a staggering 47 percent of them could not name any symptoms of gynecologic cancers.

Parallel to the important education needs is the necessity for innovative research and therapy development.

I hope the outcome of this hearing is a better picture of what efforts the Federal agencies are making to raise awareness among practitioners and among patient and medical communities of gynecologic cancers, and where there are unmet needs. In particular, I hope the agencies address their critical role in protecting the public from HPV infection and preventing more cervical cancer deaths. I also hope we can learn the status of current funding paths for innovative and cutting edge research for gynecologic cancers, and whether we are meeting the challenges to deliver new therapies.

Finally, I hope the first-hand experience and perceived needs of those who deal with gynecologic cancers as patients, family members, doctors, and researchers provide us with a better understanding of how to address gynecologic cancers.

I am now going to turn this hearing over to Congressman Cannon to chair the hearing. His daughter passed away from cancer late last year at the age of 25, and he is particularly interested in innovative research issues. I will be in and out of the hearing this morning, and I appreciate his leadership in this field and his willingness to chair the hearing.

[The prepared statement of Hon. Mark E. Souder follows:]

**Subcommittee on Criminal Justice,
Drug Policy and Human Resources**

Opening Statement of Chairman Mark Souder

"Women and Cancer: Where are We in Prevention, Early Detection, and Treatment of Gynecologic Cancers"

September 7, 2005

Good morning and thank you all for being here.

Today's hearing will examine the federal efforts targeting gynecologic cancers, specifically where we are in the areas of education, research, prevention and treatment. The hearing will also provide an opportunity for medical and research specialists, patients, and family members to discuss the relevant issues involved with gynecologic cancers and where more work is needed.

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There is an evident need to raise awareness among the patient and medical communities about all aspects of gynecologic cancers, including prevention, symptoms, screening and treatment. A recent poll commissioned by the Gynecologic Cancer Foundation found that the majority of women believe they are at risk for developing a gynecologic cancer, and fear them even more than lung cancer, which is the leading cause of cancer deaths among women. More than a third of women said they have little knowledge about gynecologic cancers, and in fact, a staggering 47 percent of them could not name *any* symptoms of gynecologic cancers.

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Finally, I hope the first hand experience and perceived needs of those who deal with gynecologic cancers as patients, family members, doctors and researchers provide us with a better understanding of how to address gynecologic cancers.

[Turn over to Mr. Cannon to chair the hearing: Mr. Cannon's daughter passed away from cancer late last year at the age of 25, and he is particularly interested in innovative research issues.]

Mr. CANNON [presiding]. Thank you, Mr. Chairman.

First of all, I would like to thank Chairman Souder for holding this hearing today. This is an issue affecting millions of Americans currently: 1 in 2 men and over 1 in 3 women will be diagnosed with cancer. In 2000, more than 1.2 million new cancer diagnoses were expected and 550,000 died from the disease. Nearly 10 million people in the United States alone were living with cancer in 2001, up from 3 million in 1971, and the American Cancer Society estimates that in 2005 nearly 1.4 million new cases of cancer will be diagnosed.

While we say that we are winning the war on cancer, the statistics don't seem to represent that. Although I am pleased to hear that we are making progress in the length of survival of those with cancers, we need to eliminate the incidents of cancer and completely cure this illness. Tremendous strides in research and treatments are being made; however, there are numerous challenges in getting those treatments to patients effectively and efficiently. There are some serious gaps in research and failures to optimize research to produce new treatments. Drug approval takes years, withholding potentially life-saving drugs and treatments from patients.

We need to look at all of these areas and optimize research among agencies, fill the gaps in research, and incentivize entrepreneurial research and produce life-saving treatments.

Today we will specifically hear from our witnesses regarding gynecological cancers, including the role of human papillomavirus and cervical cancer. Most Americans are not aware that HPV is one of the most common sexually transmitted diseases and that at any one time approximately 10 percent of women have a cancer-causing HPV infection. These HPV types cause nearly all cervical cancers, and this year about 11,000 women will be diagnosed with cervical cancer.

Additionally, as many of you may know, the Gynecological Cancer Foundation reported that men and women do not completely recognize the association between HPV and its severe health consequences. We need to better educate the public on the health risks of HPV and gynecological cancers. Although PAP test is the standard procedure to check for cervical cell changes, it is my understanding that it does not test for uterine or other gynecological cancers. I am anxious to learn how we are doing in developing tests for these other cancers.

Many of us have been personally affected by cancer, unfortunately. We now have reached a time that I believe we can all say we know someone who has been diagnosed with this devastating disease.

I thank all of our witnesses for appearing today, and I look forward to hearing your testimony about where we are on cancer research and what we need to do to win the war on cancer.

I would now like to recognize Mr. Cummings for an opening statement.

Mr. CUMMINGS. Thank you very much, Mr. Chairman. And I am very pleased that we are holding this hearing.

Breast, lung, and colon cancers are the most frequently diagnosed cancers among women in the United States. The gynecologic

cancers, including cervical, ovarian, and uterine cancers, also account for a significant number and percentage of cancer diagnoses and deaths among U.S. women.

The American Cancer Society reports that approximately 79,000 U.S. women are diagnosed with cancers affecting the reproductive organs each year. Although the survivability rate is as high as 95 percent when these cancers are detected in the early stages, each year 27,000 U.S. women die from gynecologic cancers.

Fifty years ago, cervical cancer was the leading cause of cancer death among women in the United States and around the world. Thanks to advances in cancer screening and treatment, most notably widespread use of the Pap test, the threat of mortality from cervical cancer has been dramatically reduced in the United States. Nevertheless, thousands of women are newly diagnosed each year, and the American Cancer Society estimates that more than 3,000 women will die from it in 2005.

Unfortunately, despite improved screening rates, enabled by congressionally authorized CDC screening programs, unequal access to screening remains a problem that contributes to significant disparities in cervical cancer death rates, along the lines of race, educational level, income, and age. Although racial and ethnic disparities have decreased sharply, there is more progress that must be made.

Women who belong to racial and ethnic minority groups still are disproportionately represented among the new cases of cervical cancer. Asian, African-American and Hispanic women have significantly higher mortality rates from cervical cancer than White women. Women with less than a high school education are less likely to have testing than more highly educated women. And despite the peek incidents of cervical cancer among women 40 to 55 years of age, women in this age group are less likely to have been screened than younger women. African-American women are 60 percent more likely to have cervical cancer and 33 percent more likely to die from it, as compared to White women.

The great tragedy in the American Cancer Society's estimates of the thousands of lives that will be lost to cervical cancer is that these deaths are avoidable. The Department of Health and Human Services notes in its Healthy People 2005 Initiative that the likelihood of cervical cancer survival is nearly 100 percent if early detection is followed by appropriate treatment and followup. But costs remains a barrier to access Pap tests and DNA tests for HPV.

Used together, these tests can accurately determine whether a woman is or is not at risk for cervical cancer or precursor conditions. Genital HPV infection is a necessary precursor for cervical cancer and the main cause of the disease. In recent years we have seen vigorous efforts from certain quarters to force the FDA to relabel condoms to indicate that condoms are ineffective in preventing transmission of HPV. These efforts, if they succeed, are likely to undermine progress in preventing not only HPV infection and the development of cervical cancer, but also the spread of other sexually transmitted diseases, including HIV.

The American Cancer Society specifically recognizes HIV and chlamydia as risk factors for development of cervical cancer, and condoms are widely recognized as a primary intervention for pre-

vention of HIV and chlamydia. The best available scientific evidence, moreover, supports the conclusion that condoms significantly reduce the risk of genital HPV infection and, therefore, development of cervical cancer.

In July of this year, a study entitled, "The Effect of Consistent Condom Use on the Risk of Genital HPV Infection Among Newly Sexually Active Young Women," was presented to the International Society of Sexually Transmitted Disease Research. The study found that condoms significantly reduce the risk of HPV acquisition among female university students who use them 100 percent of the time, as well as among those who use them between 55 percent and 99 percent of the time during the course of an 8-month study.

The bottom line, then, is that cervical cancer can be prevented, detected, treated, and cured, and health screening and condom use are essential components of a sound, realistic public health strategy for combating cervical cancer and the spread of sexually transmitted diseases. Unfortunately, ovarian, uterine, and other gynecologic cancers are less susceptible to prevention and early detection, and mortality rates, as a result, are much higher.

But great progress has been made in developing treatments that are highly effective when these cancers are detected at an early stage. We must therefore support efforts to promote awareness of risk factors for ovarian, uterine, and other gynecologic cancers, as well as research that can lead to development of new and better diagnostic and therapeutic tools.

That is precisely the aims of Johanna's Law, legislation pending the House and Senate named for the sister of Sheryl Silver, who will tell her sister's story during panel two of today's hearing. I am proud to be an original co-sponsor of this important bill in the House, and I sincerely hope that this hearing serves to improve the prospects for enacting this legislation.

Finally, Mr. Chairman, it is worth reiterating that we have made enormous strides in reducing cervical cancer deaths over the past few decades. Ensuring that cervical cancer death rates continue to go down for women in all parts of American society and working to duplicate that success with other gynecologic cancers are important objectives that we should fully support. Expanding access to screening and treatment for women at risk should remain the foundation of a public health strategy that puts health and wellness before ideology and science, and before politics.

I want to thank you for holding the hearing. I sincerely hope that it will lead to further advances toward eliminating gynecologic cancers as a cause of illness and death for women in these United States.

With that, I yield back.

Mr. CANNON. Thank you, Mr. Cummings.

Let me just add that you point out that we want to solve this for American society, and that is our goal. But if we solve it in America, we solve it for large parts of the world, including the many, many women who die of cervical cancer in Africa because their partners and spouses have not only brought back AIDS and other diseases, but HPV, and that ends up being a principal cause of death in Africa. If we can solve some of these problems here in

America, it is cheap and easy to solve them in other parts of the world, and that is why I think this is such an important hearing.

Are there other members who wish to make an opening statement?

Mr. ISSA. Yes, Mr. Chairman.

Mr. CANNON. Let me come over here.

Mr. ISSA. Thank you, Mr. Chairman. And I would ask that my complete statement be placed in the record.

Mr. Chairman, I want to thank you on behalf of the thousands of women fighting this fierce battle against gynecological cancer. As you know, this bill has been previously introduced in early Congresses, it has been something that we wanted to get on the front burner for 4 years plus, and I think your leadership is really making a difference in getting this bill moved and moved quickly. As you know, there are 220 plus Members of Congress who have cosponsored this. As a general rule, that means that you have enough votes to pass it on the House floor, and I am hoping that today is an important step toward that.

I won't repeat the good words that have been said by previous speakers, but I would like to simply add a couple of items. First of all, this is a cancer in which awareness can save lives. Cervical, ovarian, and uterine cancer really is, to a great extent, about what we don't know and, to be candid, as we will hear in the second panel, to a great extent what doctors don't know.

The story of Johanna is the story of misdiagnosis. It is the story not of an underserved population, a poor person or a minority; it is somebody who had professional care, and that care failed to save her life. And it has failed to save her life not out of malice, but out of a lack of the kind of information that we hope the funding we provide on a Federal level can do.

I do think that it is important. I was not an original cosponsor of this in previous Congresses, but came on board as the principal author, along with Sander Levin and others, because of an awareness that came into my office. If I may share this personally, last year I discovered first-hand the importance of early diagnosis when my legislative director, Paige Anderson, who is with us here today because of early diagnosis. She is one of the lucky ones. She stands here today a cancer survivor.

However, it was not until early diagnosis that she even learned of HPV, cervical cancer, and the importance of early Pap smears and pelvic exams. Unfortunately, her story is the story that is going to repeat itself until this legislation not only passes, but that we fully fund it and start bringing about the kind of awareness of this cancer that, candidly, we have had success stories in other areas.

This is a bipartisan bill, and I would particularly like to thank, once again, Sander Levin, who was the author of it in a previous Congress; Kay Granger; Rosa DeLauro; and Congressman Dan Burton, who will speak in a few moments. They really made a difference in previous Congresses in moving this, and now, together, we are very happy to be able to move this.

Last, but not least, I want to recognize Dr. Beth Karlan. Dr. Karlan is the president of the Society of Gynecological Oncologists. She practices medicine at Cedars Sinai Medical Center in my home

State of California. But beyond being a doctor, a researcher, a professor, and mother, Dr. Karlan has been an inspiration and motivator in the fight for gynecological cancers, and she is also the person whose efforts saved my staff person, Paige Anderson's, life. So I am looking forward to seeing the energy that she brings to the Congress, just as the energy that she has brought to her practice.

And with that I yield back.

Mr. CANNON. Thank you, Mr. Issa.

Are there other Members who would like to make an opening statement? Ms. Watson. The gentlelady is recognized for 5 minutes.

Ms. WATSON. Thank you, Mr. Chairman, for having this most critical hearing. I too had cancer visited on my family: my sister, 18 months older than I, had cervical cancer and did not survive.

It reminds me of a discussion we had in our legislature maybe 20 years ago, when we were startled to learn in the 1980's that most of the cancer testing for breast cancer was done on men. So about seven of the women in both Houses—I was in the Senate—and my colleagues in the Assembly ganged together and we said we will not vote for the budget in a block unless you put $28 million in for research on breast cancer on women.

And we got it in. We had to gang up; we had to terrorize. UCLA's Dr. Love worked with us and reported on the status of the research over the years. The women—and particularly minority women—who had breast cancer, by the time we finished up, were all dead. So we really forged ahead.

I was heading Health and Human Services for 17 years, and we forged ahead on the studies. But we required in the State of California that every woman over 40 have a mammogram yearly. We had to drop that down to 20 because we found that breast cancer was spreading faster among African-American women—we didn't know why—at an earlier age. And by the time we would get to them and we would try to follow them and profile, they were gone as well.

So in 2005 we cannot stress that we really have not made that much progress. So I do hope, listening to the panels, that you will encourage us—and particularly women—and let us know the intensity of the effort. Are we putting enough resources in? And what are America's priorities when it comes to fighting cancer? We have new kinds of cancers appearing every day. And, particularly in my State of California, skin cancer is becoming very prevalent. So we must keep pace; we must keep focused; we must keep allotting the necessary resources.

And I want to tie it in to the tragedy that we are all going through in the Gulf Coast. We need to place a priority on health; health of all Americans. And I just have to say this: When we talk about homeland security, it is not the land I am worried about; it is the people on the land. If they are weakened by disease, contagious diseases and cancer, we have no defense; we have no security. So I hope that our subcommittee will keep the focus going on the health delivery system, and specifically on the prevention and detection of cancer.

Thank you, Mr. Chairman.

Mr. CANNON. Thank you.

Other members who wish to make an opening statement? Mr. Burton. The gentleman is recognized for 5 minutes.

Mr. BURTON. I have a very, very brief statement. First of all, I want to thank Darrell Issa and Sander Levin for sponsoring this; I think it is very important and you should be congratulated for that. I want to thank Chairman Souder. He just added his name as a cosponsor of the bill, so we are up to 221 or whatever it is, so we should be able to get this passed. I want to also thank Kolleen Stacey and Sheryl Silver for being here. They have been doing yeoman's service for this cause for a long time, and I personally really appreciate it.

My wife was misdiagnosed and died about 3 years ago because of misdiagnosis on her cancer, and I just hope that part of the solution that we finally realize is making sure that the doctors across this country are educated in how to deal with analyzing the various kinds of cancer that women have. One of the big problems we have right now is, unfortunately, some of the doctors misdiagnose, and because of that the cancers spread too rapidly before we find out about it, and that is what happened with my wife.

So I thank you very much for sponsoring this bill, Darrell, and thanks for having this hearing. And I look forward to hearing the testimony.

Mr. CANNON. The gentleman yields back. I want to thank the gentleman. This is actually sort of a hard topic to talk about, isn't it, Mr. Burton?

Other Members who wish to make an opening statement? Mr. Ruppersberger.

Mr. RUPPERSBERGER. Thank you, Mr. Chairman.

Mr. CANNON. The gentleman is recognized for 5 minutes.

Mr. RUPPERSBERGER. This is an extremely important issue, and I hope this hearing today will really call attention to us and to what we need to do to bring this issue to the forefront. As we all know, gynecologic cancers, if detected early, can help the issue, and it is very important to do this.

But we do need to understand that early detection is sometimes not possible, where the symptoms demonstrated by afflicted women are identified as something else. And we must continue to be at the forefront of science and technology when it comes to diagnosing and treating these types of cancers. If adequate resources, expertise, and manpower exists, there is no excuse for delay.

I am looking forward to the testimony today from our witnesses in an effort to again raise the awareness about this type of cancer among patients and doctors, and how we, as Members of Congress, can help.

Thank you, Mr. Chairman.

Mr. CANNON. The gentleman yields back.

Mr. Waxman. The gentleman is recognized for 5 minutes.

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

I welcome our witnesses today, and I am pleased we are holding this hearing.

Over the last 30 years, the rate of lung cancer among women in the United States has more than doubled. The rate of breast cancer has increased by 20 percent. But the rate of cervical and uterine

cancers has dropped in half. And the racial disparities in diagnosis of these cancers have also substantially narrowed.

Credit for progress against cervical cancer goes largely to a single preventive health intervention: the Pap smear. By diagnosing precancerous lesions, this test permits eradication of the problem before cancer develops. By any accounting, the Pap smear ranks as one of the most major advances in women's health of the 20th century. Yet, there is much more to be done to combat gynecological cancers. Cervical cancer kills 4,000 women each year; ovarian cancer kills nearly 15,000.

The key to progress is to continue implementing sound public health practices and supporting crucial research. To start, we must make sure that all women have access to routine cervical screening. An estimated 60 percent of cervical cancer cases occur among women who did not get routine Pap smears. We also must make sure that women who screen positive for gynecological cancers have access to needed medical treatment. This is not something to be taken for granted. The President's proposed cuts to the Medicaid program threaten the basic access to care for women around the country, and, if passed, they could expect it to lead to more suffering and death from cancer.

We must take advantage of new technology. And we will hear today about vaccines that seem to be very, very promising and very successful in their tests. We need to pursue progress at the same time we resist calls to politicize policy decisions on women's health. And there are two ongoing ideological campaigns that could seriously undermine the progress that the public health system has made. The first is the call to require warning labels on condoms stating that they don't protect against HPV. This policy makes no sense.

The National Institutes of Health and CDC have both concluded that condoms reduce the risk of cervical cancer. That is the benefit, the health benefit outcome that we are all concerned about. In addition, the most recent scientific evidence indicates condoms do reduce the risk of HPV acquisition among women. In a carefully designed study of HPV and condoms by researchers at University of Washington, consistent condom use reduced the risk of HPV among young women by 70 percent.

A second attempt to politicize science involves early efforts to reject HPV vaccine. A spokeswoman from one right-wing group has expressed concern that giving the HPV vaccine to young women could be potentially harmful because they may see it as a license to engage in premarital sex.

It is a good thing that this sort of reasoning did not prevail when the Pap smear was invented. We would not have seen the major decrease in cervical cancer rates over the last three decades. The HPV vaccine offers the potential of saving thousands of lives. We should follow the advice of experts, not ideologs, in determining who should receive this intervention. After all, it is science that has guided our success in cervical cancer, and science will lead the way to continuing success.

I have looked at the list of witnesses. I think that we have a good two panels before us. I particularly want to single out Dr. Beth Karlan, who is my constituent, and welcome her to our hearing

today, and also all of the witnesses that are here to make their presentations.

Thank you, Mr. Chairman.

Mr. CANNON. The gentleman yields back. Thank you.

I would now like to recognize the Honorable Sandy Levin of the 12th Congressional District of Michigan, who will introduce Sheryl Silver, the sister of Johanna Silver.

Mr. Levin.

Mr. LEVIN. Thank you. My thanks to everyone on the panel for your eloquent statements.

My opportunity today is to introduce Sheryl Silver, who is on the second panel, and I will do just briefly so you can move on to the distinguished people here on the first panel.

Several years ago Sheryl Silver was in touch with us and in touch with me. It was the aftermath of the death of her sister, and she decided to take that tragedy in the life of her family and see if she could impact the lives of others. And for these years that has been, I think, her main preoccupation, as well as her mother, who is here today, and other members of the family.

What she brought to our attention is what has been repeated here, that wasn't well enough known: that as to gynecologic cancers, early detection almost invariably works and late detection is almost invariably fatal. So we introduced the legislation and there was a lot of interest shown across the isle and across the Rotunda. So I am here today to introduce Sheryl, who has been so dedicated to this cause, Johanna's Law, named after her sister.

Last session, Darrell Issa and I talked. He was very much moved by the experience within his own office, and we set upon a course to try to maximize the chances of passage of this legislation.

So let me just finish by suggesting the challenge here. One is for us in this Congress to prove that one person in our country can indeed make a difference, and it is up to us to do that. And, second, I think it is our charge to take personal experiences so eloquently and personally expressed here, and take personal experiences and place them into public action. And if we fail to do that, we have failed in our responsibilities as elected officials.

I am glad you are holding this hearing. I think we all appreciate the expression of personal backgrounds of personal experiences. We appreciate the interest of the scientists who are here. And I hope very much, to all of you, that the result of this hearing today will be action on the floor of the Senate and the House. We have enlisted Senators in this effort, and I think now, after you hear this, the responsibility will be ours.

Thank you for letting me proceed out of turn, and I wish you the best of luck.

Mr. CANNON. Thank you, Mr. Levin. Let me just make a personal note. I appreciate your initiative on this action, your support. I truly believe that individuals make the difference, so I appreciate your introduction, your initiative, and thank you for being here with us.

Mr. LEVIN. Thank you very much. Thank you to all of you.

Mr. CANNON. I would just also add thanks to Mr. Issa. I am a co-sponsor of this bill, and I think it is great legislation. Thank you.

A couple of procedural matters. I ask unanimous consent that all members have 5 legislative days to submit written statements and questions for the hearing record, and that any answers to written questions provided by the witnesses be also included in the record. Without objection, so ordered.

I also ask unanimous consent that all exhibits, documents, and other materials referred to by Members may be included in the record, and that all Members be permitted to revise and extend their remarks. Without objection, so ordered.

Our first panel is composed of Dr. Edward Trimble, Head of the Surgery Section, Division of Cancer Treatment and Diagnosis at the National Cancer Institute; Dr. Ed Thompson, Chief of Public Health Practice at the Centers for Disease Control and Prevention; and Dr. Richard Pazdur, Director of the Division of Oncology Drug Products, Center for Drug Evaluation and Research, U.S. Food and Drug Administration.

It is our custom as an oversight committee to swear all of our witnesses in. Would you mind rising while I administer the oath?

[Witnesses sworn.]

Mr. CANNON. You may be seated. The record should reflect that each member of the first panel agreed in the affirmative to that oath.

Dr. Trimble, thank you for joining us, and you are recognized for 5 minutes. Before you begin, let me just point out that, since we are probably going to have quite a bit of questioning, the 5-minute limit is not fixed, we don't get lightening from heaven, but if it goes beyond, I may tap just to remind you to draw your comments to a conclusion. And then we may go a second round of questioning.

But for the panel members, I intend to enforce the 5-minute rule fairly strictly, so that people who are waiting have a chance to ask questions. But, again, we may go to a second round or more of questioning if those here would deserve.

Dr. Trimble, you are recognized for 5 minutes.

STATEMENTS OF DR. EDWARD L. TRIMBLE, M.D., M.P.H., HEAD OF THE SURGERY SECTION, DIVISION OF CANCER TREATMENT AND DIAGNOSIS, NATIONAL CANCER INSTITUTE; DR. ED THOMPSON, M.D., M.P.H., CHIEF OF PUBLIC HEALTH PRACTICE, CENTERS FOR DISEASE CONTROL AND PREVENTION; AND DR. RICHARD PAZDUR, M.D., DIRECTOR, DIVISION OF ONCOLOGY DRUG PRODUCTS, CENTER FOR DRUG EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

STATEMENT OF DR. EDWARD L. TRIMBLE

Dr. TRIMBLE. I am honored to testify on the topic of gynecologic cancer for the National Cancer Institute. Over the past century, we have made major progress toward the defeat of cervical cancer in the United States. Today I would like to talk to you about some of the exciting work NCI is doing to eliminate the scourge of gynecologic cancer in the United States and around the world.

NCI scientists developed a new vaccine approach to prevent the transmission of HPV. We have licensed this technology to two large pharmaceutical companies who have recently reported that the vac-

cines were almost 100 percent effective in preventing spread of the virus. We have also been working to make screening for cervical cancer less expensive, more reliable, and more available. Even with the arrival of HPV vaccines, we will need to continue screening for many years to come.

In one of our most exciting projects, NCI is working with the CDC, the University of Alabama at Birmingham, and the Mississippi State Health Department to improve screening for cervical cancer among poor rural women in the Mississippi Delta who have had some of the highest rates of cervical cancer in the United States for the last 50 years.

Again in collaboration with the CDC, as well as with the U.S. Department of Agriculture and the American Cancer Society, NCI is implementing TEAM-UP, a national pilot program to increase cervical cancer screening among never or rarely screened women in eight underserved Appalachian States.

We are also making major strides toward the elimination of death and suffering from ovarian cancer. We are currently evaluating screening for ovarian cancer among 70,000 women through our PLCO trial. Our laboratories are developing new screening tests for ovarian cancer. One of the most promising is the identification of proteomics, protein expression in the blood, as a screen for ovarian cancer.

The NCI discovered and developed paclotaxol, or Taxol, which is now one of the standard drugs used to treat ovarian cancer. We have just completed the largest treatment trial, 5,000 women, ever conducted in ovarian cancer with the help of investigators across the United States, Canada, and five other international partner countries.

We have established four specialized programs of research excellence to foster translational research in ovarian cancer.

We are also working to strengthen our research portfolio in endometrial cancer, which is the most common female pelvic malignancy. The identification of new targets and treatments will lead us to new strategies to prevent women from developing endometrial cancer and to avoid the need for hysterectomy.

We have also developed an extensive educational program focused on gynecologic cancers. Our Cancer Information Service Partnership collaborates with local, State, and other Federal agencies to conduct outreach on cervical cancer, particularly in medically underserved populations. For example, NCI has joined with county and local officials to raise awareness, provide education, and build a community-based sustainable cancer control infrastructure for urban American Indian women in Los Angeles. We also collaborate with the CDC in addressing the needs of underserved populations using our 1–800–4-CANCER number to refer thousands of eligible women to low-cost and no-cost CDC services.

We have an extensive educational program focused on gynecologic cancer, including Web sites and educational material for both patients and medical professionals, available in English and Spanish.

Ending pain and suffering from gynecologic cancer is among the highest priorities of the NCI. We are working to implement the recommendations of the Gynecologic Cancer Progress Review Group.

We have also undertaken, in partnership with the CDC, the American Cancer Society, the International Agency for Research on Cancer, the World Health Organization, the Society of Gynecologic Oncologists, and the Gynecologic Cancer Foundation, a global initiative on women's cancer so that we can lift the burden of gynecologic cancer from women around the world.

That concludes my oral testimony. You have additional material in my written testimony. I would be happy to answer any questions.

[The prepared statement of Dr. Trimble follows:]

Testimony
Before the Subcommittee on Criminal Justice, Drug Policy and Human Resources
Committee on Government Reform
United States House of Representatives

National Cancer Institute Research and Education Efforts on Gynecological Cancers

Statement of
Edward L. Trimble, M.D., M.P.H.
Division of Cancer Treatment and Diagnosis
National Cancer Institute
National Institutes of Health
U.S. Department of Health and Human Services

For Release on Delivery
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Chairman Souder and members of the Subcommittee, thank you for the opportunity to testify on the topic of gynecologic cancer on behalf of the National Cancer Institute (NCI). Ovarian, cervical, and endometrial (also known as uterine) cancers are grouped as the major gynecologic cancers. One hundred years ago, gynecologic cancer, specifically cervical cancer, was the leading cause of cancer deaths among women in the United States. Over the past century, we have made major progress toward the defeat of this dreaded disease in our Nation. Today, I would like to talk to you about some of the exciting work NCI is doing to eliminate the suffering and death due to gynecologic cancers in the United States and around the world.

The National Institutes of Health invested $241 million on gynecological cancers research in FY 2004, including $212,527,000 at NCI. This funding supports an ongoing multi-pronged, multi-disciplinary effort in molecular biology, epidemiology, prevention, treatment, and survivorship issues of gynecologic cancers, including cancers of the cervix, ovaries and uterus.

Cervical Cancer

Cervical cancer is the second most common of cancers among women worldwide. Over 400,000 new cases are diagnosed each year, resulting in about 200,000 deaths. With the continuing education and application of early detection through pelvic examinations and Pap smears, cervical cancer is preventable or effectively treated at precancerous and early stages. Consequently, the frequency of advanced or recurrent cervical cancer has diminished in the United States. However, advanced cervical cancer is still observed and has a poor prognosis -- especially in several geographic regions with high numbers of underserved populations. We recognized that a better preventive strategy against cervical cancer is needed, and NCI investigators have developed a new vaccine approach to prevent the transmission of the human papillomavirus, the virus responsible for most cases of cervical cancer. We have licensed this technology to two large pharmaceutical companies, Merck and GlaxoSmithKline, who have recently reported that results of clinical trials indicate that the vaccines were almost 100% effective in preventing the acquisition of the virus types 16 and 18, which together account for nearly 70% of cervical cancer worldwide.

We have also been working to make screening for cervical cancer less expensive, more reliable, and more available. Even with the arrival of potential vaccines, we will need to continue screening for many years to come. An effective vaccine in combination with cervical cancer screening is expected to reduce cervical cancer rates by 90% in the United States.

NCI is working to bring state-of-the-art cervical screening to geographic regions of excess mortality. In one of our most exciting projects, NCI is collaborating with the Centers for Disease Control and Prevention (CDC), the University of Alabama at Birmingham, and the Mississippi State Department of Health to improve screening for cervical cancer among poor, rural women in the Mississippi Delta, who have had some of the highest rates of cervical cancer in the U.S. for the last 50 years. We know that cervical cancer disproportionately affects members of particular racial and ethnic minority subgroups and other underserved women.

If successful in Mississippi, we hope to promote region-specific novel screening and prevention programs with collaborators in other underserved regions such as the Mexican-U.S. border, the Pacific Rim, Native American populated regions, urban clinic populations, and centers serving migrant workers. This initiative also falls within the Health and Human Services Secretary

Leavitt's 500-day plan to support community-based approaches to close the health care gap, particularly among racial and ethnic minority populations. The NCI Center to Reduce Cancer Health Disparities recently published a report titled, *Excess Cervical Cancer Mortality: A Marker for Low Access to Health Care in Poor Communities*. This report explores the components of the problem of excess cervical cancer mortality, identifies critical needs, and recommends specific actions to eliminate cervical cancer mortality disparities suffered by women in identified geographic regions of the nation and to improve health care for all underserved women.

Ovarian Cancer

Ovarian cancer remains the most deadly of the gynecologic cancers. Reasons for this continuing poor outcome include the nonspecific and late clinical presentation of ovarian cancer and the lack of reliable and cost efficient methods of early detection. Through the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, the NCI is carrying out a major evaluation of blood tests for CA125 (a substance that suggests the presence of particular kinds of cancers, particularly ovarian cancer) and trans-vaginal ultrasounds as screening procedures for early ovarian cancer detection. Currently, 70,000 women are receiving these screening methods through this trial. When we are able to validate a screening method for ovarian cancer, the early detection alone – even without changes in current standards of treatment - will have a substantial impact on public health.

Through the NCI Director's Challenge project, we have undertaken major studies into the molecular classification of ovarian cancer. This research, being conducted at the University of Pennsylvania, the University of Michigan, Memorial Sloan-Kettering Cancer Center, and the intramural Center for Cancer Research at NCI, has helped us begin to understand the biology of ovarian cancer. In addition, we have established five Specialized Programs of Research Excellence, also known as SPOREs, to foster translational research in ovarian cancer. One of the standard drugs used to treat ovarian cancer worldwide, Taxol®, was discovered and developed by NCI in collaboration with investigators across the United States and five other international partner countries.

NCI has also begun the Proteomics Ovarian Cancer Recurrence Monitoring Prospective Trial. Among the outcomes of this trial will be a repository of tissue samples for proteomic and other biomarker validation mechanisms for the determination of ovarian cancer recurrence. Accrual of patients for this project began in June. This is a multi-institutional partnership led by NCI's intramural Center for Cancer Research in collaboration with the SPOREs. This trial will explore the opportunities of the emerging field of proteomics, which is the systematic study of proteins in a particular cell, tissue, or organism, as a way to detect early stages of ovarian cancer. Other collaborative ovarian cancer trials supported by NCI are studying the molecular characterization of newly diagnosed patients, prophylactic surgery for women at high risk for ovarian cancer, monitoring of breast cancer patients for mutations of the BRCA1 and/or BRCA2 gene (which make some women more susceptible to developing ovarian or breast cancer), as well as several trials that are looking for specific diagnostic signatures for malignancy versus benign or unaffected samples. In addition, NCI is currently sponsoring a national clinical trial aimed at evaluating a novel approach to ovarian cancer screening in women at increased genetic risk of ovarian cancer. While we recognize that more women diagnosed with this disease today are living longer, with a higher quality of life than they were twenty years ago, we also acknowledge that more work is needed to end the suffering and death that too many women still face. For women who have a high risk of

ovarian cancer, which includes a family history of breast, ovarian, endometrial, or colon cancer and a known BRCA1 or BRCA2 mutation, we recommend that they receive two yearly exams plus CA125 monitoring as well as a yearly trans-vaginal ultrasound.

Endometrial Cancer

Endometrial cancer, also known as uterine cancer, is the most common gynecologic cancer in the United States, though not the most lethal. Around 90% of endometrial cancers are diagnosed in the early stages of cancer, with an overall 85% survival rate. Population studies indicate that endometrial cancer is one where incidence and mortality are greatly affected by being overweight or obese, as measured by having a high body mass index (BMI). These data suggest that maintaining a normal body weight could prevent about one-half of endometrial cancers. However, the alarming trend of increasing BMI in the United States suggests that endometrial cancer may become more common.

NCI is able to utilize the latest technology to examine the genetic differences in endometrial cancers from women of normal and high BMI. The ability to monitor gene expression is at the heart of many research projects. This allows scientists to better understand the biology of risk, the knowledge of which will enable them to design and implement personalized preventive and therapeutic strategies. Through NCI's Clinical Trials Cooperative Groups, specifically the Gynecology Oncology Group (GOG), NCI has sponsored major anatomic and molecular staging studies of endometrial cancer. Additionally, the GOG has conducted landmark studies evaluating the roles of radiation, hormone therapy, and chemotherapy in women with endometrial cancer.

Education and Outreach Efforts to Address Gynecological Cancers

In addition to our research initiatives, NCI is also strongly committed to educational and outreach efforts in the area of gynecologic cancers and has fostered programs that reflect this commitment. NCI's Cancer Information Service (CIS) Partnership Program builds the capacity of partner organizations working in gynecologic cancer education to further the reach of their programs and services, with particular emphasis on medically underserved populations.

Our CIS Partnership Program, with more than 40 locations across the country, collaborates with local, State, and other Federal agencies. These collaborative cancer control partnership efforts focus on organizational data sharing, program planning, implementation, and training through the use of evidenced-based or evidence-informed tools. CIS also collects data on projects that inform the design and development of NCI materials and services.

Cervical cancer is a priority emphasis for our CIS Program. Every office, from Maine to California, conducts outreach on cervical cancer topics. For example, to promote community services and resources available to urban American Indian women in Los Angeles, the CIS joined county and local officials to raise awareness and provide education about the importance of cervical cancer screening. The project marks the fifth year of a cooperative campaign to build a community-based, sustainable cancer control infrastructure.

NCI also lends program planning support to cancer control outreach and research initiatives. The Human Papillomavirus (HPV) Study at the University of Hawaii is designed to determine the co-

factors that lead to persistent HPV infections, a cause of cervical cancer. Identification of these factors provides insight into the natural history of HPV infection, and may improve capacity to characterize women who are at greatest risk for cervical cancer. CIS provides support for this study in two critical areas: promotion and access. CIS is involved with development and implementation of a low-cost, culturally sensitive multimedia promotional campaign, and facilitates public access through use of NCI's 1-800-4-CANCER number to respond to questions from the public about cervical cancer. CIS then connects eligible callers to participating study centers.

For over a decade, our CIS Program and CDC's National Breast and Cervical Cancer Early Detection Program have been successfully collaborating to leverage the resources of both public health service agencies to better address the needs of underserved women. Each year, through NCI's 1-800-4-CANCER number, thousands of eligible women are referred to low-cost and no-cost CDC services.

CIS is also collaborating with the CDC, the Department of Agriculture, the American Cancer Society, and other NCI divisions to implement a national pilot program to increase cervical cancer screenings among never and/or rarely screened women in eight underserved Appalachian states. The initiative termed "TEAM-UP" has already effectively raised awareness in specific targeted areas and now the program is evaluating how much screening rates have improved. By uniting organizational resources toward a collective purpose, NCI and its partners design and implement programs with wider reach and greater impact on gynecologic cancer awareness, particularly cervical cancer education, outreach, and patient services.

NCI's Office of Education and Special Initiatives (OESI) aims to reduce the disparities related to cervical cancer with strategically planned educational programs. In addition to representing NCI on the Gynecologic Cancer Foundation's National Cervical Cancer Public Health Education Campaign, and participating in the TEAM UP initiative, OESI has an established cervical cancer education program. OESI works through intermediaries to reach rarely or never-screened women, works with Federal partners to facilitate women's access of care and participation in treatment decisions, and also enhances provider education. As part of OESI's program strategies for FY 2006, NCI is updating and developing culturally appropriate materials that address screening, follow-up, and treatment for cervical cancer. We will also be conducting formative research, developing population profiles, and setting up advisory groups for target populations in states with higher rates of cervical cancer incidence and mortality. In collaboration with the Health Resources and Services Administration-funded Community Health Centers, the Association of Clinicians for the Underserved, Area Health Education Centers, and the Department of Agriculture Cooperative Extension Agents, NCI will continue to conduct needs assessments for educational outreach and will supplement existing gynecologic cancer educational efforts.

NCI has printed several educational publications on gynecologic cancers. Earlier this year we printed a new publication, *Understanding Cervical Changes: A Health Guide for Women,* which is intended to assist women and their clinicians to understand the treatment decisions involved with abnormal Pap tests. The same booklets in both Vietnamese and Spanish are currently under development. NCI, in conjunction with the Vietnamese Medical Association, will also be promoting and disseminating the educational brochure *Cervical Cancer Risk: What Vietnamese Women Should Know.* This brochure will be available in Vietnamese and English.

Our Physician Data Query (PDQ) cancer information database, available through the NCI website, is a public access vehicle for educational information on gynecologic cancers. Through PDQ, the general public can access expert-reviewed information about factors that may influence the risk of developing cervical, ovarian, and uterine cancers and about the NCI research aimed at the prevention of these diseases.

Intramural and Collaborative Research Activities

Substantial advances have been made intramurally in the NCI Center for Cancer Research and the Division of Epidemiology and Genetics, and through collaborations with extramural colleagues who participate in the SPOREs network, the Cancer Genetic Network (CGN), and GOG clinical trials cooperative groups. Research advances made at NCI are also complemented by collaborations with private industry. In addition to the clinical trials done through the cooperative groups, NCI also sponsors Phase I and II clincial trials in gynecologic cancer through the NCI-designated Comprehensive Cancer Centers and a consortium of Canadian hospitals organized by the Princess Margaret Hospital in Toronto. NCI also co-sponsors the Gynecologic Cancer Intergroup (GCIG), which brings together investigators from all the clinical trials cooperative groups conducting trials for women with gynecologic cancers from around the world. The GCIG meets twice a year and under its umbrella, member groups have joined together to develop joint protocols and develop strategies for future research.

We are working to implement the recommendations of the Gynecological Cancer Progress Review Group, which will further strengthen our research in this area. We have also undertaken, in partnership with the American Cancer Society, the International Agency for Research on Cancer, the International Gynecologic Cancer Society, the International Union against Cancer, and the World Health Organization, a Global Initiative on Women's Cancer (GLOW) so that we can lift the burden of gynecologic cancer from around the world. This international partnership will focus on reducing the global burden of gynecologic cancer, breast cancer, and tobacco use among women. GLOW will include public and professional education, the development of a needs-assessment database, and technical assistance to countries in the developed and developing world as they work to strengthen cancer control efforts, including prevention, screening, diagnosis, treatment, palliation, and end of life care.

Conclusion

Eliminating the suffering and death from gynecologic cancer is a priority for the NCI. There is no single approach, organization, or act that will bring about an end to each of these diseases. It will require a collaborative effort between Federal agencies, private industry, States, health professionals and patients. Efforts to increase healthy life potential through interdisciplinary and interagency collaboration are well underway. Public outreach efforts, comprehensive and novel prevention and early detection strategies, and scientific pursuits to improve the standard of practice will yield the end of suffering and death due to gynecologic cancers.

Thank you, Mr. Chairman, for giving me the opportunity to present this information to the Subcommittee. I will be happy to answer any questions you may have.

Mr. CANNON. Thank you, Mr. Trimble. And I note that the light was still yellow when you finished. I appreciate that testimony.

The other members of the panel don't have to be so careful. We actually are interested in what you say.

Dr. Thompson, you are recognized for 5 minutes, or as much time as you would like to use.

STATEMENT OF DR. ED THOMPSON

Dr. THOMPSON. Thank you, Mr. Chairman. I am Dr. Ed Thompson, a specialist in preventive medicine and Chief of the Public Health Practice at the Centers for Disease Control and Prevention. It is an honor to be in front of this committee again. We appreciate the commitment of this committee to this important issue.

I would also like to thank Mr. Levin for referring to the members of this panel as distinguished. But we are distinguished by the degrees that we hold and by the positions that we occupy. The next panel will bring before you people who are distinguished by their personal courage, by their commitment to this important cause; and they are far more distinguished than we.

Gynecological cancers, cancers of the female reproductive organs—including, most importantly, those of the uterus, its endometrium, and cervix, the ovaries, and also, to a lesser extent, vaginal and vulvar cancer—are some of the most important cancers that affect women in this country. According to the most recent CDC and National Cancer Institute data—and as you have observed, Mr. Chairman—more than 71,000 women in the United States were diagnosed with a cancer affecting the reproductive organs in 2002, and approximately 27,000 women in the United States died from some form of gynecological cancer in that year.

Endometrial cancer may be the most common gynecological cancer; ovarian cancer the most deadly. Cervical cancer is the one cancer for which we currently have an effective and approved screening tool; and we will speak more about that in a moment as well.

At CDC, we are actively engaged in providing most current cancer prevention and control strategies at the community level, primarily through State and local health departments. These efforts reach hundreds of thousands of women every year in the United States. Our efforts are directed largely toward surveillance screening, where recommended, public education and awareness, health care provider education, epidemiology, and behavioral research. I would like to tell you about a few of our cancer initiatives, in particular those directed against cervical cancer. But by no means are we limiting our activities to those against cervical cancer.

The CDC's National Breast and Cervical Cancer Early Detection Program, which was established by Congress in 1991, has received growing support that helps low-income, uninsured, and underinsured women gain access to lifesaving screening programs. The national program currently provides screening support in all 50 States, the District of Columbia, four U.S. territories, and to 13 Indian tribes.

Since 1991, this program has provided more than 2.9 Papanicolaou tests and detected more than 1500 invasive cancers. Testament to the benefit of prevention and early detection is the fact that more than 74,500 cancer precursor lesions had been detected

or treated since the program's inception. The program represents a national infrastructure of more than 22,000 health care providers designed to reach those most in need.

Now, each year, between 10,000 and 12,000 women will be diagnosed with cervical cancer, and approximately 3,700 women will die from cervical cancer in the United States in 2005. The sad thing is that, in a very real way, every one of these 3,700 deaths is preventable and every one represents a failure of our American public health system.

We have achieved some success with cervical cancer mortality, reducing it by more than 70 percent over the last five decades, so that cervical cancer, once the No. 1 cause of cancer deaths among U.S. women, is now 14th. This is in large part due to widespread application of the Pap test to detect cervical abnormalities.

But as has been noted, approximately half of the cervical cancers that are diagnosed today in this country occur in women who have never received a Pap test. Another 10 percent occur in women who have not been screened within the past 5 years. So we are still not using this remarkable tool as effectively as it needs to be.

CDC also manages the National Comprehensive Cancer Control Program, which provides supports to develop comprehensive cancer control plans in all 50 States across the Nation. These plans serve as blueprints for developing and implementing cancer control activities. As an example, the California and the Florida Departments of Health, through this program, have identified and implemented strategies in their Statewide cancer control plans to identify the burden of ovarian and/or cervical cancer in local communities, strategies which include promoting referrals of ovarian cancer patients to clinical trials, promoting education and awareness within communities, and supporting ovarian cancer research.

In Alabama, the ovarian initiative focuses on enhancing the public's understanding of hereditary factors that increase the risk of developing ovarian cancer. And West Virginia's Raising Ovarian Cancer Awareness Initiative enlists ovarian cancer experts to speak with women in high-incidence counties about the symptoms of ovarian cancer and the importance of gynecological exams. Since implementing the program, the State has been able to demonstrate a 40 percent increase in participants' knowledge of the symptoms and risk factors for ovarian cancer.

In addition, CDC's national program of cancer registries collects information about incidents, diagnosis, treatment, and mortality. This data helps us to understand both the epidemiology of cancer occurrence and, in some cases, our effectiveness in bringing women to treatment.

In conclusion, gynecological cancers constitute a serious health problem in this country that CDC, along with our fellow Federal agencies, takes extremely seriously. Our role at CDC is focused on risk reduction, early detection, identifying and improving barriers to appropriate clinical practice, and to enhancing survivorship for women. There is much work to be done in all of these areas. I look forward to the opportunity to answer any questions that you may have.

[The prepared statement of Dr. Thompson follows:]

Testimony
Before the Subcommittee on Criminal Justice, Drug Policy, and Human Resources
Committee on Government Reform
United States House of Representatives

Centers for Disease Control and Prevention Public Health Work Relating to Gynecological Cancers

Statement of
Ed Thompson, M.D., M.P.H.
Chief of Public Health Practice
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services

For Release on Delivery
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Wednesday, September 7, 2005

Mr. Chairman and Members of the Subcommittee, good morning. I am Dr. Ed Thompson, the Chief of Public Health Practice for the Centers for Disease Control and Prevention (CDC).

Thank you for this opportunity to discuss CDC's public health work related to gynecologic cancers. Allow me to express at the very outset my gratitude to the Subcommittee for giving us the opportunity to talk to you about addressing the public health perspective surrounding gynecologic cancer.

The Types and Burden of Gynecologic Cancers in the United States

Gynecologic cancers are the uncontrolled growth and spread of abnormal cells originating in female reproductive organs that include the uterus, ovaries, cervix, vulva and vagina. According to the most recent CDC and National Cancer Institute (NCI) data included in the *United States Cancer Statistics (USCS): 2002 Incidence and Mortality* report:

- More than 71,000 women in the United States were diagnosed with a cancer affecting the reproductive organs; these data are from cancer registries that meet high quality data criteria and cover 93 percent of the U.S. population
- Over 27,000 women in the United States died from some form of gynecologic cancer; these death counts cover 100 percent of the U.S. population
- Endometrial cancer (cancer of the tissue that lines the uterus) is the most common gynecologic cancer
- Ovarian cancer is the most deadly gynecologic cancer

The U.S. cases (based on 93 percent of the U.S. population) and deaths (based on 100 percent of the U.S. population) for these cancers are as follows:

Endometrial (uterine) cancer:	Cases: 34,478	Deaths: 6,853
Ovarian:	Cases: 19,177	Deaths: 14,682
Cervical:	Cases: 12,085	Deaths: 3,952
Vulvar cancers:	Cases: 3,411	Deaths: 794
Vaginal:	Cases: 1,069	Deaths: 378
Other:	Counts: 970	Deaths: 432

Endometrial Cancer

Endometrial cancer is often associated with known risk factors. Women who: use estrogen replacement therapy (often used to treat menopause symptoms); use Tamoxifen and other selective estrogen receptor modulators; experience the onset of menstruation and menopause at early ages; are obese; carry the hereditary nonpolyposis colorectal cancer genetic abnormality; have polycystic ovarian syndrome; or have never been pregnant are at increased risks for developing endometrial cancer. Women who breastfeed or use combination oral contraceptives may have reduced risks for developing endometrial cancer. Currently, there are no screening tests for endometrial cancer. Most women survive this disease because of effective treatment strategies.

Ovarian Cancer

According to the CDC and NCI's USCS, ovarian cancer is the seventh most common cancer in women, and is the fifth leading cause of cancer death in women. Currently, half the women diagnosed with ovarian cancer die from the disease within five years. Ovarian cancer has been associated with certain risk factors. Factors that increase one's risk of developing ovarian cancer include the woman's age, family history of the disease, and the use of hormone replacement

therapy. Women who use oral contraceptives, have at least one child, breastfeed, or have undergone tubal ligation or a hysterectomy may have decreased risks for developing ovarian cancer. There is no reliable screening test that has been shown to reduce the risk of dying from ovarian cancer; however, several potential screening methods currently are being tested.

Cervical Cancer
Cervical cancer was once the leading cause of death for women in the United States; however, during the past four decades, incidence and mortality have declined significantly, primarily because of the widespread use of the Papanicolaou (Pap) test to detect cervical abnormalities. Regular Pap tests decrease one's risk for developing cervical cancer because they can detect precancerous cervical lesions at early, highly treatable stages. Cervical cancer is the only gynecologic cancer for which regular screening is recommended. The U.S. Preventive Services Task Force strongly recommends screening for cervical cancer in women who have been sexually active and have a cervix. Approximately half of the cervical cancers currently diagnosed in the United States are in women who have never received a Pap test, and an additional 10 percent occur in women who have not been screened within the past five years.

Human papillomavirus (HPV) infection is the primary cause for the development of cervical cancer. Increased incidence of cervical cancer is observed in women who: have multiple sexual partners; initiate sexual intercourse at early ages; have a high number of full-term pregnancies (seven or higher); smoke cigarettes; or use oral contraceptives for extended periods of time (five years or more). The relationship between these risk factors and cervical cancer is not entirely understood..

Vulvar and Vaginal Cancers
Other cancers of the female reproductive system are less common. Vulvar cancer, for example, accounts for only four percent of cancers in the female reproductive organs. HPV infection and smoking increase a woman's risk for developing vulvar cancer. Vaginal cancer accounts for approximately three percent of cancers of the female reproductive system. Young women whose mothers took diethylstilbestrol (DES) during pregnancy are at greater risk for developing vaginal cancer. The drug was given to pregnant women between 1945 and 1970 as a precaution against miscarriage. It has been suggested that HPV infection and smoking may also increase a woman's risk for developing vaginal cancer. Currently, there are no effective screening tests for vulvar or vaginal cancer, so women at increased risk need to be monitored closely.

CDC's Activities to Reduce the Burden of Gynecologic Cancers in the United States

CDC supports several initiatives specifically designed to reduce the burden of certain gynecologic cancers. For many of these cancers, prevention and early detection are essential to survival. CDC's efforts largely are directed towards surveillance; screening (where recommended); public education and awareness; health care provider education and awareness; and research.

National Breast and Cervical Cancer Early Detection Program
CDC's National Breast and Cervical Cancer Early Detection Program (NBCCEDP), which was established by Congress in 1991, helps low-income, uninsured, and under-served women gain access to lifesaving screening programs for early detection of breast and cervical cancers. The

national program currently provides screening support in all 50 States, the District of Columbia, 4 U.S. Territories, and 13 Tribes and Tribal organizations. Since 1991, the NBCCEDP has provided more than 2.9 million Pap tests and detected invasive cancers in more than 1,500 women. Testament to the benefits of prevention and early detection is the fact that in more than 38,000 women, cancer precursor lesions have been detected and treated since the program's inception. The NBCCEDP also provided diagnostic evaluation for an additional 38,000 precursor lesions for women referred to the program, as follow-up to abnormal results from screenings not provided by the program.

The NBCCEDP supports an array of strategies that include partnerships; public education and outreach; professional development; screening; tracking; follow-up; and case management services that work collaboratively to provide cervical cancer screening, diagnostic evaluation, and treatment referrals (where appropriate). The success of the program historically has depended on the complementary efforts of a variety of national organizations, as well as on state and community partners.

National Comprehensive Cancer Control Program

CDC's National Comprehensive Cancer Control Program (NCCCP) provides support in every State and the District of Columbia, as well as in several territories, Tribes, and Tribal organizations, to develop comprehensive cancer control plans. These plans serve as blueprints for developing and implementing cancer control activities. California and Florida have identified specific strategies in their cancer control plans to address the burden of ovarian and/or cervical cancer in local communities. In California, these strategies include: promoting referrals of ovarian cancer patients to clinical trials; promoting education and awareness within California's communities; and, supporting ovarian cancer research.

The program also provides funding specifically for ovarian cancer initiatives in West Virginia, Colorado, Alabama, Minnesota, New York, and Utah. Activities funded through these initiatives include efforts to increase healthcare provider education, public education, and awareness of ovarian cancer issues. In Alabama, the ovarian initiative focuses on enhancing the public's understanding of hereditary factors that increase the risk of developing ovarian cancer. West Virginia's *"Raising Ovarian Cancer Awareness Initiative"* enlists ovarian cancer experts to deliver outreach messages to women in high-incidence counties about the symptoms of ovarian cancer and the importance of gynecologic exams. Since implementing this initiative, the State has been able to demonstrate a 40 percent increase in participants' knowledge of the symptoms and risk factors for ovarian cancer.

National Program of Cancer Registries

Cancer registries collect information about incidence, diagnoses, treatment, and mortality. Data collected by cancer registries enable public health program planners to understand and address the cancer burden better, as well as evaluate the effectiveness of efforts to prevent, control, and treat cancer. CDC's National Program of Cancer Registries (NPCR), established in 1994, supports and promotes the collection and use of registry data in 45 States, the District of Columbia, and the territories of Puerto Rico, the Republic of Palau, and the Virgin Islands. The NPCR currently collects surveillance data for all cancers, including cancers of the cervix, uterus, ovaries, vagina, and vulva as reported for Whites, African Americans, Asians/Pacific Islanders,

Hispanics, and American Indian/Alaskan Natives. Data collected through the NPCR often are used by States to create burden assessments that guide program planning, outreach, and education efforts. The CDC's NPCR complements the National Cancer Institute's (NCI's) Surveillance, Epidemiology, and End Results (SEER) Registry program, which, prior to NPCR's establishment, collected cancer surveillance data for approximately fifteen percent of the U. S. population. Together, the NPCR and SEER programs collect cancer data for the entire U.S. population. These data are provided annually in the national United States Cancer Statistics report. This report can be accessed at http://www.cdc.gov/cancer/npcr/index.htm.

CDC's NPCR also is conducting Patterns of Care Studies that compare the quality of data concerning treatment and stage reported to nine NPCR registries, with data from the corresponding medical records. State tumor registries in California, Maryland, and New York are funded to support the special analyses of ovarian cancer treatment data in these medical record reviews. These studies are using population-based samples to estimate the proportion of patients in each state that received the recommended standard of care. Additionally, data on ovarian cancer outcomes and staging are being assessed by physician's specialty. Preliminary results are expected before the end of the year.

Cervical Cancer Education and Awareness Project

The CDC supports an education and awareness project through the National Organizations Strategies for Prevention, Early Detection, or Survivorship of Cancer in Underserved Populations program. The project's goal is to reduce cervical cancer incidence and mortality among working women by promoting increased cervical screening and annual follow up for women in unions. Several education and awareness brochures have been produced from focus group analyses. CDC has partnered with the National Education Association's Health Information Network to increase the circulation of their education and awareness materials among teachers and other support professionals.

Partnerships to Reduce the Burden of Gynecologic Cancers

The CDC has formed partnerships with other Federal and non-Federal organizations to improve prevention, early detection, and treatment of certain gynecologic cancers. An example of such collaboration is found in the development of *The Guide to Community Preventive Services*, which provides systemic reviews and recommendations for interventions. The task force responsible for this guide is multi-disciplinary, and includes perspectives that represent state and local health departments, managed care, academia, behavioral and social sciences, and others. This task force reviews and assesses the quality of available evidence on the effectiveness of community preventive health services, and develops recommendations for specific focus areas, including cervical cancer.

Another example of collaboration to reduce the burden of certain gynecologic cancers is the development of the *Family Healthware* Web-based assessment tool, supported by CDC, the National Institutes of Health, academia, and State health departments. The tool promotes the use of family history information to assess risk and determine prevention strategies. Specifically, the tool assesses familial risk for six chronic diseases, including ovarian cancer, and recommends

early detection and prevention strategies. Evidence strongly suggests that a positive family history of ovarian cancer increases one's risk for developing the disease.

The National Cervical Cancer Public Education Campaign encourages women to take action and get screened to prevent cervical cancer. Led by the Gynecologic Cancer Foundation and supported by partners that include the CDC, NCI, and the American Cancer Society, the educational campaign offers women and providers information about the causes of cervical cancer, as well as information about prevention and early detection. The campaign has developed educational brochures and patient presentations to help women understand cervical cancer and encourage appropriate screening and follow-up. The campaign also offers a resource list for women for obtaining cancer information and for identifying screening and patient support resources.

CDC's Research Activities to Address the Burden of Gynecologic Cancers in the United States

CDC has an active public health research program related to ovarian cancer. To guide the development of these ovarian cancer research activities, CDC sponsored workshops in 2000 and 2002 with outside experts in clinical and epidemiologic research, public health leaders from Federal and State agencies, and ovarian cancer survivors. These workshop participants identified key areas for research related to learning more about early symptoms and methods for earlier diagnosis as well as optimizing treatment and end of life care. In response to the recommendations from these workshops, the cancer epidemiology and applied research program at CDC has several ongoing studies to identify interventions that can improve the quality of life of women diagnosed with ovarian cancer. For example, research is focusing on when a woman seeks care and for what symptoms, how medical care providers respond to these symptoms; and what diagnostic practices shorten the time to diagnosis and can improve surgical evaluation and end-of-life care.

With regard to cervical cancer, CDC's program in cancer epidemiology and applied research is developing and evaluating behavioral provider and patient-based interventions aimed at increasing cervical cancer screening among Mexican women, African-American women, and low-income women. Through this research, we intend to provide evidence about effective, culturally sensitive methods to reach specific groups of women who have rarely or never been screened for cervical cancer. We also are conducting research on the attitudes, practices and training needs of providers of cervical cancer screening and follow-up using data collected through CDC's National Ambulatory Medical Care Survey and data collected about participants in CDC's NBCCEDP. In addition, CDC has been collecting data on Pap testing practices from two national CDC surveys, the National Health Interview Survey and the Behavioral Risk Factor Surveillance System, to monitor trends in Pap testing, understand the disparities in cervical cancer screening, and to identify women who are being over screened.

CDC's Publications Concerning Gynecologic Cancers in the United States

The CDC recently published several articles and a report related to cervical cancer screening. "Breast and Cervical Cancer Screening Among Mississippi Delta Women," published in the *Journal of Health Care for the Poor and Underserved* in 2004, describes screening practices and

behaviors among women in a region where cervical cancer mortality is considerably higher than in other areas.

"Adherence to Guidelines for Follow-up of Low-Grade Cytologic Abnormalities among Medically Underserved Women," published in a 2005 issue of *Obstetrics and Gynecology*, describes specific screening practices of health care providers participating in the NBCCEDP. Results from this study are used to develop strategies for educating NBCCEDP health care providers.

The National Breast and Cervical Cancer Early Detection Program: 1991-2002 National Report, released in 2005, is a CDC publication that describes screening successes and challenges.

Conclusion

Gynecologic cancers constitute a serious health problem in this country. Four of the five cancers mentioned today do not have an approved screening test. Our role at CDC is focused on risk reduction, early detection, surveillance, identifying and improving barriers to appropriate clinical practice, and enhanced survivorship. There is much work to be done in these areas for addressing all gynecological cancers. It is essential that all women in the United States, and the health care providers who treat them, have access to up-to-date, accurate information about these cancers. One way to improve access to good healthcare for women is through education and awareness campaigns for gynecologic cancer designed to increase knowledge and change behaviors. Any gynecologic cancer campaign should be population based, with an emphasis on underserved women and their healthcare providers. The campaigns should employ multiple strategies to reach all women in need and they should be evaluated and tested for effectiveness. Then, the most effective strategies should be widely disseminated through a comprehensive national campaign.

CDC has a strong presence in the field of gynecologic cancers, and is currently working in several critical areas. The CDC will continue to support:

- the **National Breast and Cervical Cancer Screening Program**, which provides access to cervical cancer screening to uninsured, poor, underserved women in this country;
- the **National Comprehensive Cancer Control Program,** which promotes the inclusion and implementation of ovarian cancer education and awareness initiatives in cancer control plans across the nation;
- the **National Cancer Registries Program**'s ongoing activities to address gynecologic cancers through the population-based collection, analysis, and sharing of gynecologic cancer surveillance data;
- research to improve education and increase awareness for the public and health care providers, and improve and maintain the development and implementation of effective screening practices and interventions; and,
- partnerships with Federal, State, academic, and community organizations to improve gynecologic cancer experiences and outcomes.

Thank you again for this opportunity to speak with you about public health issues surrounding gynecologic cancers, and CDC's work related to these diseases. I am happy to answer any questions.

Mr. CANNON. Thank you, Dr. Thompson. We appreciate that.
Dr. Pazdur. Is that an appropriate pronunciation?
Dr. PAZDUR. Pazdur.
Mr. CANNON. Pazdur.

STATEMENT OF DR. RICHARD PAZDUR

Dr. PAZDUR. Mr. Chairman, members of the subcommittee, I am Dr. Richard Pazdur, M.D., FDA's Director of the Office of Oncology Drug Products within the Office of New Drugs at the Center for Drug Evaluation and Research [CDER]. I am pleased to be here today to discuss prevention, early detection, and treatment of gynecological cancers.

The FDA's mission is to promote and protect the public health by helping to assure the safety and efficacy of human drugs and medical devices. Let me begin by informing you of recent structural changes within the FDA that are intended to provide a stronger and more consistent approach to the review process for drugs used to diagnose, treat, and prevent cancer.

In July 2005, the FDA created a new Office of Oncology Drug Products. This office has three divisions that will review applications for safety and effectiveness: the Division of Drug Oncology Products, Biological Oncology Products, and Medical Imaging and Hematology Products. Also, the Office will develop and lead a comprehensive oncology program to facilitate coordination of oncology activities across all FDA centers and ensure ongoing outreach and collaboration between the FDA, the National Cancer Institute, and other cancer-related organizations.

The Office expects to improve the consistency of review and policy toward oncology drugs and bring together a critical mass of oncologists who will help guide the development of these new therapies. Although many details of this new structure are still evolving, I am pleased to be working with many talented and dedicated scientists who comprise this new office.

The access process for cancer drugs usually starts with a sponsor seeking to develop a new cancer drug. A sponsor is usually a pharmaceutical company or a research scientist at the university or at the National Cancer Institute at the National Institutes of Health. Before clinical testing begins, researchers analyze the drug's main physical and chemical properties in the laboratory and studies its pharmacological and toxic effects in laboratory animals. If the laboratory and animal studies show promise, the sponsor submits an investigational new drug application to the FDA prior to initiating testing in patients.

New therapies for the treatment of gynecological cancer are being investigated. Hundreds of clinical trials in ovarian, cervical, endometrial, and other gynecological cancers are publicly listed. The FDA has several programs to expedite drug development and expand access to unapproved therapies. All of these programs have been instrumental in shortening the time to marketing approval for cancer drugs and biologics.

Under the Accelerated Approval Rule, the FDA can approve treatments for serious or life-threatening conditions that demonstrate the potential to address unmet medical needs on the basis of a "surrogate endpoint" that is reasonably likely to predict clinical

benefit. A surrogate endpoint is a measure of drug effect—for example, tumor shrinkage—that does not by itself show direct clinical benefit such as decreased pain or longer survival, but is thought to lead to such benefit.

Priority new drug applications and effectiveness supplements are those that could have important therapeutic impacts. The FDA's goal is to review a priority product within 6 months, rather than the standard review time of 10 months.

The fast track refers to a process for frequent and timely interaction between sponsors and the FDA during drug development. The fast track programs are designed to facilitate the development and to expedite the review of new drugs and biologics to treat serious or life-threatening conditions that demonstrate the potential to address unmet medical needs.

We are currently in the early stages of planning a workshop for oncology experts, radiation oncology, statisticians, industry representatives, and patient advocates to discuss endpoints related to ovarian cancer, and hope to hold this meeting sometime in early 2006. A steering committee including representation from the FDA, the NCI, the American Society of Clinical Oncology, and the American Association for Cancer Research is planning these workshops.

The FDA's Office of Special Health Issues works with patients with life-threatening diseases. Patients usually call to obtain information about unapproved treatments currently being researched. We direct callers to public information about clinical trials for which they might be eligible and provide additional sources of information to patients and their family members.

The formation of the NCI-FDA Interagency Oncology Task Force, in 2003, was an important strategic step toward achieving FDA's goal of increasing availability and the use of safe and effective treatments for cancer, and the NCI's goal of eliminating pain and suffering and death from cancer by 2015. The purpose of this Task Force is to leverage the expertise and capabilities of both agencies to help streamline and accelerate the overall development of the diagnostic, preventative, and therapeutic interventions of cancer.

Finally, we want to mention the FDA's Critical Path Initiative. There is growing concern that many of the new basic science discoveries made in recent years may not yield quickly more effective, affordable, and safe medical products for patients because the current medical product development path is becoming increasingly challenging, inefficient, and costly. During the past several years, the number of new drugs and biologic applications submitted to the FDA has declined. The number of innovative medical devices applications has also decreased. In contrast, the cost of product development has soared over the last decade.

A new product development tool kit—containing powerful new scientific and technical methods such as animal or computer predictive models, biomarkers for safety and effectiveness, and new clinical evaluation techniques—are urgently needed to improve predictability and efficiency along with all critical path from the laboratory to commercial product development. The FDA is in the final stages of developing a critical path opportunity list based on the input and ideas contributed both by external stakeholders and the FDA reviewers.

The FDA is working with the NCI, industry, academia, patient and other organizations to ensure that cancer patients have timely and important information about available cancer drugs, including those for gynecological cancer indications.

Thank you for this opportunity to testify. I will be happy to answer any questions the subcommittee might have.

[The prepared statement of Dr. Pazdur follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Statement of

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Food and Drug Administration

U. S. Department of Health and Human Services

"Women and Cancer – Where Are We in Prevention, Early Detection and Treatment of Gynecologic Cancers?"

Before the

Subcommittee on Criminal Justice, Drug Policy and Human Resources

Committee on Government Reform

U. S. House of Representatives

September 7, 2005

Release Only Upon Delivery

INTRODUCTION

Mr. Chairman, Members of the Subcommittee, I am Richard Pazdur, M.D., Director of the Office of Oncology Drug Products, Office of New Drugs at the Center for Drug Evaluation and Research (CDER), Food and Drug Administration (FDA or the Agency). Prior to coming to FDA, I was associated with the M.D. Anderson Cancer Center in Houston, Texas, for 11 years, where I was involved in patient care, cancer research, medical education, and administration. Because of my prior experience with patient, academic and scientific communities, I am acutely aware of how FDA's decisions and requirements can impact the public we serve.

I particularly am pleased to be with you today, during Gynecologic Oncology Awareness Month and Ovarian Cancer Awareness Month, to discuss the topics of prevention, early detection and treatment of gynecologic cancers. My testimony will focus more on the treatment of these cancers since it is the Mission of FDA in this area to promote and protect the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products and medical devices by helping to speed innovations that make medicines more effective, safer and more affordable and to help the public obtain the accurate, science-based information they need to use these medicines to improve their health. I also will share with you what our Agency is doing to accelerate the delivery of innovative cancer treatments to meet the needs of cancer patients and their families. Further, I will discuss the Agency's interaction with other government agencies, drug sponsors and the medical professional community in an effort to streamline and accelerate the overall development of diagnostic, preventive and therapeutic interventions for cancer, as well as FDA's Critical Path Initiative. In my remarks, I will use the term "drug" to refer to both traditional small molecules and to therapeutic biological products.

RECENT CONSOLIDATION OF ONCOLOGY REVIEW FUNCTIONS AT FDA

Let me begin by informing you of recent structural changes within the Agency that are intended to provide a stronger and more consistent approach to the review process for drugs and most therapeutic biologics used to diagnose, treat and prevent cancer. In July 2004 FDA announced creation of a new Office of Oncology Drug Products (OODP or the Office) within CDER comprised of three previous areas within CDER responsible for the oversight of drugs and therapeutic biologics associated with cancer treatment and prevention. Three similar but new divisions within ODP were created entitled the Division of Drug Oncology Products, the Division of Biologic Oncology Products and the Division of Medical Imaging and Hematology Products. I am honored that this past April, I was selected as the first Director of OODP.

The Office also is to develop and lead a comprehensive Oncology Program to facilitate coordination of oncology activities across all Centers of FDA, and ensure ongoing outreach and collaboration between FDA, the National Cancer Institute (NCI) and other cancer-related organizations within and outside of the government. This cross cutting Oncology Program is to facilitate cross Agency expert consultation, provide a forum to discuss and develop regulatory policy and standards and serve as a focal point for Agency interaction and collaboration with oncology professional societies, NCI and other important stakeholders. The program also is to coordinate cross cutting training and oncology education programs.

The Office expects to improve the consistency of review and policy toward oncology drugs and bring together a critical mass of oncologists who will help guide the development of new therapies. Although many details of this new structure are still evolving, I am extremely pleased to be working with the many talented and dedicated scientists who comprise the Office, in order to realize FDA's vision for it.

CLINICAL TRIALS – The Phases of Clinical Trials

FDA's primary obligations are those vested in us by Congress in the Federal Food, Drug and Cosmetic (FD&C) Act and the Public Health Service (PHS) Act, that ensure that marketed medical products are safe, effective, and properly labeled and that experimental drug studies are designed to protect the patient volunteers. Before being approved by FDA for marketing, new drugs and biological products must be proven effective in controlled clinical trials and shown to be safe. In this context, safe is defined as a determination that the foreseeable risks are outweighed by the benefits of the new product under consideration. FDA is directed, under the FD&C Act, to rely on evidence of effectiveness based upon adequate and well-controlled studies. Those persons who participate in any trials under an Investigational New Drug (IND) application must be informed fully of the risks and possible benefits of their participation, and studies must be designed adequately to protect the patients from harm.

Most clinical trials are carried out in consecutive steps called phases. Each phase is designed to gather different types of information. Patients may be eligible to participate in studies in different phases, depending on their general condition, the type and stage of their cancer, and what therapy, if any, they already have had. Patients are seen regularly by the investigators during the study to determine the effect of the treatment, and treatment is stopped if side effects become too severe.

The purpose of a Phase 1 clinical trial is to find the best way to administer a new treatment and learn how much of it can be given safely. In a Phase 1 study, a new treatment is given to a small number of patients. For a new drug, the study starts by giving a low dose of the drug and, if necessary as preliminary findings of the trial suggest, the dose may then be adjusted as new patients enter the trial.

Phase 2 studies are designed to find out whether a treatment has the intended effect. In the context of cancer therapy, Phase 2 studies are designed to study whether the treatment actually damages cancer cells or slows their growth in people. Usually groups of 20 to 50 patients with one type of cancer receive an investigational treatment in Phase 2 studies. For example, patients with breast cancer who no longer respond to standard therapy may choose to be treated in a Phase 2 study. Patients are observed closely for anti-cancer effect by repeated measurement of tumor size to see whether tumors have shrunk since the beginning of the trial.

Phase 3 studies usually compare a new treatment that appeared to have an effect in the small Phase 2 studies with standard (generally accepted) therapy, or compare the combination of the new therapy and standard therapy to standard therapy alone. Phase 3 trials require larger numbers of patients; some trials enroll hundreds or even thousands of patients. Patients usually are randomized (assigned by chance) to the treatments being studied. The group that receives the standard

treatment is called the "control" group. The researchers expect that a certain number of these patients will be helped by the treatment. Phase 4 trials may be conducted after a drug has been approved. Companies often, for example, carry out studies of new drugs in patients with different tumors or with different stages of disease. FDA also may request, and the sponsor may agree to conduct, other post-marketing studies to provide additional data to improve the safe and effective use of the drug.

Clinical Trials for Cancer Therapy

The access process starts with a drug sponsor seeking to develop a new cancer drug, which is usually a pharmaceutical company or a research scientist at a university or at the National Cancer Institute (NCI) at the National Institutes of Health (NIH). Before clinical testing begins, researchers analyze the drug's main physical and chemical properties in the laboratory and study its pharmacologic and toxic effects in laboratory animals. These are known as pre-clinical studies. If the laboratory and animal study results show promise, the sponsor submits an IND application for FDA review prior to initiating testing in people.

In addition to FDA review of a protocol submitted to an IND the protocol also is subject to oversight by a local Institutional Review Board (IRB). An IRB is a panel of scientists and non-scientists that oversees clinical research, and approves the initiation of the protocol at their respective institution. Experienced clinical investigators give the drug to a small number of cancer patients who have no other available therapy. These phase 1 studies assess the most common acute adverse effects and examine the amount of drug that patients can take safely without unacceptable side effects. Initial clinical studies also begin to clarify what happens to a drug in the human body, how it is changed (metabolized), how much of it (or a metabolite) gets into the blood and various organs, how long it stays in the body, and how the body gets rid of the drug and its effects.

If Phase 1 studies do not reveal major problems, such as unacceptable toxicity, the next step is to conduct a clinical study in which the drug is given to patients who have medical conditions that may benefit from the potential cancer drugs. Several different types of cancers often are explored in these Phase 2 studies. Researchers then assess whether the drug has a favorable effect on the condition.

Testing experimental drugs in people inevitably presents ethical questions. A general principle, agreed on internationally, is that patients in a study must not be denied known effective treatment that prevents death or serious injury. In cancer trials, patients are never denied such treatment.

FDA recommends that anyone interested in participating in a clinical trial discuss the idea with his or her physician. Doctors may be able to provide information on investigational drugs that might be of benefit to their patients and of clinical trials involving these drugs. Patients can obtain detailed information from a variety of sources, including drug sponsors, FDA (if the information is public), and NIH. In fact, industry-sponsored trials are required statutorily to be listed on *www.clinicaltrials.gov*.

Clinical trials are carried out at major medical research centers, at NIH, and even in doctors' offices. Although they may involve hospitalized patients, many clinical trials can be conducted on an outpatient basis, with participants more or less going about their normal activities. The center or institution where a study is to be carried out may run newspaper advertisements recruiting potential participants for clinical studies that tell readers where to call or write for further information.

These aspects and other implications of taking part in a clinical trial must be explained fully in advance by the people conducting the trial, and patients must agree to the conditions before they can participate. The hope of personally benefiting from a new drug or the desire to take part in research that might one day benefit millions is what makes people volunteer for clinical trials. It should not prevent them, however, from finding out all they can about being a part of the process. They also must understand that new treatments, although promising, may prove ineffective or harmful.

EXPEDITING APPROVAL OF CANCER THERAPIES

The Food and Drug Administration Modernization Act (FDAMA), enacted November 21, 1997, amended the FD&C Act relating to the regulation of food, drugs, devices, and biological products. With the passage of FDAMA, Congress enhanced FDA's mission in ways that recognized that the Agency would be operating in a 21st century characterized by increasing technological, trade, and public health complexities. Among other things, FDAMA codified many of FDA's initiatives and existing programs designed to expedite drug development and expand access to unapproved therapies. All of these programs have been instrumental in shortening the time to marketing approval for cancer drugs and biologics.

FDA programs codified in FDAMA include:

- Expediting Approval of Cancer Drugs – FDA has shown a long-standing commitment to the prompt consideration and, when appropriate, early approval of new therapies for cancer patients. In 1996, the Agency launched its "Reinventing the Regulation of Cancer Drugs" initiative with the goal of accelerating the approval of and expanding patient access to cancer drugs. This program described how FDA's Accelerated Approval Rule or Subpart H Approval (21 CFR 314.510) and for biologics Subpart E (21 CFR 601.40) would be used to approve cancer drugs earlier in their development and for expanded access programs (the treatment IND) to be used to make promising drugs broadly available prior to marketing.

    - Accelerated Approval or Subpart H or Subpart E Approval - Under the Accelerated Approval Rule subsequently incorporated into the Fast Track provision of FDAMA (section 112), FDA can approve treatments for serious or life-threatening conditions that demonstrate the potential to address unmet medical needs on the basis of a "surrogate endpoint" that is "reasonably likely" to predict clinical benefit. A surrogate endpoint is a measure of drug effect (e.g., tumor shrinkage) that does not by itself show a patient benefit, such as decreased pain or longer survival, but is thought likely to lead to such a benefit. Some surrogate endpoints are well established (blood pressure, for example) and

are a routine basis for approval. Other surrogate endpoints are not as certain, and these may now be used under our Accelerated Approval authority. The reinvention program specifically declared that FDA would rely on tumor shrinkage in refractory cancer as a basis for approval, and we have done so regularly. Since 1996, four out of nine biological products were approved under accelerated approval, and many new drug approvals have been based on this study endpoint, allowing for earlier marketing than would have been possible had FDA waited for a documented effect on such an endpoint or survival. Under accelerated approval, the manufacturer commits to study the drug's actual clinical benefit after marketing.

- Priority Review-When marketing applications are submitted they are designated as priority (P) or standard (S). Priority New Drug Applications (NDAs) and effectiveness supplements are those that could have important therapeutic impacts. A priority designation is intended to direct overall attention and resources to the evaluation of applications for products that are reported to have the potential for providing significant therapeutic advances. Specifically, FDA's goal is to review a priority within 6 months rather than the standard review time of 10 months. Since 1996, 13 biologics (9 Biologic License Applications (BLA) and 4 supplements) and 55 drugs (27 NDAs and 28 supplements) for cancer therapies have received priority review and approval.

- Fast Track refers to a process for frequent and timely interaction with FDA during drug development. The fast track programs are designed to facilitate the development of and expedite the review of new drugs and biologics to treat serious or life-threatening conditions that demonstrate the potential to address unmet medical needs. To provide clear information to industry regarding participation in the fast track process, FDA issued a guidance document on this provision in September 1998.

Fast-track designation for a clinical development program can occur at any time of the development process. It is initiated by the sponsor's request for designation and can be granted for any development program (as projected by the sponsor) that is intended to demonstrate that its drug/biologic will affect a serious or life-threatening disease or condition. This may be an improvement over existing therapy or treatment where no alternative therapy exists.

Recently two exploratory pilot programs were instituted to build on the current practice of interaction between FDA and applicants during drug development and application review.

- *Pilot 1, Reviewable Units for Fast Track Products*, provides for the review of a limited number of presubmitted portions of an applicant's marketing application (reviewable units) based on the terms and conditions agreed upon by the applicant and FDA.
- *Pilot 2, Scientific Feedback and Interactions During Development of Fast Track Products*, provides frequent feedback based on a prospectively defined agreement between FDA and applicants.

It is important to note that FDAMA did not alter FDA's effectiveness standard, except by giving explicit authority to the Agency to rely on data from a single, adequate and well-controlled clinical investigation and confirmatory evidence as support for approval in certain cases. Even for drugs intended for serious and fatal illnesses, there must be substantial evidence that the drug

will have the effect it purports to have. As noted, however, the law recognizes that the nature of the effect that needs to be demonstrated might vary depending on the urgency and clinical need.

PLANNED WORKSHOP ON OVARIAN ENDPOINTS

We currently are in the early stages of planning a workshop to discuss endpoints related to ovarian cancer and hope to hold this meeting sometime in early 2006. Planning for workshops is guided by a steering committee that includes representation from FDA, NCI, the American Society of Clinical Oncology, and the American Association for Cancer Research. Workshop participants will include oncology experts, radiation oncologists, statisticians, industry representatives, and patient advocates.

In late 2002, FDA embarked on a project to evaluate potential endpoints for cancer drug approval. Endpoints have been examined for the most common cancers: lung, colon, and prostate cancer. For each cancer, FDA held public workshops to identify important issues, and these issues were later discussed in meetings of the Oncologic Drugs Advisory Committee (ODAC). Subsequently, guidance documents will be published describing FDA's current thinking on endpoints for cancer drug approval. In June 2005, FDA co-sponsored a workshop with the American Society of Hematologists (ASH) to explore endpoints in acute leukemias.

EXPANDED ACCESS TO INVESTIGATIONAL NEW DRUG PRODUCTS

Also codified in FDAMA are the procedures known as a Single Patient IND or Treatment IND. FDA believes it is appropriate to make certain promising, but not yet approved, products available to patients with serious and life-threatening illnesses who lack alternative treatment. A major goal of the treatment IND proposed in 1982, and made final in 1987, was to make unapproved but promising drugs with appropriate evidence of effectiveness widely available prior to marketing. In the past such drugs often were available but only at selected sites. There also is a process for giving expanded access to unapproved medical devices. Exactly what to do and the Agency's role in the process are described in the oncology part of FDA's website: *www.fda.gov/cder/cancer/singleIND.html*.

LIST OF DRUGS APPROVED FOR TREATMENT OF OVARIAN CANCER

A list of the drugs approved for the treatment of gynecologic cancers is at the end of this testimony at Attachment A. New therapies for the treatment of gynecologic cancer is an area of active clinical investigations. Publicly available information on active clinical trials is available at *www.clinicaltrials.gov*. Hundreds of clinical trials in ovarian, cervical, endometrial and other gynecologic cancers are listed.

FDA OFFICE OF SPECIAL HEALTH ISSUES

FDA staff is aware of the concerns that patients with life-threatening illnesses and their families experience when trying to obtain information about potentially helpful therapies, especially when there is no treatment for their disease. In addition to staff within FDA's medical product centers that routinely provide assistance and information to consumers, FDA, in 1988, created the Office

of Special Health Issues (OSHI), with trained staff to work with patients with life-threatening diseases. The skilled staff of OSHI works with patients who have serious or life-threatening diseases such as AIDS, cancer, Parkinson's disease, or Alzheimers disease, to name a few.

Patients usually call to obtain information about unapproved treatments currently being researched. Once our staff explains that FDA cannot disclose certain confidential information about drugs or devices that are not yet approved, we direct callers to listings of clinical trials where they can locate a trial for which they might be eligible.

We are able to talk with patients about any treatment that appears in a public access database, such as the *ClinicalTrials.gov* database operated by the National Library of Medicine or NCI's database at *http://cancertrials.nci.nih.gov*. Our staff is working actively with the National Library of Medicine and the pharmaceutical industry to include more clinical trials in the *ClinicalTrials.gov* database. If a patient does not have a computer, a patient can access the NCI's clinical trials listing by calling 1-800-4-CANCER. An information specialist will search the database and send the trials information to the patient within 3 days.

Our goals in serving patients with life-threatening diseases and their family members are straightforward:

- Promptness (returning patients' and family members' calls within 24 hours);
- Accessibility (listening to the caller's concerns and giving the caller as much time as he or she needs);
- Education (about the drug approval process and his or her options); and
- Assistance (providing additional information to the patient or family member that may be helpful, e.g. other sources of information).

FDA/SPONSOR INTERACTION DURING CLINICAL TRIALS AND THE DRUG REVIEW PROCESS

FDA receives reports about on-going clinical studies to ensure that subjects who volunteer for studies are protected and that the quality and integrity of scientific data are maintained. FDA makes itself available to interact with product sponsors during the drug review process as indicated in the diagram at Attachment B, showing the Drug Development Pipeline. Formal meetings were established by Congress under the FDA Modernization Act of 1997, and FDA has committed to performance goals for such meetings under the Prescription Drug User Fee program. These meetings can occur from the pre-IND phase all the way to pre-NDA/BLA submission. FDA receives requests for and convenes over 2,000 such meetings with sponsors each year which can help sponsors clarify research questions that need to be addressed, identify earlier the unsuccessful compounds, and focus research on studies of compounds that are more likely to lead to approval.

THE NCI/FDA INTERAGENCY ONCOLOGY TASK FORCE (IOTF)

The Interagency Oncology Task Force (IOTF) was formed early in 2003 by Dr. Andrew von Eschenbach, Director of the National Cancer Institute, and Dr. Mark McClellan, then Commissioner of Food and Drugs. The formation of the IOTF was an important strategic step toward achieving FDA's goal of increasing the availability and use of safe and effective treatments for cancer, and NCI's challenge goal of eliminating suffering and death from cancer by 2015. The purpose of the IOTF is to leverage the expertise and capabilities of both agencies for the expressed purpose of streamlining and accelerating the overall development of diagnostic, preventive and therapeutic interventions for cancer.

Since its formation, the members of IOTF collaboratively have undertaken an analysis of the overall development and review process for new oncology drugs and devices and identified several specific initiatives that are directed toward optimizing drug and device development. NCI is working to specifically gather and synthesize the scientific support needed by FDA to address specific regulatory issues. FDA is working cooperatively with NCI to address important scientific issues including:

- Committing to encourage physicians and scientists to become expert in clinical research, the clinical approval process and the translation of laboratory science into new products for cancer through high quality training,

- Developing markers of clinical benefit using imaging in oncology drug development, collaborative development of the scientific data needed to establish improved surrogate endpoints for cancer clinical trials, and the potential utilization of advanced technologies,

- Utilizing bio-informatics technology to expand the use of an electronic form of the IND application,

- Establish a process to facilitate the interaction between NCI-supported investigators and FDA during any phase of the regulatory review process,

- Enhancing scientifically driven review of the pre-clinical requirements for IND filings; and

- Developing the scientific base for consistent review of cancer prevention agents.

The IOTF is meeting regularly and actively addressing issues that can ultimately speed the development of new advanced interventions for cancer. The IOTF subcommittees are currently developing resource materials that will assist investigators in preparing the data needed for FDA's regulatory process. FDA has already responded with guidance documents (such as a recent guidance on pharmacogenomics) and process changes.

FDA's CRITICAL PATH INITIATIVE

On March 16, 2004, FDA issued a report entitled, "Advancing America's Health; Advancing Medical Breakthroughs." This "Critical Path" paper calls for academic researchers, product developers, and patient groups to work with FDA to help identify opportunities to modernize tools for speeding approvable and innovative products to market to improve public health. The report provides FDA's analysis of the current pipeline problem -- the recent slowdown, instead of the expected acceleration, in innovative medical therapies reaching patients, and suggestions for addressing this problem.

Today's revolution in biomedical science has raised new hope for the prevention, treatment, and cure of serious illnesses. However, there is growing concern that many of the new basic science discoveries made in recent years may not yield quickly more effective, affordable, and safe medical products for patients. This is because the current medical product development path is becoming increasingly challenging, inefficient, and costly. During the last several years, the number of new drug and biologic applications submitted to FDA has declined significantly; the number of innovative medical device applications also has decreased. In contrast, the costs of product development have soared over the last decade. Because of rising costs, innovators often concentrate their efforts on products with potentially high market return. Emerging contenders for resources include the development of products targeted for important public health needs (e.g., counter terrorism), less common diseases, prevalent third world diseases, prevention indications, or individualized therapy is becoming increasingly challenging. In fact, with rising health care costs, there now is concern about how the nation can continue to pay even for existing therapies. If the costs and difficulties of medical product development continue to grow, innovation will continue to stagnate or decline and the biomedical revolution may not deliver on its promise of better health. Attachment C to this testimony demonstrates this for drugs and biologics through 2002.

A problem, in FDA's view, is that the applied sciences needed for medical product development have not kept pace with the tremendous advances in the basic sciences. The new science is not being used to guide the technology development process in the same way that it is accelerating the technology discovery process. For medical technology, performance is measured in terms of product safety and effectiveness. Not enough applied scientific work has been done to create new tools to get fundamentally better answers about how the safety and effectiveness of new products can be demonstrated, in faster time frames, with more certainty, and at lower costs. In many cases, developers have no choice but to use the tools and concepts of the last century to assess this century's treatment candidates. As a result, the vast majority of investigational products that enter clinical trials fail. Often, product development programs must be abandoned after extensive investment of time and resources. This high failure rate drives up costs, and developers are forced to use the profits from a decreasing number of successful products to subsidize a growing number of expensive failures. Finally, the path to market, even for successful candidates, is long, costly, and inefficient, due in large part to the current reliance on suboptimal assessment methods.

A new product development toolkit -- containing powerful new scientific and technical methods such as animal or computer-based predictive models, biomarkers for safety and effectiveness, and new clinical evaluation techniques -- is needed urgently to improve predictability and

efficiency along the critical path from laboratory concept to commercial product. Superior product development science is needed to address these challenges -- to ensure that basic discoveries turn into new and better medical treatments. More efforts need to be directed at creating better tools for developing medical technologies. Finally, we need a knowledge base built not just on ideas from biomedical research, but also on reliable insights into the pathway to patients.

FDA is planning and beginning an initiative that will identify and prioritize (1) the most pressing development problems and (2) the areas that provide the greatest opportunities for rapid improvement and public health benefits. This will be done for all three dimensions along the critical path -- safety assessment, evaluation of medical utility, and product industrialization. It is critical that we enlist all relevant stakeholders in this effort. We are in the final stages of developing a Critical Path Opportunity List, based on the input and ideas contributed both by external stakeholders and FDA reviewers. Concurrently, FDA has refocused its internal efforts to ensure that we are working on the most important problems and intensified our support of key projects. We are working closely with NCI under the IOTF on proposals to advance the science of cancer drug development.

Through scientific research focused on these challenges, we can improve the process for getting new and better treatments to patients. Directing research not only to new medical breakthroughs, but also to breakthrough tools for developing new treatments, is an essential step in providing patients with more timely, affordable, and predictable access to new therapies. We are confident that, with effective collaboration between government, academia, and the private sector, these goals can be achieved.

CONCLUSION

FDA is working with NCI, industry, academia, patient and other organizations to ensure that cancer patients receive safe and effective drugs. FDA also is working hard to improve patient access to promising cancer treatments without compromising patient safety. Furthermore, we are working to ensure that patients have timely and important information about available cancer drugs including those for gynecologic cancer indications. Our goal is to improve upon a system that supports all cancer patients, and all other patients seeking access to new drugs and treatments for their disease.

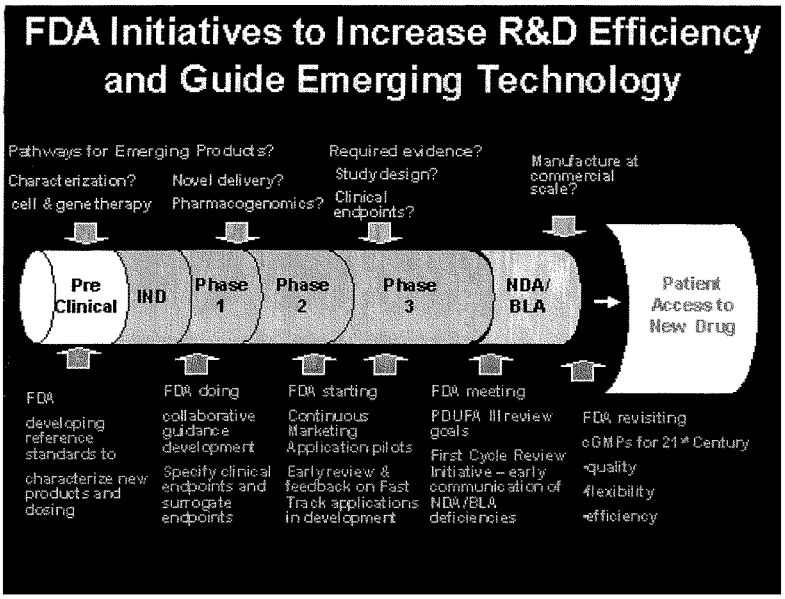
Thank you for this opportunity to testify. I will be happy to answer any questions the Subcommittee might have.

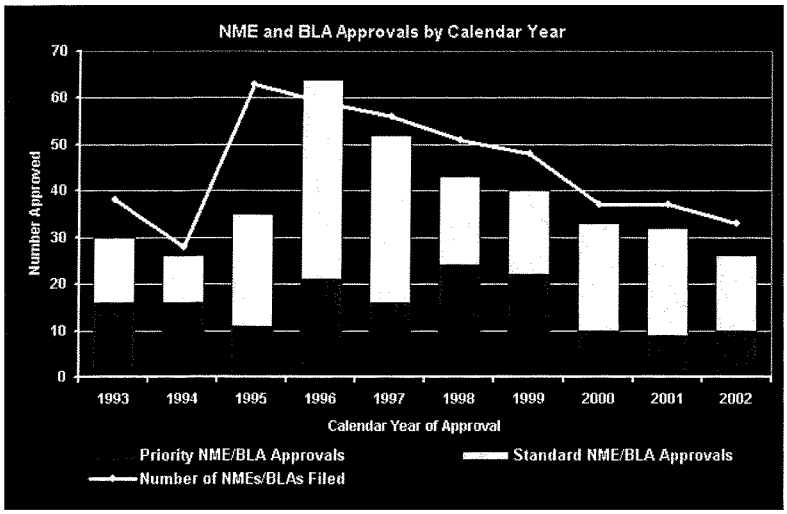
FDA APPROVED TREATMENTS FOR GYNECOLOGICAL CANCERS

CANCER OF THE OVARY:

DATE	DRUG	INDICATION
Dec. 1978	Platinol (cisplatin)	Metastatic ovarian tumors - in established combination therapy with other approved chemotherapeutic agents: Ovarian-in established combination therapy with other approved chemotherapeutic agents in patients with metastatic ovarian tumors who have already received appropriate surgical and/or radiotherapeutic procedures. An established combination consists of Platinol and Adriamycin. Platinol, as a single agent, is indicated as secondary therapy in patients with metastatic ovarian tumors refractory to standard chemotherapy who have not previously received Platinol therapy.
June 1980	Alkeran (melphalan)	palliation of non-resectable epithelial carcinoma of the ovary
Dec. 1987	Adriamycin PFS (doxorubicin HCl)	used successfully to produce regression in disseminated neoplastic conditions such as acute lymphoblastic leukemia, acute myeloblastic leukemia, Wilms' tumor, neuroblastoma, soft tissue and bone sarcomas, breast carcinoma, ovarian carcinoma, transitional cell bladder carcinoma, thyroid carcinoma, gastric carcinoma, Hodgkin's disease, malignant lymphoma and bronchogenic carcinoma in which the small cell histologic type is the most responsive compared to other cell types
March 1989	Paraplatin (carboplatin)	Palliative treatment of patients with ovarian carcinoma recurrent after prior chemotherapy, including patients who have been previously treated with cisplatin.
Dec. 1990	Hexalen (altretamine)	Single agent palliative treatment of patients with persistent or recurrent ovarian cancer following first-line therapy with a cisplatin and/or alkylating agent based combination.
July 1991	Paraplatin (carboplatin)	Initial chemotherapy of advanced ovarian carcinoma in combination with other approved chemotherapeutic agents.
Dec. 1992	Taxol (paclitaxel)	Treatment of patients with metastatic carcinoma of the ovary after failure of first-line or subsequent chemotherapy.
June 1994	Taxol (paclitaxel)	New dosing regimen for patients who have failed initial or subsequent chemotherapy for metastatic carcinoma of the ovary
May 1996	Hycamtin (topotecan)	Treatment of patients with metastatic carcinoma of the ovary after failure of initial or subsequent chemotherapy.

April 1998	Taxol (paclitaxel)	For first-line therapy for the treatment of advanced carcinoma of the ovary in combination with cisplatin.
June 1999	Doxil (doxorubicin liposomal)	Accel. Approv. (clinical benefit not established) Treatment of metastatic carcinoma of the ovary in patient with disease that is refractory to both paclitaxel and platinum based regimens. ***Recently converted to full approval.**
June 2000	Taxol (paclitaxel)	First line ovarian cancer with 3 hour infusion.


FDA Initiatives to Increase R&D Efficiency and Guide Emerging Technology
Pathways for Emerging Products?
Characterization?
cell & gene therapy
Novel delivery?
Pharmacogenomics?
Required evidence?
Study design?
Clinical endpoints?
Manufacture at commercial scale?
Pre Clinical
IND
Phase 1
Phase 2
Phase 3
NDA/ BLA
Patient Access to New Drug
FDA developing reference standards to characterize new products and dosing
FDA doing collaborative guidance development
Specify clinical endpoints and surrogate endpoints
FDA starting Continuous Marketing Application pilots
Early review & feedback on Fast Track applications in development
FDA meeting PDUFA III review goals
First Cycle Review Initiative – early communication of NDA/BLA deficiencies
FDA revisiting cGMPs for 21st Century
•quality
•flexibility
•efficiency


NME and BLA Approvals by Calendar Year
Number Approved
70
60
50
40
30
20
10
0
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
Calendar Year of Approval
Priority NME/BLA Approvals
Standard NME/BLA Approvals
Number of NMEs/BLAs Filed

Mr. CANNON. Thank you.

May I begin the questioning by asking you members of the panel, generally, are you familiar with Abasian statistics or its evolving cousin, complexity theory? Mr. Trimble. Are you experts in either of those areas?

Dr. TRIMBLE. I am not expert. I do have statistical colleagues at the NCI who are very qualified in those topics.

Mr. CANNON. Dr. Thompson.

Dr. THOMPSON. I can answer an unqualified no, I am not an expert in either of those, although, likely, we do have colleagues at CDC who can provide additional information if needed.

Mr. CANNON. Dr. Pazdur.

Dr. PAZDUR. Likewise, I am not a statistician; however, the FDA obviously has a complete cadre of statistical analysis.

Mr. CANNON. Are you all familiar with some of the concepts embedded in Abasian theory or complexity theory? Just generally familiar?

Dr. TRIMBLE. I would have to tell you, Mr. Chairman, that I am sufficiently familiar with it to get myself into real trouble if I attempt to explain anything according to those lines.

Mr. CANNON. You are probably a lot better than I am. I ask that question because it seems to me that we have the opportunity in America today to make some dramatic changes in the way we do things and improve things. Let me go through a series of questions for each of you.

I met with Dr. Eschenbach from the National Cancer Institute. I think he is a remarkably delightful, interesting person, but the delightful part doesn't extend to the gravitas that he brings to bear on these subjects. He is highly committed and I have enjoyed my conversations with him along these lines. NCI and NIH are to be commended for the extensive database work they have done in developing databases on ongoing clinical trials. This is a terrific step forward.

But, Dr. Trimble, is there any database you are aware of that lists off-label use of currently approved drugs or devices for medical treatment?

Dr. TRIMBLE. There is a compendium which lists the available data to support off-label use of drugs in various clinical situations.

Mr. CANNON. Would that be like a study that somebody reported, so it is a compendium of studies?

Dr. TRIMBLE. That is correct.

Mr. CANNON. Is there a centralized Internet database that physicians or patients can refer to that outlines current treatment protocols for a given medical condition?

Dr. TRIMBLE. The NCI's PDQ database lists standard recommendations based on a comprehensive review of the literature for cancer prevention, screening, treatment, treatment of symptoms, palliative of care and end of life care.

Mr. CANNON. Tell me a little bit about where that database comes from, how it is developed, and how new protocols get into the system.

Dr. TRIMBLE. The NCI convenes panels that are independent panels. They include both representatives from academic institutions as well as from NCI and from other Federal agencies. They

review the current literature on a regular basis. Some panels meet yearly, some meet every 3 months, depending on the volume of literature. They then draft statements which summarize the literature, which reference the literature, and those statements are placed on the NCI's PDQ Web site so that it is widely available.

Mr. CANNON. You know, we have this mammoth number of highly educated doctors in America. Sometimes they don't actually recognize the problems. But when we have this huge group of people that are well educated, tend to be academic, tend to be clinicians, but with a creative mind-set, is it possible in your mind to capture that capability, that academic ingenuity out there in some form that would allow protocols that doctors are using to be brought into a database so that other doctors could look at those protocols and then develop sort of an Abasian context in improved treatments?

Dr. TRIMBLE. Well, as I said, the PDQ database makes or summarizes what is——

Mr. CANNON. Let me just make a distinction. The problem with PDQ is that this is a bureaucratic and long process, as opposed to a database process or a process that grows from practitioners up. Is it possible to shift gears away from the long process that says this is OK and to a process that says we would like to know what you are doing out there, we would like to compare it to what other people are doing, and we would like that information to be made available to other doctors?

Dr. TRIMBLE. We have made an effort to reach out to the community in a pie project for certain cancers to find out how these cancers are being treated in the community, what is the effective treatment upon outcome upon quality of life; and we are analyzing that data currently to see how effective it is and to see whether we should be expanding this program to other cancer sites.

Mr. CANNON. You are probably familiar with the development of childhood cancer responses. When I was very young, my best friend's younger brother was found to have leukemia, and we thought he would be dead within 3 months. It turns out there was a treatment that somebody had identified, tried on the young boy, and he wasn't cured, but he didn't die. This happened four or five times in my childhood, where he became critical, was ready to die, and then a new treatment came forward. As a result, I saw him 6 months ago; he has a family, he is happy and in his fifties now. So we have a case of success.

What happened there—and I have talked to a number of people throughout the pediatric world—is that there was so little focus on pediatric medicine, especially oncology, that what we had was a high level of communication. And that high level of communication meant that it started out with telephones, later went to faxes and to e-mail. It meant that people who discovered something that might work communicated it to everybody else, everybody else tried it, and those things that really worked tended to be focused on and then became the base of treatment. That has been incredibly effective; not just in the single case that I am aware of, but the view of all people involved in childhood oncology recognize that as a great source of success.

We have the ability to communicate those things on all levels and for all cancers much more rapidly. Is anybody looking at that

at NIH or NCI that you are aware of, Mr. Trimble, to try and replicate with the massive increase in technology the great successes we had in that one area?

Dr. TRIMBLE. Certainly, the progress that we have made in pediatric cancer has been tremendous, and we are trying to see if we can replicate that progress. There are a number of things that the pediatric oncology community has done which are admirable.

For example, probably 90 percent of children less than age 12 diagnosed with cancer are treated at pediatric cancer hospitals. This is in contrast, for example, to adult cancers, where only 5 percent or 10 percent of patients are treated at NCI-designated cancer centers. So the fact that the pediatric oncology community has been able to concentrate the care of children with cancer in specialized cancer hospitals has been tremendous.

They have also——

Mr. CANNON. Excuse me. The access to data is radically greater today for all cancers, including adult cancers as opposed to child cancers. In other words, I don't want to understand why we are successful with childhood cancers. I think I get that. The question is is it possible to systematize access to data so that we do it much more rapidly.

Dr. TRIMBLE. Well, another area which has made the pediatric cancer world so successful is that more than 70 percent of children with cancer go on clinical trials. So we capture data on how they are treated, their response to treatment, and their quality of life. We are trying to increase the number of adult patients going on clinical trials. In addition, we are trying to extend our database so that we can capture more information on all adults who are diagnosed with cancer.

Mr. CANNON. I apologize for that diversion. Have you finished on that point?

Dr. TRIMBLE. Yes, I did.

Mr. CANNON. OK. In the case of my daughter—let me just ask the panel of this generally.

I think we should do a second round of questions. On this committee there is a tendency to go longer for the chairman and the ranking member. I am not going to abuse that too much.

But in the case of my daughter, she had a rare cancer that maybe 30 young women typically a year get in America. I called a friend of mine, as my daughter was going through the MRI, who is a radiologist, and said after she is done, would you mind taking a look at the pictures, and he said, hold on a second. And then he said, OK, I am looking at them now.

I said, how could you be looking at them; she is in the MRI machine right now. And he was not at the same site. So he said, well, the miracle of modern science. And then the next words out of his mouth were, "Oh, this is bad." Not exactly the kind of thing you want to hear from a doctor.

Now, if he had been sitting—it was in her knee and he said it's involved in the tendons, and that is bad. Now, what she had was clear cell sarcoma of the tendons and aponeurosis. But he didn't remember the whole name; he just remembered having bumped into this rare cancer that was associated with tendons. And if he typed into the freaking machine that he had in front of him, if he had

a database that allowed him to type in sarcoma in tendons, the treatment for my daughter would have been radically different. Just a simple little information context there.

Now, we have done radical things in information. My favorite on earth is Napster. You need to think about Napster, because that was a peer-to-peer system that allowed anybody to get online and identify information that was out there. In particular, it means that a doctor can make information available.

You are telling me how you want to structure data so that it is available and put people in clinical trials. We have people who are essentially in clinical trials because they have cancer and they are being treated by people who understand information and systems. In my daughter's case, she worked for the guy later on who actually did the MRI that I had mentioned earlier, so when the cancer came back, she did a number of MRIs, because it didn't cost anything and because her boss was a very gracious guy and a good friend.

Now, in the course of her disease, there were no treatments. We found one treatment of a person in Japan who had the disease and had remission. But there are no accepted protocols for her disease. That meant that we tried various different kinds of things with medical guidance, including using the most standard or common treatment for malaria throughout the world today, which is an herb that the Chinese came up with.

Today, there are millions of people taking that herb with no side effects, so we tried it on her. But we had no guidance; the idea of how much to give her or how often to give it to her. So we experimented with it for 6 weeks. We didn't really understand it, but going back now we see that in her case the MRIs before she took it and after she took it indicate that there was a dramatic slowing of the growth of the tumor.

Now, that information seems to me to be quite important to somebody else who has the same kind of disease. And the only way you can get that information, the only way is by having access to her records. So if you have a database that is like a Napster directory and you can find clear cell sarcoma of the tendons as aponeuroses and see who has treated what and then say, wait a minute, here is something that might have an effect, that could actually save people's lives.

There is no way to get that data in our current system. You can go online and you can see all the—well, I shouldn't say that. There are many people who have used this and they have their ideas about how to use this, but there is no context where you can give it scientific integrity, where people can build on the ideas.

What I am asking you—and let me just leave it at this point with this panel and then we will go to Mr. Cummings—is does it make sense to create in our data-rich environment a context for practitioners, medical doctors, people who are trained in medicine, to identify the best treatments that are out there, and then build upon those and create a database as we did in pediatric oncology, and move from that base forward? This is not, are your institutions going to do it? The question is, does that make sense? Because we probably have to make some changes here for you guys to be able to do that. But does it make sense?

If I could ask the three of you to respond to that, I will then yield back and defer to my friend, Mr. Cummings.

Dr. THOMPSON. Mr. Chairman, you have just identified one of the primary reasons why Secretary Leavitt is committed for the Department of Health and Human Services to work toward developing an electronic patient record system in this country. It would provide the sorts of database that would allow the sort of research you are talking about to be done. It is not something that we now have on a large scale basis.

You have identified one institution that had that aspect of it and was able to use it very well, but we don't yet have it standardized; we don't have it in enough places. We have not yet solved the problems of privacy and confidentiality that must be solved.

But if we can develop a common patient record that is electronic and accessible in the ways you just described, it will not only provide better direct patient care with the medical knowledge that we have now, it will allow the type of research you have just described.

Dr. PAZDUR. I think you hit on the head some really important areas here, and one of them being treatment of patients that are not on clinical trials. We do a great job, I think, of collecting data, and perhaps too much data, on patients that are on clinical trials, and one of the real issues is how does a drug work once it gets out there in a post-marketing situation as well as in the treatment in off-label uses such as in rare diseases where there are not going to be large clinical trials.

So a database that reflects how the drug is actually used in the intended indications as well as in off-label uses I think would be an extreme important step to provide guidance, especially in areas where you have relatively rare and unusual tumors, because considering the frequency of some tumors, they are very important tumors, but somebody is not going to do a large size clinical trial, just due to the rarity of some of these diseases.

Dr. TRIMBLE. The only additional point I would add is that we desperately need a system to track who has been screened for cancer, for example. We have no national database to tell us who has had a Pap smear within the last 10 years, who has had a mammogram; do we know one place where we can capture the images of those mammograms so we can compare them.

Mr. CANNON. Thank you. Let me make a distinction and a comment. The distinction is you are thinking in terms of clinical trials. And what we have are many, many, many practitioners who use protocols sometimes, who adapt protocols for the use of their patients, and who are accumulating huge amounts of data. The question is not how do we make this all fit into a clinical trial, but how we capture the data from the practitioners. If you would think about that.

Dr. Thompson, Secretary Leavitt is actually from Utah, interestingly, and he may not appreciate actually how good we are in Utah, but there is a company in Utah that is the leading light in these kinds of issues, and I am going to get you the name of it, it is called NexLight, or sometimes eBridge. They have developed an incredibly thorough system for managing patient data using all the rules of HIPAA and other requirements and allowing the staff.

And I am going to get you a card on that and ask for, in a written request, your response as to what that kind of a program could do for allowing us in America to accumulate data on individuals based upon their consent, their understanding of the law and their consent, and giving access by those patients to people like doctors or people running clinical studies or other scientists so that we can actually move that issue forward.

I am going to ask some more questions, but I will save those until the next round.

Mr. Cummings, if you have questions, you are recognized for 5 minutes.

Mr. CUMMINGS. Yes.

Dr. Thompson, in your opinion, what do we need to do to increase access to the existing interventions like Pap smears? You know, the sad part is that we have people dying.

Dr. THOMPSON. It is. And what we need to do is to learn to use the science we now have more effectively so that it reaches everybody. The Congress took an important step in 1991 in enacting the legislation that created the Breast and Cervical Cancer Screening Program, because what this does more than anything else is make it true in this country that today no woman should be without cervical cancer screening or breast cancer screening simply because she lacks the ability to pay for it, because any woman at or below 250 percent of the Federal poverty level qualifies for this program and can receive screening services through it.

So cost should not be a barrier. And yet we know we are still not reaching all of the women we should. The figures that I cited to you I think are figures we should be proud of. We are reaching many women and they are low-income women. But we know some things that are troubling to us, and we want to work to make them different.

This is not published information, it is simply what we have observed in looking at some of the States implementing it, but we know, in the State of Ohio, for instance, that they tell us that although they are utilizing the program effectively, the women in the upper half of that income range, 250 percent and below of the Federal poverty level, are the ones who seem to be taking advantage of the program, and women in the lower half, the very lowest of the low-income women, seem to be less often reached by the program. So we are looking and need to be looking at things that influence women's choices as to how they use these programs, whether they know about them.

We have now gone passed the point where it is laboratory research that is needed. In these areas it is the sorts of behavioral research that will help us learn why people do and don't use medical programs and things that may be necessary to facilitate that. That is the sort of research that CDC engages in along with our colleagues at the National Institutes of Health. But the bottom line, the answer to your question, we have simply got to learn how to bring these techniques to the people that need the most and often are the ones who know the least about them.

Mr. CUMMINGS. The program is one going back to 1991, so it is about, I guess, 15 year anniversary. That is a long time. And I am just wondering, do you know how that research is done? Is it focus

groups? You know, one of the things that I do believe is that people who have similar experiences in life probably shed the best light on other people in like circumstances.

And I am just wondering. Sometimes I think what happens is that, say, for example, if I wanted to know about why do women in the lower economic rung of the ladder did not access, I would go and talk to other women. I sure wouldn't go to a man; I would go to a woman. Sometimes I just find that a lot of our government programs don't do that. A lot of times we don't go to people who could probably help us with it.

For example, in my community there is a big glaucoma problem. And my mother, having lost sight in one of her eyes with glaucoma, I am in tune; I get it. So I am always talking to people about their eyes. But some kind of way I think we also need to use people who see the light, perhaps, to help spread the word. And I was just wondering how much we do of that, too. That is, people who may fall into those categories and have a relationship, therefore, and can spread that word. You follow what I am saying?

Dr. THOMPSON. Yes, sir, I do. And this is an area in which we in the medical professions maybe are coming a bit late to the idea that we should ask those who we are trying to reach how best to reach them. But we are doing that now. And at CDC in particular we have established a new center, it is the National Center for Health Marketing.

That doesn't mean we are selling people things, it means we are literally marketing health. And we are doing research by asking people, both in studies and in focus groups, how it is that you make your decisions about how you seek your health care of all sorts and how we can improve your ability to do that. So we are beginning to use those techniques of approaching the community we are trying to reach much more extensively.

Mr. CUMMINGS. Now, as far as doctors are concerned, they know about these options that women have with regard to free screenings and whatever. Do you think that plays a major role? Are you following me? Somebody comes to the doctor. Do you think because they know this is something available, that they make women aware of it?

Dr. THOMPSON. My colleagues can probably address this better than I. But although we as doctors believe we know everything, the truth is most of us don't know enough even about our own specialties, and all have things that we can learn. So professional education is a part of CDC's programs. I know it is also part of the National Cancer Institute's approach.

Mr. CUMMINGS. Dr. Trimble.

Dr. TRIMBLE. We have seen data showing that obstetricians and gynecologists are the most likely to recommend that women undergo Pap smears and mammography. They are followed by family practitioners. Unfortunately, many adult internal medicine specialists are less likely to do a pelvic exam or obtain a Pap smear.

So as Dr. Thompson mentioned, we need to redouble our professional educational efforts. In addition, the routine Pap smear screening has now been instituted as a mark of quality in health care provider organizations, so we think that this will increase the recommendation of Pap smears for all women.

Mr. CUMMINGS. Dr. Pazdur, you know that rising costs and a lack of commitment to applied science in emerging various new drugs and devices to treat cancer and other deadly diseases. What can be done to encourage applied science research and technology?

Dr. PAZDUR. Well, I think this is one of the considerations that the FDA had in establishing the critical pathway, because there is a tremendous funding of discovery of drugs. But I think where we have been lacking in the whole drug development area has been in the clinical and the development of drugs after they may have been initially discovered, and that is the clinical development of the drugs and the preclinical development.

And that is why we are working with the NCI and have this project. What are paradigms that can be shifted from conventional evaluation of drugs to facilitate bringing drugs that are safe and effective, not compromising safety and efficacy—we never want to do that—but expedite drugs cognizant of the fact that they have to be safe and effective; looking at new non-clinical ways to develop in animal models.

For example, what would be a minimum data package that could be accepted to bring drugs into a life-threatening situation; what are different statistical tools that could be used to give us confidence that a drug is safe and effective, rather than the traditional statistical methods that have been used? So I think this is an area that is an extremely important area that we want to focus on, because we are cognizant of that and really need to work not only in the FDA but with our external stakeholders, not only in government, not only in industry, but with the academic and patient community.

Mr. CUMMINGS. Thank you.

Mr. CANNON. The gentleman yields back.

Mr. Issa, did you have questions?

Mr. ISSA. Yes, Mr. Chairman.

Mr. CANNON. The gentleman from California is recognized for 5 minutes.

Mr. ISSA. Thank you.

Dr. Trimble, you mentioned in your opening statement the vaccine for HPV, and my understanding is there are 150 or so different strains, if you will. How many is it effective against?

Dr. TRIMBLE. Well, there are a variety of HPV subtypes. Only a subset, perhaps 20 or 30, seem to be bad actors in terms of going on to cause cancer. The two companies that are developing the vaccine have gone furthest with the prophylactic vaccine and have focused on the most common subtypes, 16 and 18, which are responsible for a majority of cervical cancers around the world and in the United States.

Mr. ISSA. And I would like to concentrate my questions not on, if you will, the new discovery side of it for a moment, because Johanna's Law really is about awareness, with $5 million going toward and $10 million per year going initially toward demonstration projects to try to improve early diagnosis.

My first question—and I will take any of them, but I think, Dr. Trimble, I would start with you—is it enough? Is this the amount of money that you believe would start saving lives in large enough

numbers, or are we kidding ourselves? And even with the leveraging of public-private partnerships, will we need more?

Dr. TRIMBLE. Well, I concentrate my own work on promoting gynecologic cancer research and developing trials in gynecologic cancer, so obviously from my own perspective I always like to see more money focused on gynecologic cancer. And it should be said that about 5 percent of the NCI's budget is, as we know, earmarked and goes toward gynecologic cancer research. And there is a lot of basic science research as well that is specific to gynecologic cancers, but may well influence us and help us develop new treatments, new screening tests.

So I think it is a very hard question for me to answer. Yes, I would love to see more money going into gynecologic cancer; on the other hand, we have a limited pot of money and there are a lot of other cancers that we have to study as well.

Mr. ISSA. Dr. Thompson, maybe in your case, right now I would say there are tens of millions of dollars a day worth of free air time warning the people of New Orleans and the south, but particularly New Orleans, not to drink the water and the contamination. I don't know how many people are going to heed that warning.

It does seem a little strange that we are all going to be aware, unless of course, we are in the affected area, where we don't have a television. But maybe somebody will go in and tell the person who doesn't have a television or water what they need to do. From your experience, is this a sufficient first step to have a real impact both on the misdiagnosis side and on the need for testing side?

Dr. THOMPSON. Well, certainly we will never have spent enough on cancer prevention and cancer detection until no one dies of cancer. But at the same time there are other priorities that we have to balance back and forth.

I think certainly the concept of educating particularly providers about the latest techniques, about the latest knowledge, about how to appropriately screen, how to evaluate symptomotology is always worth the effort. Whether this will accomplish the end I think we will only know when we attempt it and then we evaluate whether or not we have accomplished it, and if not, what is then required to finally accomplish it.

Mr. ISSA. Last question, and I am staying on the same subject of money. My understanding is it takes about three quarters of a billion dollars to bring a new drug to market. Any one drug coming to market, from your experience—and Dr. Pazdur might be the best to answer this—any one drug probably would save, at a maximum, 3,000 to 5,000 deaths a year for nearly $1 billion, perhaps more; $15, $20 million, would you say, any of you from your experience, that an effective awareness campaign could save 3,000, to 10,000 lives a year between the three cancers? Would you say, on balance, that this $15 million—as compared to the $1 billion of one new drug—could save as many or more lives?

Dr. PAZDUR. The answer to your question is yes. Obviously, prevention and early detection of cancer is always better than the treatment of advanced disease, even early stage disease. But especially when one takes a look at advanced disease, patients that have metastatic disease, where most of the drugs in oncology are

being developed, most of those situations have to be considered palliative types of therapies, unfortunately.

So efforts to really eradicate cancer and to truly make an impact on the burden of cancer really needs to be addressed in the early stage awareness, getting the community to see their physicians. Doctors know generally what to do; however, if the patients are not coming to them, that is where the gap could be, and I think that is a need for community recognition of the disease and the importance of getting screened, etc.

Mr. ISSA. Thank you, Mr. Chairman.

Mr. CANNON. The gentleman yields back.

Ms. Watson. The gentlelady is recognized for 5 minutes.

Ms. WATSON. Thank you, Mr. Chairman.

This question goes to Dr. Trimble. In your testimony you state that an effective vaccine in combination with cervical cancer screening is expected to reduce cervical cancer rates by 90 percent in the United States.

I am finding out that there are those who began to oppose the HPV vaccine. A spokesperson for the Family Research Council said that giving the HPV vaccine to young women could be potentially harmful because they might see it as a license to engage in premarital sex. So from a public health perspective, does the Government typically withhold vaccines because of the unsubstantiated claims that they will affect people's attitudes and behaviors?

Dr. TRIMBLE. Well, let me start by seeing if Dr. Thompson would like to comment in terms of the—I know the CDC has a vaccine advisory committee which carefully measures the risks and benefits associated with vaccines and makes recommendations, so perhaps Dr. Thompson——

Ms. WATSON. Fine.

Dr. THOMPSON. First, Ms. Watson, let me thank you for the imagery you used earlier about homeland security being not about the land, but about the people on the land. With your permission, I am going to use that with attribution, occasionally.

Ms. WATSON. Please do.

Dr. THOMPSON. As my colleague has said, CDC has a process for evaluating the usage of vaccines. Now, the first issue is whether it becomes licensed, and there my colleagues from the FDA must make the decision. But once a vaccine is licensed, we have a committee, it is called the Advisory Committee on Immunization Practices, that meets regularly. It consists primarily of scientific experts, but also of public health practitioners.

I had the privilege of serving on that committee myself for 4 years before coming to CDC. And it also makes provision, extensive provision, for public input and public comment. Based then on the science and the policy implications of the use of a vaccine, they make scientifically informed decisions recommending to CDC, and from CDC thus to the Department of Health and Human Services, what use the vaccine should be put for.

That process is ongoing now. The ACIP has already addressed the issue of HPV vaccine in some of its meetings in anticipation of licensure, and will be doing so again. So it is critically important that persons interested in this issue bring their concerns to the

committee through the public comment process and make sure that their voice is heard.

Ms. WATSON. The encouraging words that you used were based on science.

Dr. THOMPSON. That is correct.

Ms. WATSON. Not based on ideology or negative attitudes. We have been accused in our public school system—I was a member of the board in Los Angeles—when we passed out condoms upon request to block the spread of AIDS, we were accused of encouraging young people to engage in sex.

I carried the needle exchange bill for 8 years—it was passed after I left—and was accused and made to sit on the hot seat because there were those attitudes out there that everything we did was encouraging people to have sex. So I am assured by your response that you operate based on the facts and on empirical evidence gained from your scientific research when you make these decisions, correct?

Dr. THOMPSON. I can assure you, both from having been on it and knowing the people that are on it now, that the ACIP bases its decisions on scientifically verifiable fact and will not deviate from it.

Ms. WATSON. From a public health standpoint—and this is back to Dr. Trimble—we in Government, we decisionmakers must put policies out there that will help the public and reduce the risks that they face, even if it goes against some people's religious beliefs. I am a Roman Catholic, and I support choice, I support condoms, I support all kinds of other things that will reduce the risk to the public. So I just wanted to make that statement real clearly. And I appreciate, Dr. Thompson, your response.

Thank you, Mr. Chairman.

Mr. CANNON. Thank you. Without objection, I think we will go through another round of questioning.

Let me just followup on what Ms. Watson was just asking. What rate of vaccination is that 90 percent figure you talked about predicated upon? In other words, what percentage of women and girls does such an outlook presume will be vaccinated?

Dr. TRIMBLE. I am not sure where the 90 percent figure came from. My impression is that we may well have said that the rate of cervical cancer has fallen so dramatically in the United States with the introduction of Pap smears, but I am not sure that we discussed in our testimony the projections for vaccine adoption and implementation in the future.

Mr. CANNON. Thank you. Just along those lines, I am going to ask a couple of questions that my colleagues wanted to ask but are not here.

For the FDA, your testimony references cervical cancer only once. This subcommittee informed your agency that we are very interested in issues that the FDA failed to address in our hearing on cervical cancer last year. Your agency was provided with questions that we expected to be addressed, specifically on the matter of the agency's failure to comply with Public Law 106–554, signed by President Clinton in 2000, requiring that condoms be accurately labeled to reflect the fact that condoms do not protect women from HPV infections. Why aren't you addressing this issue?

Dr. PAZDUR. I personally can't answer that issue. The condoms are handled and the approval of condoms are handled by the Center for CDRH, so I do not have personal knowledge of that area. We will provide to the committee a written response to this question within 5 days.

Mr. CANNON. Thank you.

Since Public Law 106–554 was enacted requiring accurate condom labeling, more women have died of cervical cancer than from AIDS among non-injection drug users. The FDA has still not complied with this law. Can you tell this committee why it has taken so long to act on this critical public health matter and require accurate condom labeling?

Dr. PAZDUR. Here again I will reference my previous answer, that we will provide an answer to the committee in writing.

Mr. CANNON. Thank you. It is not a personal thing, but institutionally we did have a hearing, and we expect a response. Thank you.

Now I would like to move on to other issues. Are any of you familiar with protein testing to identify whether a woman or, for that matter, man has had HPV and which of the HPV viruses the individual has had?

Dr. TRIMBLE. There are currently approved by the FDA tests for women to evaluate whether they have an active infection of HPV and some subtyping of the various high-risk types is available for that. In addition, we do have some serological studies which evaluate antibodies in blood that can show a history of HPV infection.

Mr. CANNON. Are those definitive; can you say to a woman you have not had or you have had a HPV infection based upon those studies?

Dr. TRIMBLE. Certainly the tests for active HPV infection does have a false negative rate, so one would need to do a series of tests over weeks to months to say for sure that a woman does not have an active infection at this point in time. The serological tests can fade over the years, so you may no longer have an immunological memory of having HPV, although in one point in life you may have had it.

Mr. CANNON. For you, Dr. Trimble, but also for CDC, it would seem to be important that if you had a test that could identify what HPV a person has had in his or her system, would that be significant in the cost of identifying and treating people that may have or get cervical cancer?

Dr. TRIMBLE. Certainly with the development of accurate HPV tests, we have begun to study whether we should or could modify the existing screening program so as to screen first with a HPV typing and then only followup with Pap smears in people who were found to have HPV infection. This might well work for women let us say 25 and older in whom HPV is rare.

Among younger women, though, HPV infections are common, so one would not want to start with a primary HPV screening test because there would be many false positives. And the vast majority of individuals, both men and women, who are exposed to HPV quickly resolve that infection and have no adverse health effects from the HPV infection.

Mr. CANNON. But when you say no adverse health effects, doesn't it take years of the infection to create a cancerous lesion?

Dr. TRIMBLE. Well, we think that the average age of infection is probably less than age 20, and the median age for diagnosing cancer is around 65. So, yes, there are years to decades.

Mr. CANNON. Thank you.

Dr. Thompson.

Dr. THOMPSON. We do currently, through CDC's breast and cervical cancer screening program, provide for the use of HPV DNA testing in certain clinical situations where it can be used as an adjunct to Pap testing. But at this point it has not yet been determined that it is a useful tool for across-the-board screening.

So we use it in very special circumstances, such as when a woman has had a low-grade abnormality detected by a Pap smear. And after a period of time she has had negative colposcopy, we can then use HPV DNA screening and Pap screening to determine what sorts of followup are necessary. So in some circumstances we use it even today.

Mr. CANNON. You know, there have been some terrific transformations in science. I read 2 or 3 weeks ago in Time magazine about Craig Ventner, who is traveling the world in a yacht and testing the DNA set every 20 miles or so, and he is able to do this because the cost of decoding DNA has fallen dramatically, from about $10 a pair, when we started the Human Genome Project, apparently, now down to like less than a penny a pair to decode. So it is cost-effective for him to do that even on his boat. And I think there are new technologies that are going to bring that down by another order or two orders of magnitude.

It seems to me that this is an area where we need to change our thinking about how we are looking at disease, because the cost of decoding what is going on is so much, almost infinitely, lower than it has been. Could the three of you respond to how your agencies are dealing with the lowered cost of protein identification, DNA or RNA and other proteins, and what that means for the future of science? And what it might mean for complexity, how we ought to start looking at these diseases in an environment of Abasian or complex theory.

Dr. Trimble, Dr. Thompson, then Dr. Pazdur.

Dr. TRIMBLE. Well, certainly cost is an important issue. The Gates Foundation, for example, has made a large contribution or earmarked a large contribution of money to help develop inexpensive HPV diagnostic tests for use in the developing world. And we have had some discussions with the Gates Foundation, as that research progress, as to whether we might be able to use some of those inexpensive diagnostics in the public health sector.

At present, we only have a few tests which have been approved by the FDA, and some individuals have commented that the prices attached to them, prices placed on them by the companies which market them, make them less than optimal for use in the public health setting. But we obviously have no influence over the price of a proprietary diagnostic.

Mr. CANNON. Thank you. I have a friend who complains that in every other sector of the economy innovation means lower prices, except in the medical sector, where prices skyrocket. That is an

issue, but perhaps maybe the issue really is—and if I could skip over you just for a moment, Dr. Thompson, because this is probably an issue of most importance to you and what you are doing—but what do we do about the cost of getting approval when the nature of the ideas that are coming before the FDA is changing? In other words, you know more about what you are dealing with when you have decoded a protein than you do when you are dealing with a substance which may be toxic, but it may also affect disease.

Dr. PAZDUR. I think what you are really talking about is a concept which we refer to as enrichment, and that could the fields that you are referring to, proteomics and genomics, really identify a population of patients that are more likely to respond to a therapy. For example, if you have a DNA chip which identifies a subgroup of cervical cancer patients or ovarian cancer patients that are more likely to respond to a given therapy, that is a great step forward, because obviously these drugs are toxic drugs, for the most part, and you could spare people that have a very reduced chance of benefiting it from receiving drugs that they are not going to benefit from. Likewise, you are going to select a group of patients that are most likely to benefit.

Mr. CANNON. What you just said is perfectly agreeable, but what I asked is slightly different. What are you doing at the FDA to encourage the identification of proteins and then your process for approving those proteins based upon what they are, as opposed to what historically we have done with toxicity? In other words, you may have a patient who responds better, as you have just pointed out, because of proteins that he or she has.

On the other hand, you may have causative agents that you can identify, like HPV viruses, for which you may have serological remnants, or you might have an active culture. What are you doing at FDA to help speed up that process, where we are not dealing with the likelihood of death, but we are dealing with the likelihood of certainty that an agency is present?

Dr. PAZDUR. What we are doing in the area of genomics, we have specific groups of people that are working on guidances on how this data should be submitted to the agency. Obviously, this is an evolving field of science. So we are working with industry, inviting them to come in, share their data with us. We are organizing conferences, discussing how this data will have an influence on subsequent clinical trials. We are well aware of the scientific advance. It is an evolving science that has to really have a partnership with the FDA and both the academic community as well as the commercial community.

Mr. CANNON. You call this an evolving area of science. It is not. That is what you called a transition of understanding what germs were over 100 years before we got vaccines that we actually understood why they worked. This is a revolution; this is an explosion; this is a transformation. And what you are talking about is a process that makes it a lot more expensive and, by the way, impedes the health care of Americans and people worldwide.

May I suggest that the FDA needs to think differently about this? Because it is not the same as what has been, and much of what has happened can be left up to practitioners who specialize and who deal with the issues. So what I view the FDA here as is

a big door, a big hurdle, a big cost increaser that needs some thought.

I know you are thinking about it, but your answers are answers that are in the context of a bureaucratic and outcome-oriented context, rather than how to help people's health, which is what the focus ought to be. You really need a transformation of thinking at the FDA.

And I know you have done many things. I am a big fan of the FDA. I have been a big opponent of reimported drugs and things like that. But the FDA needs to evolve at a rate that is somewhat maybe lagging, but at least near the rate that the transformation in science is happening.

I don't mean to lecture so much, but it is an area of deep frustration.

And, Dr. Thompson, clearly this is a matter of great importance to you and your agency. Do you have some comments?

Dr. THOMPSON. Well, in public health it is really simple: the lower the cost of a screening test or an intervention, the more people we can provide with the benefit of it. So it is up to our colleagues in the regulatory sector, in the research sector to develop and certify these products, but once they reach our hands, the less they cost, the more people we can serve with them.

Mr. CANNON. Thank you.

Mr. Burton, I have one more question, but did you want to ask questions of this panel?

Mr. BURTON. I just have one question, but go ahead.

Mr. CANNON. Let me just point out what our discussion has been and where I think, as a community, we need to be headed. Much of the answering of the questions I have asked has related to controlled clinical trials, and I have continued to come back to what a practitioner does with his patients and what his experience is, and what we can accumulate from that process. It is a paradigm shift. It is a dramatic paradigm shift, but it is a shift that makes pretty significant sense, especially when you view the world from the point of view of the tools we have that are capable of helping us accumulate data.

Of course, I have to say my questions may have, at some times, been harsh, and I apologize for that, but it is an awfully personal thing. But your agencies are really wonderful agencies, and there is no criticism of the agencies, it is just a road I hope you would see to get to the next position. And all three of your agencies have a piece of this and you are doing remarkable work, but the cost of medicine is skyrocketing. The access to medicine is diminishing.

When I was elected to Congress, 65 percent of Americans had employer-based health insurance; today, 45 percent of Americans have that. And the answer is either we go to a controlled, socialized single payer system, which 65 percent of Americans now want, by the way, understanding that means socialism—as opposed to 45 percent when I first got elected; the numbers have inverted themselves—or we go to a system where the American way actually succeeds, and that is open markets, free access to information, choice by consumers, choice based upon access to information. In some cases that is a matter of cost; in the case of my daughter, it was

a matter of life and death. It was an ignorant set of doctors who prescribed badly, didn't know what they were doing.

What happened to my daughter was an abomination, and it was an abomination that I couldn't fix. I mean, I am a Member of Congress; I was a Member of Congress then. I didn't have access to the information to figure out what was going on with my daughter. Now, that has been ameliorated somewhat in recent times, but we still have problems in that area.

Here, the three of your institutions are very different and represent different elements of the puzzle. But we have a huge cost hurdle that is transforming the rights and choices of Americans in a way that I think is wrong. So as you look at this, may I just suggest when a patient and his doctor or her doctor has access to information, they will make better decisions.

We have ways of massively expanding information, and one of them, just to be thinking about, when we passed AHSEA, we had 2 million people in America that got involved in that act, that became activists. I suspect you have 5 or 10 million today, because the number of people that are using nutritional supplements has increased significantly. And if you go to the NNFA, which is the National Nutritional Foods Association, Web site, nnfa.org, they have an incredible presence. They reach many people.

And if the CDC said here is a set of questions we would like to know about your health and here is how we will protect the data, I suspect you would have millions of people who would respond. In other words, if you think about how you get data, you can get it much more cheaply than we have ever done before. The cost of obtaining data from individuals has plummeted, just like the cost of decoding a DNA pair has plummeted.

So if you would think in those terms, I suspect you would see that there are great opportunities for improved health in America, for improved control by individuals of their health in America, and for a system that protects without impeding, without causing death and destruction, which in fact often happens with our medical system. That is probably not your fault, it is actually largely doctors who are ignorant of what they are doing. But it would be nice to allow patients to have some access.

And I have ranted here, but I would like you all to think about that. We are going to followup with some written questions.

Now, Mr. Ruppersberger, I know that you are next, but I think Mr. Burton only had one question. Would you mind if we go to him for that question and then come back to you?

The gentleman from Indiana is recognized for 5 minutes.

Mr. BURTON. Thank you, Mr. Chairman. I will just be real brief here.

First of all, I presume that you gentlemen would be supportive of Johanna's Law. That authorizes $15 million over 3 years for public service announcements and $55 million over 3 years for grants to establish local and national nonprofits and community-based health centers to test different outreach and education strategies. I am sure you know all that.

Are our health agencies doing anything in this area right now? Do they have any kind of an outreach program or educational program for gynecological cancers in women?

Dr. TRIMBLE. The NCI does have an extensive educational program, both for the lay public as well as health professionals, focused on gynecological cancer. We work closely with our Cancer Information Service and the CDC in terms of disseminating that information.

Mr. BURTON. The reason I asked is when my wife was suffering from cancer, I never saw any manifestation of that. Can you tell me, real quickly, how much money is being put into that program?

Dr. TRIMBLE. I will have to get back to you with the amount of money that we put into cancer information, but it is a large portion of our budget and our activities.

Mr. BURTON. I would like to have that. Thank you.

Mr. CANNON. The gentleman yields back.

Mr. Ruppersberger. The gentleman is recognized for 5 minutes.

Mr. RUPPERSBERGER. Mr. Chairman, thank you.

There have been a lot of issues discussed here today. I think one of the frustrations that we have sometimes in Congress is that we raise some issues and then there is not implementation. And I would hope that we could benefit from this panel, and I know that the chairman feels very strongly about this issue because of some of his unfortunate personal situations that we really implement and move forward.

In order to avoid any repetition, there is one issue that I think hasn't been addressed, so I will just ask that to the panel and that is all I have.

In the past, the NIH and CDC has found that there was evidence that condoms can reduce the risk of cervical cancer, but there wasn't enough data to determine if condoms prevented the spread of HPV. Earlier studies were insufficient to answer this question because they asked people to recall past condom use, they didn't track people's behavior over time or they didn't know people's STD status before the study.

Now a recent study has addressed many of these issues. Researchers tracked young women over time and gathered precise data on condom use and sexual behavior. The study found that consistent condom use reduced the risk of HPV acquisition among women by 70 percent and reduced the risk of cervical HPV by 80 percent.

My question to anyone on the panel, if anyone has an opinion: Do you think this is the kind of study that the FDA should take into account when considering labels for condoms?

Dr. PAZDUR. Here again, I have not reviewed the study, but obviously I think we should take account of all information. I can't make a commitment to you on a specific study without obviously seeing the data that is presented, but from your description of it it is something that we would be very interested in looking at and including into product labeling.

Mr. RUPPERSBERGER. I am not just saying looking at. I would recommend that you look at the study and if we are going to have momentum and move forward on this entire issue, I think these are things that we just shouldn't talk about at a hearing; we need to get the research done and follow through.

Dr. PAZDUR. By "look at" I meant evaluate appropriately.

Mr. RUPPERSBERGER. And then deal with FDA.

Dr. PAZDUR. Correct.

Mr. RUPPERSBERGER. Thank you.

Mr. CANNON. The gentleman yields back.

Mr. Issa, did you have further questions?

Mr. ISSA. Yes.

Mr. CANNON. The gentleman is recognized for 5 minutes.

Mr. ISSA. Thank you.

I would like to followup on a question Mr. Burton asked. If there is a lot of money being spent on outreach, why is it that it doesn't get to the end of the pipeline? Because Johanna's Law and this authorization for funding specifically is the result of an observation that it doesn't get to the end of the pipeline.

So where is it being spent if we can't see it where we believe it should end up? Is it just that it is being spent elsewhere or something? It is befuddling to both Mr. Burton and myself.

You could just not answer, and we will assume that is no, it isn't getting there, and we can move on. But go ahead.

Dr. THOMPSON. We can give you the figures as to how much CDC spends on programs aimed at preventing or early detection in all of the different kinds of gynecologic cancer. That is not going to answer your question, however; it will just tell you relative amounts of dollars spent.

Our focus at CDC has been primarily on provider and patient education, but it has been limited. It has been limited primarily to demonstration projects trying to gain a little more knowledge about how we can most effectively use those dollars. We do not yet have a large-scale campaign that is population-based and nationwide. It has been very focused.

Mr. ISSA. So, following up, should this bill become law, it would enable you to take that next step; certainly not nationwide, but it would give you the tools to do that, is that correct?

Dr. THOMPSON. Certainly from the standpoint at CDC, legislation that provides resources to expand our programs would give us the opportunity to expand them. But, at this point, HHS currently has not established a position formally on this particular piece of legislation, but its provisions and the concepts embodied in it are certainly those that I think we could all support.

Mr. ISSA. OK.

I would yield to the gentleman from Indiana.

Mr. BURTON. Let me just say that I watch old movies and stuff on television, and I see advertisements and stuff all the time, public service announcements saying, you know, prostrate cancer is a growing thing; gentlemen, get tested for that. And I just can't understand when I never—and when my wife was suffering from cancer, I never saw any ads, never saw any public service announcements, never saw anything.

And I was just talking to this young lady back here, who is a cancer survivor, and she says she has a master's degree, and when she tried to go to the Web site to find information about the cancer she was suffering from, she and her husband, they had to go through all kinds of hoops to get the information. And it seems that if our health agencies have money in the pipeline to educate the public about these various forms of cancer, it would be manifested in television ads or newspaper ads.

I just saw this ad in the Roll Call magazine that was paid for by Angelina Jolie. You know, it just seems people would be educated to know, especially about the kind of cancer that is not readily discernible.

I mean, if you guys are spending money on telling people about this, I sure haven't seen it, and my wife died 3 years ago. So I would just like to know, if you are spending the money, where in the world is it going?

Dr. TRIMBLE. We would be happy to get you the information on the budget that NCI spends on educating the public and professionals about gynecologic cancer. But, nonetheless, the size of that budget is substantially less than that of, say, what major corporations use to promote new products. So in many cases we can't afford to buy TV time on national network TV.

That said, I think we make a very energetic effort to make sure that our Web site is as comprehensive as possible; that we have publications which are available in low literacy form, both in English and Spanish; that we have a 1–800–4-CANCER number with cancer information services available around the country that can help people find appropriate care, to find clinical trials, to find contact for support organizations.

We know we need to do more, but we have developed a close working relationship between NCI and CDC, between NCI and CDC and the professional societies and advocacy groups so that we can multiply our investments and make sure that the information gets as widely as possible.

Mr. BURTON. Well, let me just say that maybe you need to hire an ad agency or somebody to come up with some ads that could be put in public service announcements so people could be made aware of these things. My wife was misdiagnosed, and I think it was because even the doctor didn't have the kind of educational background to tell her what she should do.

I just think if we are spending money in that area, and I hope we pass Johanna's Law to help augment this, but if we are spending money in that area, we ought to make sure the public can see it in one way or another. So you should just take that back as a recommendation. And I would like to see, if you could send it to us, a list of the ways that you are spending the money to inform the public, because I haven't seen it, and I would like to see it. Thank you.

Mr. ISSA. Mr. Chairman, I would ask unanimous consent for 1 additional minute.

Mr. CANNON. Without objection, so ordered.

Mr. ISSA. Mr. Chairman, I would yield to you for that minute.

Mr. CANNON. Thank you. If the gentleman would yield back, I will just make my final comments. The gentleman yields back. Thank you.

Mr. Trimble in particular, but others, have any of you been involved with the rulemaking relating to making federally funded studies available? That is an issue for another time and another panel, but of course goes right to the heart of access for information.

Just a final question. Actually, we want a commitment from each of you on behalf of your agencies, so you have to be careful. You

are not limited to what you are able to actually do, but you know your internal circumstances. FED has made some commitment along these lines that I am sure you are aware of.

I want from each of you a commitment, those of you who can give it, on behalf of your agencies that you will work together and with Congress, with my office, to work on the issue of making more information available, developing databases that appropriately can have information available to doctors, researchers, and others, especially in the context of the lowered cost of database access and the lowered cost of protein decoding.

If we could start with Mr. Trimble, whatever you could commit to, I would appreciate.

Dr. TRIMBLE. Well, I know this is a high priority of Dr. von Eschenbach, our Director, is making information more widely available, as well as building on the Nation's expertise in informatics. And as part of that he has established a cancer bioinformatics project called CIBIG. And I think that there are a number of components to that, but one of them would include the emphasis that you, Congressman Cannon, have put on, in terms of gaining data from the way an individual doctor, an individual patient, their experiences so other people are aware of that and can learn from that.

Mr. CANNON. Thank you. I appreciate the clarity of that commitment. I actually spoke to Dr. von Eschenbach about this. I believe that he clearly understands the benefit of capturing data from practitioners. So I appreciate that.

Dr. Thompson.

Dr. THOMPSON. As I mentioned earlier, the Department of Health and Human Services is already solidly behind the development of an electronic patient record which would facilitate many of the things that you are describing. At the level of CDC, our commitment to this is, I think, demonstrated best by the establishment only a few months ago of a new center called the National Center for Public Health Infomatics, which will address this and other needs for health information to be more readily collected and more readily available.

Mr. CANNON. Thank you. And I assume that includes also a commitment to work with other agencies and to get clinical information from practitioners available to others.

Dr. THOMPSON. Yes, sir, it does, particularly the electronic medical record effort is one that is cross-cutting throughout the Department of Health and Human Services, and all of the divisions of the Department are potentially involved in this.

Mr. CANNON. Thank you.

Dr. PAZDUR. As I stated in my testimony, we have an Interagency Task Force that is a joint effort between the FDA and the NCI, and I think that this is an excellent project for that task force really to capitalize on. It is not solely an FDA problem; it is not solely an NCI problem; it is not solely a CDC problem; but something for us to work on together. And I think that task force provides at last a framework to begin the process that you have outlined.

Mr. CANNON. And is this a fairly substantial commitment on the part of FDA, from your perspective?

Dr. PAZDUR. Yes, it is.

Mr. CANNON. Thank you.

I find myself sitting here frowning through this hearing. That is because this is a rotten subject to be talking about, especially if you have had the kind of loss that Mr. Burton and I have had. And I hope that frown has not been viewed as negative. What your institutions are doing is incredibly important. You are remarkably effective. We don't want to change the world, but we want to help you all adapt and we want to create the legal context for that adaptation.

Let me just say finally, before we leave, Mr. Rosenfeld, would you mind raising your hand? This is a molecular biologist over here, a friend of mine and a brilliant human being. You may want to meet him as you go out and get his card, or stay and listen to his testimony, which I think is going to be remarkably interesting. He was a molecular biologist before I think that was popular, and has been a leader in some of these areas, particularly in cervical cancer and the identification of proteins related to that.

So, with that, unless there are further questions, we appreciate your time. This panel is dismissed.

If we could have the second panel join us.

We had a question from a witness regarding the appropriateness of videotaping, that is, a family member videotaping the testimony. Without objection, the chair is inclined to allow that. So, without objection, so ordered. The family may videotape the hearing.

And, if you would like, without objection, Ms. Silver, you can have her put a chair up here so she can videotape the table, if you would like. Without objection, so ordered.

All right, now, if we could have you raise your right hands.

[Witnesses sworn.]

Mr. CANNON. The clerk will note that all members of the panel have nodded in the affirmative.

We will just go member by member, starting with Dr. Karlan. We appreciate your being here, and you are recognized for 5 minutes.

STATEMENTS OF DR. BETH KARLAN, PRESIDENT, SOCIETY OF GYNECOLOGIC ONCOLOGISTS; DR. MARK JAY ROSENFELD, SCIENTIST/RESEARCHER; SHERYL SILVER, SISTER OF JOHANNA SILVER; AND KOLLEEN STACEY, OVARIAN CANCER SURVIVOR

STATEMENT OF DR. BETH KARLAN

Dr. KARLAN. Thank you, sir. Chairman Cannon and members of the subcommittee, thank you for inviting me to testify at today's hearing. I am honored and heartened by the interest of this subcommittee in this important issue.

My name, as you heard, is Beth Karlan, and I practice medicine at Cedar Sinai Medical Center in Los Angeles. There, I am the director of the Women's Cancer Research Institute, the Division of Gynecologic Oncology, and the Gilda Radner Hereditary Cancer Detection Program. I am also professor of Obstetrics and Gynecology at the UCLA Geffen School of Medicine.

This year I was elected to serve as the 37th president of the Society of Gynecologic Oncologists [SGO]. Our organization's purpose is to improve the care of women with gynecologic cancer by encouraging research and disseminating knowledge. Our overall effort is focused on raising the standards of practice in the prevention and treatment of gynecologic malignancies through cooperation with other organizations that share our interest in women's health care, oncology, and related fields. SGO members make us the leading organization of gynecologic oncologists in the United States.

At the outset, I want to clearly state my belief that Congress can take action that in the immediate future will save the lives of thousands of women. Today in the United States, one women will be diagnosed with a gynecologic cancer every 7 minutes. That is over 200 women just today and close to 80,000 women this year. If detected early, a majority of these cancers can be cured.

But, frankly, many women don't know what symptoms to worry about and, therefore, they are unable to ask the right questions of their health care providers. Complaints such as bloating, abdominal or low back pain, or constipation may bother all of us occasionally. But when these symptoms are persistent and progressive for as little as 2 weeks, they should alert a woman to see her physician and ask about gynecologic cancer. With the help of the Federal Government, we can make this happen. We can make this happen.

I would like to bring to your attention H.R. 1245, the Gynecologic Cancer and Awareness Act of 2005, commonly referred to as Johanna's Law. This legislation would serve to increase the education and awareness about the early warning signs of gynecologic cancer. That is the purpose of Johanna's Law: so no woman has to face a diagnosis of gynecologic cancer late in her disease just because she did not know the associated symptoms, risks, or where to turn.

As a clinician and surgeon, I can recount hundreds of stories of women who came into my care too late because they did not recognize the warning signs their bodies were sending to alert them to the presence of cancer. These anecdotes, however, are validated by a recent poll of 800 women across America that was conducted by Research America in conjunction with SGO's foundation, the Gynecologic Cancer Foundation. This poll surveyed women about their knowledge of gynecologic cancers and is submitted as an attachment to my written testimony.

Here are just a few of the astonishing statistics: 47 percent of women surveyed could not name one symptom of a gynecologic cancer, not one; and almost 60 percent of women surveyed could not name one step they could take to decrease their personal risk of developing a gynecologic cancer.

Mr. Chairman, these statistics do not lie. We need to make a difference, and we can make it now. We have achieved much, but women are still dying. Congress's commitment to expanding the boundaries of medical research has been a vital weapon in our war against gynecologic cancer, and for that we are immensely grateful. However, there is still a tremendous gap between the science and the realities of clinical care. All of our scientific advances are useless if women do not know when, where, or how to access care.

Representatives Issa, Levin, Granger, and DeLauro have introduced Johanna's Law, which is cosponsored by many members of this committee. In fact, there are now 221 co-sponsors of this important legislation. Under Johanna's Law, the Department of Health and Human Services would conduct public education and awareness programs to get facts about the early warning signs of gynecologic cancer into the hands of women of this country.

I cannot over-stress the importance of arming women with the basic facts about gynecologic cancers. Education is our front line defense in the battle against these killers of women. Your support will make this education and awareness possible.

Once again, thank you for the opportunity to testify here today. I am constantly inspired and humbled by the strength and determination shown by women with cancer who are just trying to survive. I believe your leadership on this issue will give even more women the full lives they so richly deserve.

Thank you, and I look forward to answering your questions.

[The prepared statement of Dr. Karlan follows:]

STATEMENT OF BETH Y. KARLAN, MD

BEFORE THE SUBCOMMITTEE ON CRIMINAL JUSTICE, DRUG POLICY AND HUMAN RESOURCES

SEPTEMBER 7, 2005

Mr. Chairman, Ranking Member and members of the subcommittee, thank you for inviting me to testify at today's hearing. I am honored to be here and heartened by the interest of the subcommittee in this important issue.

My name is Dr. Beth Karlan, and I am the President of the Society of Gynecologic Oncologists. I practice medicine at Cedars-Sinai Medical Center and the Oschin Cancer Institute in Los Angeles, California, where I am the Director of the Women's Cancer Research Institute, the Division of Gynecologic Oncology and the Gilda Radner Hereditary Cancer Detection Program. I am also Professor of Obstetrics and Gynecology at the University of California, Los Angeles' (UCLA) Geffen School of Medicine.

The Society of Gynecologic Oncologists (SGO) is a national surgical specialty society of physicians. Our membership is trained in the comprehensive management of women with reproductive cancers. Our purpose is to improve the care of women with gynecologic cancer by encouraging research and disseminating knowledge. Our overall effort is focused on raising the standards of practice in the prevention and treatment of gynecologic malignancies through cooperation with other organizations interested in women's health care, oncology and related fields. SGO's members make the Society the leading organization of gynecologic oncologists in the United States. As gynecologic oncologists, we are women's cancer specialists who have received an additional three-four years of intensive post-graduate medical training in the comprehensive treatment of gynecologic cancers, including cancers of the ovary, endometrium, cervix, vulva and vagina.

At the outset, I wish to clearly state my belief that Congress can take action that will, in the immediate future, save thousands of women from dying from these cancers. Today, in the United States, one woman will be diagnosed with a gynecologic cancer every seven minutes. That's over 200 women today and close to 80,000 this year. Over one-third of these women will die unnecessarily. Early education and prevention, as well as effective screening, could save many of these lives. Sadly, too many women are unaware of the early symptoms of gynecologic cancer. If detected early, the vast majority of these cancers are curable. Without fact-based information, many women are unable to ask the right questions of their physicians -- questions that can save their lives. Through the establishment of a federal program, women could receive education about the early warning signs for and the effectiveness of early detection of gynecologic cancer.

Arming women with this critical knowledge is the purpose of H. R. 1245, the Gynecologic Cancer Education and Awareness Act of 2005 – commonly referred to as "Johanna's Law." Passage of "Johanna's Law," which I will describe in more detail, could immediately prevent needless deaths from these cancers.

From my vantage point as a surgeon specializing in the treatment of gynecologic cancers, and as president of SGO, I can assure this subcommittee that today's hearing performs a critical public service. The paucity of public discussion and attention about gynecologic cancers is literally killing

thousands of women in our country because they do not know, nor do they understand, their risks of developing a gynecologic cancer. I could sit here and recount hundreds of first person stories of women who came into my care too late, and did not know the warning signs that their own bodies sent to alert them to the presence of cancer. Had they known what to watch for and how to listen to their bodies, we could have intervened earlier and saved their lives.

To better illustrate the job I believe we must do, I like to draw a parallel between gynecologic cancer and breast cancer. I believe we are all old enough to remember when little was known about breast cancer, screening was in its infancy, and a late stage diagnosis often meant physically deforming surgery, scorching radiation therapy, and many times death. In 20 years we have revolutionized breast cancer care and survival by advocating for heightened awareness, improved screening and novel treatments. Open discussions about risks, early detection and intervention have saved thousands of lives. It is our firm belief, and the intention of this legislation, that we must achieve the same outcome for gynecologic cancers, and create an environment where gynecologic anatomy can be named and visualized just as comfortably as the anatomy of the breast.

We don't come to you with only a vision, we have data to support our case for this legislation. Today, SGO's Foundation, the Gynecologic Cancer Foundation (GCF) and Research!America released the results of a poll of 800 women across America that asked women about their knowledge of gynecologic cancers. The poll report is submitted as part of my testimony.

Here are just a few of the astonishing statistics:

47 percent of women surveyed could not name one symptom of gynecologic cancers, not one!

45 percent of women surveyed were not aware of any personal risk factors that increased their chance of developing a gynecologic cancer.

Almost 60 percent of women surveyed could not name one step they could take to decrease their personal risk of developing a gynecologic cancer.

Clearly this data suggests that with even a modest improvement in outreach and education, we can save lives and precious healthcare resources, and improve the health of our nation's women. This legislation will accomplish that – through education of both women and their health care providers.

To help you better understand each of the gynecologic cancers and our opportunity to improve survival for every one of them, I have submitted for the congressional record a copy of the 2005 State of the State of Gynecologic Cancers. Each year at the beginning of September, Gynecologic Cancer Awareness Month, SGO and GCF publish this report to the women of America describing each gynecologic cancer---their risks, symptoms, incidence rates, and most importantly, the advances made during the past year. For the purposes of my testimony, I will briefly discuss the three most common female reproductive cancers -- cervical, ovarian and uterine cancer and invite you to consult the report for information about the less common gynecologic cancers.

Cervical cancer begins in the cervix, the lowest portion of the uterus or womb that opens into the vagina. It results when abnormal cellular changes go undetected and invade the underlying cervical tissue. Cervical cancer is the only gynecological cancer that can be prevented by regular Pap smear screening, yet over half of the women dying from cervical cancer in the United States have never had

a Pap smear. Cancer of the cervix usually affects women between the ages of 30 and 55 but has been found as early as the teenaged years. This year an estimated 10,370 cases of invasive cervical cancer are expected to be diagnosed and result in approximately 3,710 deaths. Because this cancer is totally preventable, each one of these deaths is, sadly, an unnecessary death.

Ovarian cancer usually arises from the cells on the surface of the ovary and can be extremely difficult to detect. But it is not a silent disease. Recent studies demonstrate that approximately 40 percent of women with ovarian cancer saw their physicians 4-12 months before the diagnosis was made and complained of symptoms including abdominal pain, bloating and gastrointestinal distress. As you will hear from other witnesses on this panel, this delay in diagnosis often makes it too late for medical intervention to be effective. Ovarian cancer ranks fourth in cancer deaths among women and causes more deaths than all the other cancers of the female reproductive tract combined. It is estimated that there will be more than 22,220 new cases diagnosed this year and approximately 16,210 women will die from this disease. Knowledge of the symptoms of this cancer can literally save women's lives. Johanna's story makes this point so poignantly clear.

Uterine cancer usually begins in the lining of the uterus, or endometrium, when cells in the lining grow out of control and invade the muscle of the uterus. It most frequently occurs in women around perimenopause or in the postmenopausal years but may occur in younger women as well. Cancer of the endometrium is the most common of the female reproductive cancers. This year it is estimated there will be 40,880 new cases of uterine cancer diagnosed, and that this will result in 7,310 deaths. The GCF-Research!America poll found that women over 65 do not feel that they are at risk of developing a gynecologic cancer, especially when compared with women 35-44 years of age. Again, we must change this number. For in the case of uterine cancer and ovarian cancer, it is these postmenopausal women who are at the greatest risk.

We have made enormous strides in identifying the risk factors and causes of these cancers, including hereditary, environmental, and biological contributors. In the past 10 years our identification of the genes responsible for two hereditary gynecologic cancer syndromes, familial breast-ovarian cancer syndrome and hereditary non-polyposis colorectal cancer syndrome (HNPCC), has contributed greatly to our ability to detect a woman's risk for developing a gynecologic cancer.

Women who are part of the familial breast-ovarian cancer syndrome have inherited a deleterious mutation in either the BRCA1 or BRCA2 genes, which places them at much greater risk for breast and ovarian cancer. On average a woman has a 13 percent risk of developing breast cancer and a 1.8 percent risk of developing ovarian cancer. Women with these BRCA1 or BRCA2 gene mutations have an almost 90 percent risk of developing breast cancer and a 15-40 percent chance of developing ovarian cancer. HNPCC is a cancer family syndrome due to inherited genetic mutations in a different group of genes and results in a predisposition to cancers of the colon, endometrium and ovary. For women with HNPCC syndrome, the lifetime risk of ovarian cancer and endometrial cancer is approximately 10 percent and 40-60 percent, respectively.

Mr. Chairman, we clearly need to know more about why all cancers, including gynecologic cancer, develop and how to detect them early and treat them effectively. But what we already know about gynecologic cancers is significant. We know that some people are at enhanced risk of developing such cancers and, perhaps most critically, that early detection vastly increases the odds of prolonged survival and cure for all of these cancers. One of our biggest problems is that we have not been able

to effectively communicate these facts to the vast majority of the women in our country. And the results of the GCF-Research!America poll dramatically illustrate this point.

You will undoubtedly hear from witnesses today about their personal experiences, as well as the experiences of their loved ones, in discovering and treating their cancers. As I mentioned earlier, in my role as a physician I often see tragic stories that did not have to end tragically -- lives lost that could have been saved with more timely interventions and treatment. Congress' commitment to expanding the boundaries of medical research has been a vital weapon in our war against gynecologic cancer. However, all the treatments in the world will not work if women do not know when, where and how to seek them.

Representatives Issa, Levin, Granger and DeLauro have introduced Johanna's Law, which is co-sponsored by many members of this committee. In fact, there are 220 co-sponsors of this important piece of legislation. Under Johanna's Law, the Department of Health and Human Services (HHS) would conduct public education and awareness programs to explain the facts about the early warning signs of gynecologic cancers to the women of this country. The activities HHS would undertake would include various forms of communication (written materials, public service announcements and more), as well as outreach in cooperation with nonprofit organizations. Johanna's Law would entail modest levels of funding ($15 million annually), but these monies would be significant in our fight to end cancer as a threat to women. I cannot over-stress the importance of arming women with the basic facts about these cancers. It is our front line defense in the battle against these killers of women.

An ad calling attention to "Johanna's Law" appeared today in "Roll Call" through a generous donation from Angelina Jolie. Maybe you saw it. It portrays a woman alone, sitting on an examination table with a look on her face of overwhelming sadness. The caption reads, "If only she had known sooner." I believe that no woman should have to face a diagnosis of gynecologic cancer because she did not know the risk factors and symptoms. This is the purpose of "Johanna's Law.

I look forward to answering your questions and thank you for the opportunity to testify today. I am constantly inspired and humbled by the strength and determination of women to live. I believe your leadership on this issue will give even more women the full lives they so richly deserve. Thank you.

Mr. CANNON. Thank you, Dr. Karlan. Among those women are my five remaining daughters and wife who appreciate your testimony, and there are some startling statistics there.

Dr. Rosenfeld, you are recognized for 5 minutes.

STATEMENT OF DR. MARK JAY ROSENFELD

Dr. ROSENFELD. I am grateful to the subcommittee for the opportunity to discuss my professional experiences and opinions on progress against gynecologic cancers. I come from a different perspective than most here. No. 1, I am a researcher; No. 2, most of my work has occurred not only in the United States, but the bulk of it in places like China.

Given the time constraints, I have made much of my presentation a written one, and covers such issues as the financial incentives that perpetuate inefficient and costly diagnostic methods; the need for disruptive or analytic or diagnostic technologies to achieve pervasive high-quality and inexpensive medical care; and whether cervical cancer vaccines can actually achieve significant use in our lifetime.

Perhaps not an intended topic at this meeting, but the ways in which we have pursued cancer for several decades have, over all, been a failure, in my opinion. There have been some clear successes. With the possible exception of Pap smears, gynecologic cancers are not blatantly prominent among these. Perhaps the greatest improvement, as actually has been mentioned, has been treating childhood cancers. Overall, our inability to lower the cancer death rate, despite expensive efforts spanning more than 35 years since the war on cancer began, shows the need for major change in strategy.

I am now going to somewhat digress—although it is in my written presentation—digress from what I had originally prepared because of comments made by people. For example, Dr. Thompson talked about the 2.9 million Pap smears that had been done to achieve the finding 1,500 patients with invasive cancers. That is great, because that cost $75 million and an average of $40,000 to $60,000 to find each of those cancers.

Now, I am happy that these people were discovered. I hope that they were treated; I hope that it was successful. On the other hand, that is a lot of money. And it is a lot of money that if we could be more efficient in terms of the way in which we pursue our medicine and the way in which we pursue our diagnostics, then we could reach more people.

This gets into questions such as we discussed a few minutes ago, or actually throughout this entire proceeding, and that is how do we reach people? We can only reach people if we have the kind of technologies, if we have the kind of methods that will allow us to reach them for a good economic price. Most of the democratic side, in fact all are not here right now, but, on the other hand, they had talked literally about that, the black community, and reaching the black community.

I talk in my written work about the financial incentives that perpetuate inefficient and costly diagnostic methods. Look at the Pap smear industry. It is a $7 billion industry. I am not condemning Pap smears. But if something new, something revolutionary, some-

thing disruptive came along—and there are those things on the horizon as we speak—how do we contend with that? These people are making a living.

So either consciously or subconsciously, they are going to buck the trend because they are spending $2 billion per gynecologic exam in this country that leads to a Pap smear. There is $1.2 billion being spent on average each year now for Pap smears alone. When you have a Pap smear that is questionable, you go to colposcopy. Colposcopy is a microscopic examination of the cervix; $3.6 billion is being spent there. Yet, over 80 percent of colposcopies, fortunately for the patient, show that the patient has nothing wrong. We just spend over $2 billion for nothing, in a sense.

Things need to be done. There is a need for disruptive technologies. Bringing down costs is mandatory. We have to shift in a grander way to earlier detection and treatment. This is something that I push very aggressively in China.

And I think that if you look at the war on cancer, speaking more generally, but also to gynecologic cancers, we have to concentrate more on less advanced states, where treatment effects may be better. For example, when we go to FDA approval and we are looking at a new drug, what is happening with a new drug is that, typically, the patient that is being treated is the sickest patient.

Now, I am not saying sick patients should or should not be treated, but the sickest patient with a drug is oftentimes a patient that won't respond anyway; and maybe a person who is not as sick could benefit more from that drug. This is something that really needs to be looked at very, very seriously.

In any case, I am rather passionate about changing the system, and hopefully during my question and answer period I can help you in terms of what else I have to offer. Thank you.

[The prepared statement of Dr. Rosenfeld follows:]

U.S. House of Representatives
Subcommittee on Criminal Justice, Drug Policy and Human Resources

Women and Cancer – Where Are We in Prevention, Early Detection and Treatment of Gynecologic Cancers?

September 7, 2005

Statement by

Mark J. Rosenfeld, Ph.D.
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Statement

I am grateful to the Subcommittee for the opportunity to discuss my professional experiences and opinions on progress against gynecologic cancers. Given the time constraint, I have made much of my presentation a written one, which covers not only what I shall now verbalize but also topics like the financial incentives that perpetuate inefficient and costly diagnostic methods; the need for disruptive analytical or diagnostic technologies to achieve pervasive, high-quality inexpensive medical care; and whether cervical cancer vaccines actually achieve significant use in our lifetime. Perhaps not an intended topic at this meeting, but the ways we have pursued cancer for several decades have overall been a failure. There have been some clear successes. Gynecologic cancers are not blatantly prominent among these, and perhaps the greatest improvements are in treating childhood cancers. Overall, our inability to lower the cancer death rate, despite an expensive effort spanning more than 35 years since the War on Cancer began, shows the need for a major change of strategy. In my written presentation, the issue of lacking progress is dealt with in detail.

I have considerable experience on cancers of many sorts, but my gynecological experiences center largely about cervical cancer in the United States and China. As an invasive condition, this is a disease that strikes about 500,000 women worldwide annually, and 300,000 die each year. On a global basis, it is the most frequent female cancer in developing nations. In the United States, between 250,000 and 1 million women each year are annually diagnosed with cervical dysplasia. Dysplasia means abnormal growths. Without treatment, 30-50% of these could progress to invasive cancer. Almost 13,000 new cases of invasive cervical cancer are diagnosed each year, along with more than 50,000 cases of malignancy still confined to the surface of the cervix (carcinoma in situ). The American Cancer Society estimates that almost 5,000 women will die this year from cervical cancer. This represents 18% of American deaths from gynecological cancers.

A virus called HPV (or human papillomavirus) causes virtually all cervical cancers. Given that HPV is largely transmitted via sexual intercourse, cervical cancer should be considered a sexually transmitted disease.

To identify abnormal cells typical of cervical cancer, a Pap test (also called a Pap smear) is typically done. It is an examination done with a microscope of cells collected from the cervix, and it requires highly-trained specialists. In the United States and other developed countries, where Pap tests are widely available and easily accessible, deaths from cervical cancer have plunged. Given that most cancers in the United States are on the rise, this is indeed an achievement. It is more so the case upon consideration of Pap test deficiencies. The sensitivity of a single Pap test for detecting cancerous growths is as little as 50%. The National Institutes of Health estimates that any single Pap smear has a 20% chance of being a false negative. False negatives can vary be up to 55% for invasive cervical cancers, and 80% for preinvasive conditions.

The poor sensitivity of a Pap test is compensated by frequent repetition to improve detection. In other words, the American cervical cancer screening system consists of doing Pap tests again and again – with about 60 million done in the United States each year. Repeat Pap testing is costly, burdensome, and time consuming, as well as needing highly trained specialists to successfully perform. This makes Pap testing rare or non-existent outside of North America, Western Europe and Japan. For the developing world, the inability to screen for cervical cancer in its earlier stages literally means death for hundreds of thousands of women each year.

A major deficiency is that Pap testing has primarily been effective against squamous cell carcinoma only. Pap tests have been of little worth for detecting cervical adenocarcinoma, a cancer that starts in glandular tissue. Meanwhile, this is an aggressive, life-threatening condition for which incidence in the United States has increased by about 40 percent over the last 10 years for unknown reasons. Since its early detection is not doable with Pap tests, adenocarcinomas become obvious when larger and harder to successfully treat. Also, an excessive number of adenocarcinoma victims are in their teens and 20s, instead of the 50s more typical for squamous cell cancers detected with Pap tests -- while current molecular methods that might assist in diagnosing adenocarcinomas are mandated by the FDA only for women more than 30 year

Not only missed with Pap smears, adenocarcinomas are likewise difficult to recognize via colposcopy -- especially in early stages. Difficulties in detecting cervical adenocarcinomas with Pap tests point out the dire need for novel detection methods since Pap testing actually does not work. Pap testing does not work, and a molecular-based alternative is needed.

Statistics point to a particularly greater risk of developing adenocarcinoma in the 20-30 year age group, and adenocarcinomas have even been found in females as young as 16 years old. This propensity for adenocarcinomas to occur in younger women calls for revised age guidelines for cervical cancer screening. Current standards for HPV-related testing mandate diagnostics only for women greater than 30 years of age. Meanwhile, molecular testing has the potential to facilitate accurate diagnosis of this disease and younger women seem to be at greater risk.

Although inefficient, there is incredible financial incentive to perpetuate inefficient Pap screening and to otherwise slow down or prohibit the commercial penetration of emerging molecular methods into the cancer detection marketplace. About $6 billion are spent each year to look for cervical disease. Almost all cervical cancer scrutiny today starts out with a Pap test. Two billion dollars are paid out just for the examination during which Pap smears are taken – in other words, a primary source of revenue for many physicians. As for gynecologic oncologists, a major "bread-and-butter" procedure is colposcopy-directed biopsy, a microscopic examination of the cervix during which tissue samples are taken. In essence, patients are referred for colposcopy when Pap smear results seem abnormal, and a colposcopy-directed biopsy costs $350 to $450. If the colposcopy-directed biopsy does not show why the Pap smear was abnormal, a cold cone biopsy might then be done. A cold cone biopsy is $1,200 expense.

In the United States, about 3.5 million Pap tests are classified as equivocal (atypical cells of undetermined significance, or ASCUS) each year. Current guidelines specify colposcopic follow-up to an equivocal Pap test, but since a woman with a minor abnormality and an otherwise normal cervix has only a 7% chance of ever needing treatment, the benefit of such scrutiny is unclear but expensive. The National Cancer Institute reports the average cost of managing an abnormal Pap smear at about $1,200, and costs for dealing with discrepant Pap findings at about $3.6 billion each year. Of this amount, about $2 billion goes to those doing the colposcopies. This means that a gynecologic oncologist can make hundreds of thousands of dollars each year from colposcopy alone.

What if an inexpensive molecular test became available for diagnosing cervical cancer? Real financial incentives exist to restrict its use. There is a considerable Pap test industry encompassing the diagnostic laboratories which process Pap smears and the cytopathologists who interpret the results (American Society of Cytopathologists). With 60 million Pap smears given yearly and a single test costing $25-50 to process and interpret, well more than 1.2 billion dollars are involved.

Given that around 80% of colposcopies turn out negative, at least $1.5 billion a year could be saved if the first look for cervical disease were sensitive and specific enough to preclude unwarranted colposcopic examinations. Molecular tools have such promise, along with an unrealized potential to be inexpensive. If these could be appropriately constructed, then both Pap tests and most colposcopies could be relegated to obscurity.

Recognizing that HPV causes cancer has provides clarity and otherwise needed perspective to the diagnosis and management of cervical dysplasias and cancer. HPV-related diagnostics can be unambiguously directed at disease instead of just infection, and that aspect is being actively developed. For example, an immunotest from a commercial entity in the western United States is showing great promise in clinical studies here and abroad as to being able to detect cervical disease with great sensitivity.

In extrapolating to the more than 60 million Pap smears done each year in the United States, an HPV-related test on equivocal Pap tests, using current FDA-approved but still inefficient technology, portends an annual cost savings of at least $150 million from just eliminating repeat visits for another Pap test.

The potential of molecular HPV testing is that detection could be done not only sensitively but also rapidly and cost-efficiently. However, implementation will undoubtedly impact moneymaking by gynecologic oncologists and other health care professionals.

A major trend in medical diagnostics has been to higher resolution or specificity – but without serious, or any, attention to cost. This is indeed the case for current,

molecular HPV or cervical cancer tests – and it is more so a factor driving national health expenditures to grow at four times the rate of inflation.

In actual fact, molecular tests for cervical cancer and the associated highly-complicated analytical machinery needed to do the tests are expensive – which thus makes them available to privileged patients, with those in rural and low-income regions relegated to obscurity in the process. Indeed, more than one in four Americans are now faltering under the burden of health costs, while the rest include those who say they worry about whether they will be able to pay routine medical bills in the future and those who have already started cutting corners healthwise because of the costs.

New disruptive healthcare technologies to reverse this situation are mandatory and these need to be encouraged if serious progress is to be made on not only providing cost-effective and even inexpensive, pervasive early detection of cervical cancer but the same for so many other cancers – and to succeed across the board in so many ways as to the War on Cancer. However, the medical naysayers will assiduously protect their financial turf and, consequently, retard progress.

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Mr. CANNON. Thank you for recognizing the light. We probably wouldn't have tapped you silent, given the kind of information you were giving, but we will come back, I can assure you, with questions to give you more opportunity to explain some of these things.

Ms. Silver, you are recognized for 5 minutes.

STATEMENT OF SHERYL SILVER

Ms. SILVER. Thank you so much, Mr. Chairman, for your leadership, for holding this hearing today, for your passion for this issue. I am so sorry for your loss, and I express my deepest condolences.

And to so many of you on this committee who have also been personally touched by cancer and who have led this fight for us, we are so grateful to you, Mr. Issa, our lead sponsor in the 109th Congress; to Mr. Burton, who has been such an advocate for us; Mrs. DeLauro; Mrs. Granger; and, of course, Mr. Levin, the original author of Johanna's Law. We are just indebted to all of you for taking up this fight for us, and for millions of American women at risk. That is really the issue here.

And as the person who first proposed Johanna's Law, I suppose I should give my name: Sheryl Silver. I am the founder and president of Johanna's Law Alliance for Women's Cancer Awareness. Most proudly, I am the younger sister of Johanna Silver Gordon, after whom this legislation is named.

I feel a responsibility on behalf of millions of grieving family members in this country who have lost hundreds of thousands of their mothers, sisters, daughters, and other loved ones, to sound an alarm today. I know everyone in this room is supportive, and we are grateful for that, but there will be many who read and hear this testimony.

So I want to go on record today as saying we have a national tragedy that is not being addressed adequately. Unlike the tragedy of September 11th and Hurricane Katrina, which thankfully have only happened once in this Nation's history, this is a tragedy that is going on year after year in this country, as we lose, this year, nearly 30,000 women to gynecologic cancers. Nearly 10 times the number of Americans we lost on September 11th we are now losing every single year.

In just the last 10 years we have lost over 250,000 of our mothers, sisters, daughters, and other loved ones. Although we are grateful for its progress and absolutely for the 221 cosponsors in the House, the time to act is now. In just the nearly 3 years since I proposed it, over 75,000 more women in this country have run out of time, run out of medical options and died, and left behind millions of us grieving for the rest of our lives.

And what magnifies the tragedy of these deaths, and all of them from these cancers, is that they are not inevitable. A diagnosis does not have to be a death sentence, as we have heard today. Diagnosed at the earliest stage, ovarian, uterine, and cervical cancer—which account for over 90 percent of all new diagnoses in this country every year—these three cancers all have 5 year survival rates greater than 90 percent, with women diagnosed early commonly going on to live normal, long, healthy lives.

And yet thousands of women, tens of thousands are diagnosed after this earliest stage every year in this country. With ovarian

cancer, the problem is particularly common. Eighty percent of women are diagnosed after the cancer has progressed to more advanced and less survivable stages.

And a common ingredient in those late-stage diagnoses are the delays that occur simply because women don't recognize or know the symptoms of the disease or its risk factors, and so are not seen quickly enough, appropriately enough. This is exactly the life-threatening information gap that contributed to my sister's late diagnosis and death.

Despite being the daughter of a physician, the sister yet of two other physicians, and a health-conscious woman who saw her gynecologist annually for pelvic exams and Pap smears, who ate nutritiously, exercised regularly, did everything she knew of to live a long, healthy life, despite that, the one thing my sister did not know is that persistent heartburn, bloating, and constipation were common symptoms of ovarian cancer. She assumed they were to do with a minor gastric problem. She took antacids.

When the symptoms persisted, she made an appointment to see a gastroenterologist; waited several weeks as a new patient for that first appointment, never thinking the delay may be life-threatening. And by the time she saw her gynecologist and appropriate tests were performed, she was immediately scheduled for major surgery that led to the shocking diagnosis of stage 3C ovarian cancer, of only four stages, a late stage. She was only given a prognosis of 12 to 18 months to live; and with aggressive surgery, multiple surgeries, treatments, chemotherapy, different kinds of chemotherapy, clinical trials.

We searched for everything. She went to leading cancer centers, she had great insurance, access to care at UCLA, MD Anderson. But nothing helped because she was diagnosed so late. And she spent the last 8 months of her life tethered to an IV pole for her basic nutrition and hydration, and eventually pain medication 24 hours a day to dull her agony. This is a horrible way for a dynamic and loving and health-conscious woman to lose her life.

But we are not here because my sister was an unlucky, uninformed woman. I didn't propose Johanna's Law 3 years ago because of that. I proposed it because this tragedy is happening day after day, year after year in this country, unchecked. And whatever we are doing, it is not enough, because the death toll from this group of cancers is not going down.

Two years ago the death toll from ovarian cancer went up. It may go up further as this population ages. Our Nation is an aging population, and women over 50 are at higher risk for both ovarian and uterine cancer. So we have to do more to improve early detection and develop better treatments, all of it, or else we will see this death toll continue to climb.

Last week—I am going to also cut my testimony short. I am already over that time. Let me just say the following, and I will submit, if I may, my written testimony in its entirety.

Last week our President said the Federal Government's job is to save lives because every life is precious. I absolutely agree. And we have already lost too many of our precious mothers, daughters, sisters, and other loved ones and dear friends, simply because they didn't get the information in time.

This is not the behavior of a compassionate Nation. We know that acting quickly can spare needless suffering, just as we know that acting quickly in the wake of Hurricane Katrina—and this Congress can move quickly when it needs to, as it did last Friday in granting major funding for relief. We know that moving quickly in the case of natural disasters will spare needless suffering and death.

And the coalition of doctors, nurses, cancer survivors, and family members who have advocated for Johanna's Law these last 2 plus years, we do it because we all believe that we can improve early detection; we can save lives by educating women. They will take action given the facts.

So I beg this Congress, we have the best chance we have ever had because we have over half the members already co-sponsoring. Please let the legacy of the 109th Congress be that in addition to responding to the challenges of terrorism, homeland security, natural disasters, and other challenges facing this Nation, this was the Congress that finally took the action so long needed and created the urgently and desperately needed program of gynecologic cancer education.

By doing that you will not only save lives by improving early detection, you will finally give a measure of healing to millions of us in this country who grieve the loss of our loved ones and who will know, by the existence and the passage of Johanna's Law, that our loved ones did not suffer and die in vain, but that their stories and our retelling of their tragedies have finally been the catalyst to create this long overdue and urgently needed national program of gynecologic cancer education.

I thank you for your patience and indulgence. Thank you.

[The prepared statement of Ms. Silver follows:]

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Testimony for Sheryl Silver
September 7, 2005 Hearing on Women and Cancer:
"Where Are We in Prevention, Early Detection and Treatment of Gynecologic Cancers?"

I'd like to thank the subcommittee for this opportunity and focus on the urgency of the need to create a national program of education to improve early detection of gynecologic cancers in the U.S.

As the person who first proposed Johanna's Law, legislation that would create a national program of gynecologic cancer education, I feel a responsibility to sound an alarm today, to make sure this subcommittee and anyone reading or hearing my testimony knows that we have a national tragedy that needs to be addressed. Unlike the national tragedies that have thankfully taken place only once in our history – like the tragedy of Sept 11th and the tragic devastation we have just witnessed from Hurricane Katrina, the national tragedy I'm referring to has been going on for years and years and years.

This national tragedy relates to the thousands and thousands of women lost each year in this country to gynecologic cancers. In the last 10 years alone, we have lost over 250,000 American women to these cancers. In just the last 4 years, since the tragic events of 9/11, we have lost over 100,000 American mothers, sisters and daughters on domestic soil---not from terrorist attacks, thank God --- but just as tragically, from gynecologic cancers. In the nearly 3 years since I proposed Johanna's Law, legislation that would create a national program of gynecologic cancers, we have lost 75,000 American women --- 25 times the number of Americans lost on 9/11 --- in less than 3 years.

And what magnifies the tragedy of all these deaths is the fact that they are not inevitable. A diagnosis does not have to be a death sentence. Diagnosed at the earliest stage, ovarian, uterine and cervical cancer---which account for over 90 percent of all new diagnoses in the U.S. each year--- these 3 cancers all have 5-year survival rates greater than 90 percent, with women diagnosed early commonly going on to live normal, healthy lives for many years.

And yet, tens of thousands of women in this country each year are diagnosed after their cancer has progressed beyond the earliest and most survivable stage. The problem is particularly common with ovarian cancer, which is diagnosed approximately 80 percent of the time at stages that are much less survivable. Contributing to these late stage diagnoses is a lack of knowledge about the symptoms of the disease that commonly leads to lengthy delays in diagnosis. My sister Johanna was a victim of this life-threatening information gap.

We were stunned when Johanna was diagnosed with advanced ovarian cancer. We had no family history of the disease. What's more, my sister was a vigorously healthy and health conscious

woman who visited the gynecologist regularly for recommended pelvic exams and Pap smears. She ate nutritiously, exercised regularly. She did everything she knew of to live a long, healthy life. Unfortunately, the one thing she didn't know was that persistent bloating and heartburn were two of the common symptoms of ovarian cancer.

When she began to experience these symptoms, she assumed they were due to a minor gastric problem. She took antacids. When the symptoms persisted, she made an appointment to see a gastroenterologist and waited patiently several weeks for that first appointment, never thinking the delay might be life-threatening.

By the time Johanna saw her gynecologist and the appropriate diagnostic studies were performed, she was scheduled for major surgery a few days later. That surgery confirmed the shocking diagnosis of advanced ovarian cancer.

Although Johanna's doctor initially predicted she had just 12 –18 months to live, with aggressive treatment that included 4 surgeries, endless rounds of chemotherapy and participation in two clinical trials, my determined and courageous sister survived 3 ½ years. She was, however, rarely in remission and lived the last 8 months of her life tethered to an IV pole 12 hours a day for her basic hydration and nutrition --- and eventually 24 ours a day for the pain medication that dulled her agony. This was a horrible way for a loving, dynamic and health conscious daughter of a doctor to lose her life. Yes, my dad was a physician. So is my brother and yet we were as stunned by Johanna's diagnosis as every other family impacted by this disease that I've met in the 8 years since my sister's diagnosis.

That's why I proposed Johanna's Law --- not because my sister was one unlucky, uninformed daughter of a doctor but because her story is tragically common. In the days after Johanna's diagnosis, nearly every woman friend and family member we told about her situation was shocked ---not only to learn that their vigorously healthy friend had been diagnosed but that the gastric symptoms she'd had were common symptoms of ovarian cancer. They hadn't known it.

Neither had the ovarian cancer survivors I met in Johanna's support group at Gilda's Club or at national conferences on ovarian cancer I started attending the year Johanna had her first recurrence. Woman after woman had nearly identical stories. Nearly all had been diagnosed at advanced stages of ovarian cancer. All but one HAD LEARNED ONLY AFTER BEING DIAGNOSED that the symptoms they had experienced for months were common symptoms of the disease. And sadly, when their doctors attributed their symptoms to benign conditions with similar symptoms, without first ordering the appropriate diagnostic studies to detect ovarian cancer, since these women had no idea their symptoms could be due to ovarian cancer, they couldn't even say to their doctors: "Shouldn't we first rule out the most lethal cause of these symptoms, ovarian cancer, before assuming something benign is the problem?"

This is the deadly status quo Johanna's Law is designed to address. By providing women information about the symptoms and risk factors of gynecologic cancers, the program of gynecologic cancer education it would create can empower women experiencing symptoms to recognize them as potentially dangerous, prompting them to seek appropriate medical attention quickly and ask questions that ensure a gynecologic cancer is considered among the possible causes during a first visit, not months later as has so often occurred.

This problem is not new. I've heard stories of women who went through the same terrible experience decades before Johanna's diagnosis. And I hear about the same problem occurring today --- nearly 9 years after my sister was diagnosed and five years since she died. Commonly I hear of women who had symptoms and searched for answers for months before they were diagnosed, and who died within 1 - 5 years of being diagnosed with late stage ovarian cancer, despite multiple surgeries and aggressive chemotherapy regimens.

The needless suffering and deaths resulting from women not knowing the symptoms of ovarian cancer has gone on too long --- and cost too many precious American lives. And frankly, it's about time this national tragedy was adequately addressed and the source of it eliminated.

As President Bush said last Friday during on-camera remarks about Hurricane Katrina, "The job of the federal government is to save lives because every life is precious."

I absolutely agree with the president on that point. Every life is precious --- and just as we know that responding quickly with adequate resources can spare needless suffering and death following hurricanes and other natural disasters, we who have advocated for Johanna's Law believe that we can similarly spare more American families needless suffering and death by creating and funding a program of gynecologic cancer education.

We know that women, given the right information, will seek appropriate and complete medical attention sooner. Had my sister Johanna known that she possessed risk factors for ovarian cancer --- which she did --- or that she was experiencing common symptoms of the disease, she would have rushed to see her gynecologist and made sure the right diagnostic studies were performed. Every ovarian cancer survivor I've ever met would have done the same had she known that her symptoms could have been related to this deadly disease, which kills more women in the U.S. each year than all other gynecologic cancers combined.

But none of these women ever had the chance to take the actions that might have led to earlier detection and their long-term survival. None of them had the chance because none of them ever got the information about symptoms until after they were diagnosed at a late stage when even aggressive treatment couldn't save most of their lives.

My sister had planned to be around to watch her daughter marry and have children. She looked forward to being a grandmother and to being there to help our aging parents in their later years. And again, my sister was not alone in having such dreams and goals.

And yet my sister and hundreds of thousands of wonderful women in this country have been robbed of all those precious moments. Their families have been robbed of all those memories with them because their loved ones died decades before they should have simply because we lack better tools for earlier detection of this cancer and because they learned about the symptoms of this cancer too late to take advantage of existing diagnostic tools.

This is a national tragedy that has gone on for decades --- but we have a chance right now, this year, to stop it. The thousands of family members and survivors across the country who have contacted their legislators, many for the first time in their lives, have asked them to co-sponsor Johanna's Law in hopes of sparing other American families the terrible nightmare we have all lived through. The program of education we are hoping to create can't spare our families this agony. It can, however,

give us a small measure of healing to know that our loved ones have not suffered or died in vain but that our federal government has heard our pleas --- and responded quickly, compassionately, and appropriately --- to create the national program of gynecologic cancer education this nation has so long needed.

Let it be part of the legacy of the 109th Congress that this Congress created this long overdue program --- and that along with addressing homeland security, natural disasters and other challenges our country faces --- let it also be known that this Congress acted this month, during Gynecologic Cancer Awareness Month, to spare more American families the needless suffering that comes with a late stage diagnosis of ovarian and other gynecologic cancers.

We may not save every life with a program of education, but we can save more than we have been and we can give women a fighting chance to be detected in time for their lives to be saved.

As a compassionate nation known for valuing every one of its citizens, we must do all we can --- as quickly as we can --- to improve early detection. That means that while we wait for research breakthroughs which we desperately need and hope will bring us vaccines and even better tools for early detection and treatment of late stage cancers, while we wait, the one thing we can do now, this month, is create a national program of gynecologic cancer education.

Just last week, we saw how quickly the House moved to provide the funding needed to help the families devastated by Hurricane Katrina. **We know this Congress can move quickly whenever it deems a particular issue or situation a crisis or top priority. I am here today to say that this situation, too, must be considered a top priority, a national tragedy that has gone on for years --- quietly, desperately, in hospices, hospitals and homes.** And even though these tragedies are not seen on our television screens, the agony endured by families impacted by late stage gynecologic cancers is excruciating. There is terror and desperation for every one of us as we helplessly watched those we love run out of medical options and then die.

I apologize if these comments offend anyone who hears or reads them. I am merely trying to express the magnitude of the agony felt by all of us who have supported our courageous loved ones through their battles with ovarian cancer and then helplessly watched them die.

We want to spare the millions of American women at risk for gynecologic cancers --- and their families – this same excruciating agony. The members of the 109th Congress can help us achieve that goal by creating a national program of gynecologic cancer education and awareness. Besides saving lives through early detection, such a program will finally give a measure of peace to millions of grieving family members. It will assure us that our loved ones did not suffer and die in vain but rather, that their stories served as the catalyst for creating America's long overdue --- but urgently needed --- national program of gynecologic cancer awareness and education

I thank the Subcommittee for its patience in listening to the pleas of a grieving sister.

Johanna's Law is named after Johanna Silver Gordon, a dynamic and health conscious woman who died 3 ½ years after being diagnosed at an advanced stage of ovarian cancer.

Mr. CANNON. Thank you.
Ms. Stacey.

STATEMENT OF KOLLEEN STACEY

Ms. STACEY. Good morning Chairman Cannon and committee members. Good morning Mr. Burton, my Congressman. I want to thank you, Mr. Burton, for everything that you have done for me as a survivor. I am very honored to be here to speak to you about something very dear to my heart, Johanna's Law.

Last year I went to an advocacy training meeting and I heard Sheryl Silver speak about her sister Johanna and her motives for Johanna's Law. That speech gave me hope that some day something will be done to make women and health care professionals more aware of the signs and symptoms of gynecological cancers.

Sheryl, I want to thank you for taking the initiative to propose a bill long overdue.

Johanna's story and mine were so much the same that it gave me cold chills. Unfortunately, thousands of other women have the same story, caused in great part by a lack of knowledge of the symptoms of ovarian cancer. The need for education and awareness is crucial. Johanna's Law will provide that campaign that will definitely save lives.

For the last 8 years I have suffered through numerous surgeries, reoccurrences, countless hours of chemotherapy and radiation. Why? Could this suffering have been prevented, or at least lessened?

I learned, after diagnosed, that I had all the symptoms. I wasn't aware that indigestion, heartburn, pressure on the bladder, unusual bleeding were symptoms of ovarian cancer. Nor did I know that a Pap smear didn't screen for ovarian cancer. I visited doctors for each one of those symptoms, but no one put it all together.

It took an entire year for me to be diagnosed correctly. By then the cancer was stage 3C, an advanced stage of ovarian cancer, with only a 38 percent chance of a complete cure. Had it been discovered in an early stage, I would have had a 90 percent chance of complete cure.

Today, 8 years later, nothing has changed. I still meet with women who did not learn about the signs and symptoms until after diagnosed. Together, Congress, we can do this. We can educate people until scientists come up with an early detection test.

I may look good to you today, at least I hope so, however, that hasn't always been the case. Time won't permit me to go into all the details of my experiences over the last 8 years, but let me tell you what I have gone through just this year alone. I had a PET scan last December that showed a tumor in my lymph node in my neck. Surgery was scheduled for January to remove the tumor.

It turned out to be much worse than the doctors expected. On January 7th I woke up with incisions up and down my neck, stapled. I had two drainage tubes coming out, six radiation catheters, all hanging out my neck. I could tell people were frightened to look at me. They were shocked by the way I looked. My friend said, you have a good Frankenstein look going, Kolleen.

Then I saw the fear in my family's eyes and I was immediately scared too. I was then told that my cancer had spread, and the surgeon had to remove two nerve clusters and my juggler vein.

Just 4 weeks after surgery and radiation treatments, a followup PET scan was done. My cancer had spread again. We had no choice but to be aggressive with treatment. I just finished chemo 2 weeks ago. I felt like giving up. This isn't fun.

My family is tired of seeing me with pain. I live with a terrorist every day. I have multiple side effects that will be with me the rest of my life. My quality of life has dramatically changed. I have an equilibrium problem that makes me unable to walk in the dark.

I have numbness in my feet and hands, continuous pain, constant fatigue, and I was forced to go on disability. Being on disability affects my pride. This year, the 8th year, I wanted to give up, but I knew I could not. I have to fight for my family and for other women that are going through this horrible experience. Cancer isn't just a physical condition, but also an emotional roller coaster for me, my family and my friends. I could not have done it without their love and support.

In closing, I would like to leave you with a feeling of hope. As children, we hope to grow up to be big and strong. As adults, we hope to be healthy and live a long, happy life. If we are not healthy, we hope that our experience will help the people around us to make the right decision.

Congress, by passing Johanna's Law, each of you has a chance to make the right decision and give hope back to me, to women, and grieving families that have been victims of this deadly disease. This year, 28,000 women will die from gynecologic cancers.

Thank you.

[The prepared statement of Ms. Stacey follows:]

September 7, 2005 Testimony by Kolleen Stacey

I am very honored to be here today to speak to you about something very dear to my heart...Johanna's Law.

Last year I went to an Advocacy Training Meeting and heard Sheryl Silver speak about her sister Johanna and her motives for Johanna's Law. That speech gave me Hope that someday something will be done to make women and health care professionals more aware of the signs and symptoms of gynecologic cancers.

Sheryl, I want to thank you so much for taking the initiative to propose a bill long overdue. Johanna's story and mine were so much the same that it gave me cold chills. Unfortunately, thousands of other women have the same story...caused in great part ... by a lack of knowledge of the symptoms of Ovarian Cancer. The need for education and awareness is crucial. Johanna's Law will provide a campaign that will definitely save lives.

For the last 8 years I have suffered through numerous surgeries, recurrences and countless hours of chemotherapy and radiation. Why? Could this suffering have been prevented or at least lessened? I learned after diagnosis that I had all the symptoms. I wasn't aware that indigestion, heart burn, pressure on your bladder, unusual bleeding were symptoms of Ovarian Cancer. Nor did I know that a PAP smear test did not screen for Ovarian Cancer. I visited doctors for each of those symptoms, but no one put it all together! It took an entire year before I was diagnosed correctly. By then the cancer was stage 3C, an advanced stage of ovarian cancer with only a 38% chance of complete cure. Had the cancer been discovered in an earlier stage I would have had a 90% chance of complete cure!

Today, eight years later, nothing's changed. I am still meeting women who did not learn about the signs and symptoms until after diagnosis. Together, we can change this.

I may look good to you today...at least I hope so. However, that hasn't always been the case. Time won't permit me to go into great detail of all my experiences over the last eight years. But, let me tell you what I have gone through this year alone. I had a PET scan last December that showed a tumor in a lymph node in my neck. Surgery was scheduled for January to remove the tumor. It turned out to be much worse than the doctors expected. On January 7, I woke up with incisions up and down and across my neck that were stapled together. I also had 2 drainage tubes and 6 radiation catheters hanging out of my neck. I could tell people were frightened and shocked by the way I looked. My friends said "you have a good Frankenstein look going Kolleen." I saw the fear in my family's eyes and I was immediately scared too. I was then told my cancer had spread and the surgeons had to remove two nerve clusters and my jugular vein.

Four weeks after surgery and radiation treatments, a follow-up PET scan was done. My cancer had spread. We had no choice but to be aggressive with treatment. I felt like giving up.

This is not fun! My family is tired of seeing me with pain. I have multiple side effects that will be with me the rest of my life. My quality of life has dramatically changed. I have an equilibrium problem that makes me unable to walk alone unless I have sufficient lighting. I have numbness in my feet and hands; continuous pain; constant fatigue; and I was forced to go on disability. Being on disability affects my pride. This year, the eighth year, I wanted to give up, but I knew I could not. I have to fight for my family and to save other women from going through this horrible experience. Cancer is not just a physical condition but also an emotional roller coaster for me, my family, and my friends. I could not have done it with out their love and support.

In closing, I would like to leave you with a feeling of hope. As children, we hope to grow up to be big and strong. As adults, we hope to be healthy and live a long happy life. If we are not healthy, we hope that our experience will help the people around us to make the right decisions. By passing Johanna's Law, each of you has the chance to make the right decision and give HOPE to me, women, and grieving families who have been victims of these deadly cancers.

This year 28,000 women will die from a gynecologic cancer.

Thank you.

Mr. CANNON. Thank you, Ms. Stacey. It is hard to believe all that by talking about it or hearing about it. Thank you for sharing that with us.

My sense is that we are going to make great progress with Johanna's Law. I am pretty sure the House will pass it. Unfortunately, we had to pass the bankruptcy bill eight times before the Senate got around to it. In this case we may have more. I think there is some kind of prohibition against speaking ill of the other body, so let me just say we have high hopes that they will be reasonable on this issue and move relatively quickly.

I view Johanna's Law as part of a larger context. You were all here and listened to me talking with the people that control the purse strings in America for much of what is going on here and control, to a large degree, the research, so I would like your comments as we go through this on that research.

But, Dr. Karlan, if we could start with you. You are a practitioner. You run a research institute. You are one of those people that is—I think most doctors really view themselves as scientists anyway. But you really straddle both worlds; you treat people and you run a research institute.

Can you comment on what we talked about, what the earlier panel dealt with to some degree, about the role of practitioners, what it would mean to health care generally if we had access to more information from practitioners and their patients as to treatments, and how best practices could be spread and how new ideas could be generated? Is that something you have thought about and would you like to comment on that?

Dr. KARLAN. I clearly thought about it in the last 2 hours during this panel, but I think previously we at times exchange the anecdotal observations that you described so clearly earlier with regards to your daughter's response on the MRI to her Chinese herb. I think sharing those observations are often seminal on the research side of things. One takes that observation and then asks how and why, as well as sharing it with others.

I think that the information system that you described is one that we do colloquially in our communities, we do it through the society at our annual meetings where we talk about our patient experiences or the amazing survival or the things we have seen, and exchange those stories. I think an information database as you described could perhaps allow us to collate those anecdotes, begin to make observations that would have better power by seeing are they consistent or is it anecdotal to that person's immune system or other aspects of her genetic makeup, and then translate that. As a clinician-scientist, I look at those observations and try to understand the molecular biology as to why they occurred.

So, yes, that type of information, where every single patient, and not to at all make patients' experiences and take it out of the human nature, but allow those data points to be captured so we can learn more and more from every single patient's experience, because I do think that is going to be our future. But individualized care, molecularly directed and targeted care, and we are going to need those data, that opportunity to move that forward.

Mr. CANNON. Are you familiar at all with complexity theory or Abasian statistics? That is a mean question, but I don't mean it to be.

Dr. KAPLAN. Not in any great detail, sir.

Mr. CANON. But from your point of view, having dealt with many patients and with clinical studies, you get the sense of how, if you had much data, you could sort that and bring a great deal of decision-enhancing information to bear on any given patient.

Dr. KAPLAN. Absolutely.

Mr. CANNON. Thank you.

Dr. KAPLAN. I think that is what we are all dealing with now with genomics, proteomics, that we have enormous amounts of data, but we need to mine that data so that we find those gold cores, that ore that allows us to see the light, see how the dots are appropriately connected. So we need all those patient——

Mr. CANNON. Exactly. That is exactly it. Thank you.

I wish the prior panel were all here. Thank you for staying with us.

But, yes, thank you, that is exactly the point. And while I suspect all doctors may not be as smart or as attractive as you, almost all doctors actually care about their patients and want to see better processes, better treatment, better devices available for their health.

And in the case of my daughter, by the way, there were like 100 studies, animal studies on the artemisinin that we used that showed pretty dramatic success. But no bridge from those studies to practice. How do you dose a human being? Whether that drug would have worked or not, I don't know. There was some obvious evidence that it was working to some degree, but we are not building at all on that experience for other people who have this or similar diseases, despite the fact that there are some really very powerful, profound studies out there with animals, and yet no opportunity to translate that to others.

Thank you very much, Dr. Karlan.

Dr. Rosenfeld, we have talked somewhat about some of these issues. Do you have other things you wanted to talk about in response to the other panel, or would you rather that I ask you questions?

Dr. ROSENFELD. I am used to questions from you. Ask me a question.

Mr. CANNON. You talked about disruptive technologies in your presentation. And clearly, with the earlier panel, we talked about the effect of the disruptive technologies that have resulted in a much lowered cost of identifying proteins. Can you talk a little bit about what has happened in that field, where we are headed, and what that means for patients in America? Ms. Silver talked about 250,000 mothers and sisters in America. We are talking 20 or 30 times that many people worldwide. So if you would talk a little bit about what progress in America means to the rest of the world, I would appreciate that also.

Dr. ROSENFELD. Sure. Disruptive technology actually has its own definition, it is an innovation that, due to its revolutionary nature, can actually replace an existing or dominant technology. We already know of those things in other contexts. For example, every-

body knows what a CD is. My kid doesn't know what a vinyl record is. So a point made there.

A disruptive technology oftentimes, also, if you read, for example, Clayton Christianson, who has written extensively about that, from the Harvard School of Business——

Mr. CANNON. And a good Utah boy, I might add.

Dr. ROSENFELD. You better believe it. You can tell I am from Utah too.

A disruptive technology oftentimes also does several things. No. 1, it very frequently brings down costs. An example that comes to mind, of course, is the computer industry. You get a lot more bang for the buck today from a computer than the little 8088 that I bought in 1981.

In any case, disruptive technologies are also interesting in the sense that they have odd origins. Oftentimes they don't come from academia. For example, the CD, although it was from an MIT professor, it actually came through a private enterprise route. And the reason is that academic institutions are oftentimes interested or follow down a path which are called evolutionary technologies; that is, you build A to B to C of the same technology. Where a disruptive technology is a revolution.

Now, with that in mind, what is on the horizon, what is actually working now? And please realize that I am very, very interested in health care delivery to rural populations, to developing nation populations. So, from my perspective, I want to see people everywhere get the kind of health care that is only affordable now at some of the big medical centers or the big reference laboratories.

But with regards to, for example, DNA and DNA analyses, right now the current methods used to look at, for example, PCR DNA to look at human papillomavirus in a laboratory, to set up that laboratory would cost you $100,000 for the device alone. Set up the lab and so on, you are in for another $100,000. You have to run it with specially trained personnel, etc., etc., etc.

There is now disruptive technology that will allow that same DNA analysis to be done on a device that would retail probably for a couple hundred dollars, for chemistries that will allow you to do this for a couple pennies per patient. And that is the kind of disruptive technologies I am talking about. These technologies will allow you to do things anywhere.

Mr. CANNON. So the common lab today, a current lab with PCR technology, it costs something like a penny a pair to decode?

Dr. ROSENFELD. Well, it is not a penny a pair, but by the time—I can actually, if you want me to produce this, I can actually give you a spreadsheet; I have this broken down. But to do a patient in a laboratory with all costs right now would probably cost in the neighborhood of tens of dollars to do an analysis: do you have HPV; do you have ovarian cancer. Those kinds of things would cost a lot of money. And what I am talking about is now the technology is in place for doing this for pennies; and away from offices and away from laboratories.

Mr. CANNON. And when you say pennies, you are talking about the whole analysis, not each pair.

Dr. ROSENFELD. Yes, I am talking the whole analysis.

Mr. CANNON. So if you are decoding several pairs, you are talking about a fraction, a very small fraction of a penny per pair.

Dr. ROSENFELD. In fact, there is a meeting tomorrow at Johns Hopkins University in that regard I will be participating in.

Mr. CANNON. So what does that mean for the FDA or for the CDC or for NIH or for the National Cancer Institute in terms of this massively plummeting cost of decoding proteins in comparison with what should be available to Americans and the rest of the world in terms of treatment? What should happen? How should that transformation drive treatment technology?

Dr. ROSENFELD. Well, I mean, it is obvious. If it is disruptive technology that has brought down cost, we should be able to deliver whatever that is to the patient for cheaper. So, for example, if it is to diagnose cervical disease, I should be able to diagnose cervical disease for a couple of dollars instead of tens of dollars.

And, by the same token, if we are talking, though, the FDA, CDC, I don't hold them blameless, but the FDA, with regard to that bureaucracy, they are going to have to start looking at things differently. Things have to be done differently, because I don't think we can afford not only to neglect new technology, but we can't afford to approve technologies the way in which our infrastructure is set up as we speak.

Mr. CANNON. We have three people who have had a daughter or a wife or a sister die of cancer here in the group and a cancer survivor with us, and we are talking about clinical testing and protocols that get set at a high level, when what you are telling me is we have now in place technology that enables a physician at the lowest level to be doing things that could only be done at the most expensive labs on Earth less than a decade ago.

Doesn't that seem to you—in fact, you, in your earlier testimony said something—I made a little note somewhere. You are fairly critical, I think, of the FDA and its reaction, and I suspect that the key here is the historic context of the FDA versus the transformed future of medicine.

Dr. ROSENFELD. It is time for the FDA to change. The world has changed. It is time for them to change. They are operating on a system that is predicated, in my opinion, on the way in which things used to be done prior to the advent of molecular biology. The FDA still has not even adjusted to molecular biology as a term. There is one molecular biology test in the entire planet that is FDA approved, one, with regards to gynecologic cancers.

Mr. CANNON. Wow.

Dr. ROSENFELD. And not only that, the technology for that one HPV—it is an HPV test—is 20-year-old molecular biology technology. There is lots of new stuff, there is lots of good stuff. There is molecular testing that could be done for ovarian as we speak, and it is not in the pipeline.

Mr. CANNON. I want to explore this for a bit. But first I would like to get some bona fides on the table. Would you mind giving us your academic background, what you are doing in China, the committees you are serving on? I know that is a long list, but you don't have to do it all, just some of the high points.

Dr. ROSENFELD. OK, if I talk about China, remember I am a loyal American.

I have graduate degrees from both the University of Utah and the University of British Columbia. I am a molecular biologist, also a geneticist. I am former faculty at the University of Utah School of Medicine. Our department used to be called the Cellular, Viral, and Molecular Biology Department.

I went into private enterprise actually because I feel very strongly about the direction that I feel medicine needs to take, and have been involved with innovative technologies as a consequence. I have been involved predominantly with gynecologic cancers and, in particular, cervical cancer, and I hold one distinction, and that is that I actually sit on the China State Council on Medical Reform. I am the only American.

And I am very proud of that because China has made great strides with regards to reforming their medical system. They want a system that really works for people, and that is something that I think is, from my perspective, I am apolitical on that; if they want to do it, I am willing to help. And just because it is fun, I also breed giant pandas when I am in China. I am in charge of giant panda reproduction at Peking University.

That is my background on reproduction endocrinology.

Mr. CANNON. Do you also work with the Mandalay? Do you also work with the pandas——

Dr. ROSENFELD. Oh, the Mandalay Bay fiasco? Yes.

Mr. CANNON. I didn't know it was a fiasco. That is because of the trust that the Chinese have in your judgment.

Dr. ROSENFELD. Yes. I am also the English version—if you go on the net, the English version of the China 5 year cancer policy, I am actually the author.

Mr. CANNON. So you spend a lot of time in China. Why?

Dr. ROSENFELD. What?

Mr. CANNON. You spend a lot of time in China working on cervical cancer. Is there a reason for that?

Dr. ROSENFELD. Cervical cancer in particular, because China is probably the epicenter for cervical cancer. Last year, for example, over 90,000 died of cervical cancer. And I have been on wards where I have seen, on a given afternoon, as many as 70 women with terminal invasive cervical disease. So China is a place that is necessary if one is to get a handle on gynecologic cancers, in particular cervical.

The other reason is that I really do have a true commitment to taking technology and introducing it into rural and developing regions, and working with the Chinese has been good from that perspective. So, for example, I am down in Guangxi Province, which is a remote area of China, and looking at whether or not we can indeed deliver such things as molecular biology services in the middle of nowhere.

However, the spillover, I think, is great, and that is this, that the commitment is that this be provided also here. So, for example, when we heard discussions earlier today about the need for Black populations to be able to achieve pervasive early detection screening, I believe that can only be achieved if we change the diagnostic paradigm, and that is the kind of technologies that I work with.

Mr. CANNON. I know the Chinese Cancer Institute is among the highest quality in the world, with highly trained people, and they

are not compromising that at all. But China has a problem: they don't have the wealth that America has, so they can't do things the way America does them and still reach people in China, which is really Johanna's Law. How do we do things in America? Well, we are going to spend a lot of money on it.

Dr. ROSENFELD. That is a plus.

Mr. CANNON. But the Chinese are different. Would you talk about that, why that is a plus?

Dr. ROSENFELD. It is a plus because we are spoiled and they are not. And the plus is this: again, I said it earlier, and that was 2.9 million people, we spend $75 million, $60,000 per cancer. We are willing to spend that kind of money. We throw money left and right in health care. That has been a problem here. We throw money out for research, but where is the accountability in the end?

There is a wonderful article that I actually photocopied and put in, called "Why We Are Losing the War on Cancer and How to Win It." Read that. That is what is wrong with cancer in the United States, and that is why the Chinese don't have that problem. You know, they are very practical-minded. How did they deliver the most to a country that is three or four times the size of our country, and for little money?

Mr. CANNON. It seems to me there are probably three disruptive technologies or things that have happened in America.

And, Dr. Karlan, I would appreciate your comments on this as well.

In the first place, you are talking about DNA decoding, that technology and how that has plummeted in price. That is dramatic. I don't know how you can state how dramatic it is, because everything that derives from it is unanticipated. You never thought in terms of looking for a genetic marker for a disease when the cost was tens of thousands of dollars. But now, if you are talking about pennies, it means a different kind of thing; it is a whole new mindset.

In the second place we have what I call the Napster phenomenon, that is, I am a big fan of Napster, I wanted them to have a model where people paid. We don't want them to rob music. They wanted a model where they paid. But that kind of peer-to-peer technology is disruptive, I think it is fair to say. And when you add that to the other kinds of database technologies we have, the informatics approach, where you organize information, as opposed to the peer-to-peer work, where information organizes itself, it seems to me you have another two kinds of transformations.

And then the third kind of thing that is happening is that as people are aware of these transformations, wholly new ways of viewing medical problems are arising. And those are principally coming, I think, from medical practitioners, but they are also coming from a lot of other folks, because as nutritionists, as dieticians, as people that like nutritional supplements, as drug companies look at off-label uses, you are getting this incredible increase.

So you take a drug that you know the toxicity of, that may be very effective for one thing, and you say what are the molecules. And, of course, we can tell what those molecules are better now because of these other technologies. Then you can look at what the chain of reactions is within a body and do some significant predict-

ing. In other words, as a derivative of these other things, you have this massive number of people who are empowered then to do creative things.

Is it important to the two of you in particular that we create a data context for that to happen? And if you are aware enough of the difference between a database like the informatics database that has been testified about earlier and a peer-to-peer database, I would like your comments on that. And what else can we do to help this tide or this dam that has broken and now is flooding down, what else can we do to help that be channeled and effective for improving treatments for people?

Let us start with Dr. Karlan, if you would, and then Dr. Rosenfeld.

Dr. KARLAN. Thank you, Mr. Chairman. I think you have eloquently outlined the breakthroughs, the shifts in paradigm that have resulted from the human genome project, and then the advances in informatics that allow us to look at gigabytes of data and suddenly see the tree and get through it and see the next steps forward.

Johanna's Law, though, processes and tries to take the disconnect between our breakthroughs in the laboratory and what we see on the corner. Shoppers, come in and get your Pap smears now. How do we bring these advances to all of our kitchen tables before we get cancer? When you get cancer, then you start logging on, you do extensive searches.

Mr. CANNON. Almost everybody in America uses Google. And to the degree you can make information available—and there are many forms of that—then you have the ability for people to educate themselves, so you don't have to suffer with four or five different symptoms, you go to four or five different doctors, and way too late you find out that you have one problem that is causing them all.

Dr. KARLAN. But I think Mr. Burton hit on it earlier. When you start to have the symptoms, when you start to have the problems, when you begin to ask those questions, then you go to Google.

Mr. CANNON. Right. Exactly.

Dr. KARLAN. But how do you process that information? How do women——

Mr. CANNON. Let me make a suggestion. I understand what you are saying, and I want Johanna's Law to pass. But I want some other transformations in the medical system, which I would like your opinion on, because I believe, to your point now, to the degree that people understand that there are transformations in medicine, then they will look. Mr. Burton laid it out very well: The problem is how do you look in the right place and know what you are actually looking for? But the transformations that derive, that is, as you see from a database, from other sources, new treatments and new opportunities, then people say, "What are my symptoms?" And they will go back.

So I think it is actually an iterative process. In other words, I am not just ignoring Johanna's Law here. I am saying, how do we make it all come together in a system?

Go ahead.

Dr. KARLAN. No. Again, as we get these new technologies, a better basic understanding, if you would allow me, why some people

live and others do not survive their cancer, and we communicate better that cancer is not a death sentence, we will then also open up that door.

And I will digress, if you allow me, one moment. We did an outreach project in Los Angeles, in the inner city church system, where the pastor was very much in support of Pap smears, and we did see and treat; get your Pap before mass, go to mass, come out, have your treatment. And we published those data about the findings of Pap smears. It was predominantly a Latina population.

Afterwards, the pastor was very interested in the women who did not participate; came to church every single Sunday, but did not partake in this problem. We did these focus groups in Spanish with social workers, not with the physicians themselves. And there was this pervasive fear of a passive coping mechanism of why do I want to find out if I have cancer? Cancer is a death sentence.

So to your point again, informatics, genomics, targeted therapies, when we can better use Johanna's Law to communicate cancer is a curable disease—the article that you referred to. When we look at heart disease as the paradigm, where have we been able to see the death rate from heart disease plummet? It is because we have educated people so effectively about lowering your cholesterol, taking your aspirin, exercising, watching your weight, watching your diet.

We need to do something similar for cancer; understand what we need to do to prevent it. And the way we are going to get that information, the way we are going to be able to roll out the molecular tests that are being developed is by integrating all these data effectively and seeing how to move forward.

Mr. CANNON. And you struck me with what you said earlier. You talked about gigabytes of data. In other words, you are talking about big, big, big numbers or data points that you are crunching to identify this, which means you really have to have another paradigm shift, which is a paradigm toward complexity and toward the kind of computing that is now so cheap, that will allow you to sort the massive number of data points and come up with indicators of where we should go.

Dr. KARLAN. Yes. And thank goodness our computational colleague scientists, who understand Abasian theory much better than I myself, can put together these four-dimensional type of networks that allow us to look at those massive volumes of data.

Mr. CANNON. We are actually looking now, as we speak, at trying to get funded a complexity center in Utah, which is not just my home State, but a place where a lot of this activity is going on. So I am going to take that comment as in support of a massive computer that would be shared by University of Utah's Medical Center and various other places around the country.

We have talked a lot, but, Dr. Rosenfeld, do you want to followup and comment on those things?

Dr. ROSENFELD. Yes. I actually have a couple comments. No. 1, technologies are in place now, for example, for a lot of gynecologic cancers, that you could, on your way into the mall, literally have your finger pricked and an analysis instantly done. And from that analysis you could find out such things as ovarian status; you could find out such things as your Pap status, that is, whether or not you

have not only HPV, but whether or not that has progressed to cervical dysplasia.

Now, that goes to what Dr. Karlan was saying, and that is why some of these people who went to church did not participate. I contend a lot of them do not want to participate because a gynecologic examination, whether you like it or not, means you have to get up in stirrups, and it is very uncomfortable or discomforting for patients. And there is some good information on that.

So if we are able to diagnose new ways, and not only new ways in terms of the technique, but new ways in the sense that you don't have to at least initially go for a gynecologic exam, then I think that we are going to be able to obtain much broader reach of people and get disease at its earliest stages.

I will say one last thing, and that is that we can get—and we have done this already—we can get as little as one molecule and find that one molecule, which means that we can find disease in perhaps its earliest state. And if we find it in its earliest state, it is the easiest to treat.

Mr. CANNON. Thank you.

Mr. Burton, would you like——

Mr. BURTON. Yes, Mr. Chairman.

Mr. CANNON. The gentleman from Indiana is recognized for 5 minutes.

Mr. BURTON. I am sorry, I have to leave in just a few minutes. So I appreciate you yielding to me, Mr. Chairman.

First of all, I was reading part of this article that you referred to, "Why We Are Losing The War on Cancer and How To Win It." And I promise you I will read it all. But I wasn't aware that in 2004 cancer will claim or did claim some 563,700 people. That is an amazing figure to me.

I am glad Dr. Trimble is still here. Are you awake, doctor? Your eyes are closed. I just want to make sure you are still with us.

The President signed a proclamation on August 29th making this month National Ovarian Cancer Awareness Month, and he said because the early signs of ovarian cancer are easy to miss and often resemble the signs of other conditions, it is important for women to talk with their doctors about detection and be aware of the risk factors and symptoms of this cancer. That is true of so many cancers, not just ovarian cancer.

And I would like to go back to what I said to you, doctor, a while ago, and I am really glad you are still here. You know, it is one thing to come up with technical advances that will help in the war against cancers of various types. It is another thing for people to know about them. There has to be some balance between the technology advances and the research that is taking place, and the people knowing what in the world to do.

It really bothers me from a personal standpoint—and, you know, as I said, three members of the panel have had people die from cancer, and we have people out here who have suffered from cancer or had loved ones die from cancer, and they simply didn't know the signs.

There should be a significant part of the budget—we give our health institutions billions and billions of dollars every single year for research. That research amounts to nothing if the people who

are affected by cancer don't know that it works and don't know how to utilize it. And you say you don't have money in there for public service announcements and that sort of thing. That is nonsense.

I mean, if you could find that 90 percent of the people are going to survive more than 5 years if they know how to deal with their cancer and you don't tell them about it, that is almost criminal. In fact, I think it is criminal. Why are we spending these billions and billions and billions of dollars, and people like my wife or these other people we are talking about, aren't even aware of what they can do to protect themselves, or their doctor? Her doctor misdiagnosed her, for God's sake.

I should have sued her for malpractice, but when you are in politics, you can't do that because it is all over the papers you are trying to take advantage of somebody. So we didn't do that. But my wife died. And everybody I have talked to said had she been aware of her early signs, she would be alive probably today, 3 years later.

I just have to tell you—and I hope you will take this message back, because I was looking at your background here. You are the Head of the Surgery Section, Division of Cancer Treatment and Diagnosis at the National Cancer Institute. For God's sake, go back and tell them to spend some money on advertising and telling people what the hell is going on.

[Applause.]

Mr. BURTON. That is what Johanna's Law is all about, and that is why I am glad we are having this hearing today. And I wish there were a lot more Members of Congress here. But to do all this research and spend all these billions and billions of dollars—I don't want to beat a dead horse—and to not have public service announcements so people know that bloating and constipation, bleeding, and different kinds of things are signs of some form of cancer so they can go get checked out, it just boggles my mind.

You know, there just has to be some balance there. So we have talked about, just a minute ago, maybe introducing a resolution, a congressional resolution saying that the National Institutes of Health and National Cancer Institute should spend a certain percentage of their budget on advertising so people are aware of the various kinds of cancer they may be subject to.

[Applause.]

Mr. BURTON. And I think we will probably introduce that legislation, but it is unnecessary, because all you guys have to do over there is say, hey, look, we have to make sure the public is informed.

And I want to tell you, in my district right now we did some public service announcements this week about the hurricane, and every television station was very anxious to put on public service announcements informing people what was available to them to help them survive. And with 563,000 people dying in 1 year from cancer, you would think we would spend part of our budget telling them what it is all about, especially since we are doing all this research.

Anyhow, that is all I have to say, Mr. Chairman, except I do want to say one thing that is a little bit humorous. Your curriculum vitae, Doctor, is very impressive, but it is nothing compared to the woman sitting right next to you. She has got 33 pages, and

that is only since 1999. I am so impressed with you. Are you married?

Dr. KARLAN. Twenty-five years.

Mr. BURTON. I am just teasing. You tell your husband he is very lucky to have such an intelligent woman at his side. I understand he is a psychologist, too.

But let me just say, Mr. Chairman, I really appreciate your giving me the time to do this. And I hope that the people at our health agencies and the National Cancer Institute will take this to heart. Spend some money on telling people. And if you do public service announcements, just get them produced. Get an ad agency to produce them. I promise you, you get them to me in Indiana, they will be shown. I will get them shown. You just get them produced. Thank you.

Mr. CANNON. The gentleman yields back. Thank you for your comments.

Mr. Issa, did you have questions?

Mr. ISSA. Yes, Mr. Chairman.

Mr. CANNON. The gentleman is recognized for 5 minutes.

Mr. ISSA. Thank you, Mr. Chairman.

Dr. Rosenfeld, you talked about the pin prick blood test. How much is that per each examination?

Dr. ROSENFELD. Right now, the pin prick, just so you understand what it is, Congressman Cannon had referred earlier to an immune or protein test for cervical disease, and we have one actually working now. Our actual cost of doing it at the moment—realize that we haven't gone through the FDA hurdle. And, by the way, it is $802 million, on average, for a drug or tests, not three-quarters of a billion. So it is even higher.

Mr. ISSA. I have been in Congress for 5 years, so that is about how far out of date I am on all my facts.

Dr. ROSENFELD. Oh. But, anyway, it is costing us 14 cents.

Mr. ISSA. What is it going to cost the patient if it becomes FDA approved?

Dr. ROSENFELD. Well, in our discussions we are hoping a couple bucks, literally. Again, realize that everything I do centers around low resource settings, so that my eye is on the economy.

Mr. ISSA. I appreciate that. That sounds very promising, and we look forward to—it is too bad we lost our FDA guy. We really could have put him on the spot on that one.

Dr. Karlan, California is sort of the starting home of HMOs, and health maintenance organizations were designed to do things early, provide care early in order to spend less money, and the theory was that you actually got less expensive health care by doing certain things early.

How do you accomplish that in the—let me back up a little. In order to accomplish that, which is a truism, I think, that we all understand from the last couple of hours here, in gynecological cancer, how can we take the dollars that we are authorizing in this bill and leverage those in public-private partnerships to get that effect?

Dr. KARLAN. As you said, we have a lot of experience with the prepaid health care system in California, and I go back to Mr. Burton's impassioned words a few moments ago: we need to get the

message out there. There was a recent study published a few months ago in the Journal of the National Cancer Institute looking within the Kaiser system.

They looked at specifically cervix cancer, and they looked at women in the Kaiser system who had access to paid health care, and if they had Pap smears in the 4 to 12 months prior to the diagnosis of cervix cancer. About two-thirds of them had been in the system. Eighty percent of them had actually come in for an outpatient visit three times or more and did not get a Pap smear.

So I guess my comment about public service announcements, getting the information out there, new technologies is what they call inreach. Instead of outreach, inreach assessment. When you come in for your vision care—because you look at where gynecologic cancers hit in women, let us say, in the perimenopause, menopause, and older, and you say what types of needs are those women accessing the health care for, and remind them to get a Pap smear. At Kaiser it is almost a four vital sign. When you go in to get your prescription checked, they will ask you, "Here is information about gynecologic care, have you had your Pap smear?"

There has to be this access, this education of both the women as well as health care providers. I think we have heard over and over again ob-gyns are more likely to think about gynecologic cancers, but so many women, especially after they finish childbearing, their primary care physicians are not their obstetrician-gynecologist, and they may go misdiagnosed for months to years.

There was recently a study published out of California looking at the Medicare records, and those women who were diagnosed with ovarian cancer—and they looked at their doctor visits in the 4 to 12 months prior to the diagnosis of ovarian cancer, and 40 percent of them went to the doctor. Forty percent of women with ovarian cancer went to the doctor 4 to 12 months before their diagnosis with a complaint of one of the main symptoms, bloating, abdominal, low back pain, or constipation, and never had it worked up. So that is an enormous impact we can make right there.

Lower cost. If you make an early diagnosis, costs a lot less to cure someone with stage 1 disease. And then not only the financial cost, the human cost: they live a full life, they are cured of their disease.

Kolleen was very brave today both to come here and to take the time to share with us her story. If she was diagnosed at stage one, it would have been 8 years ago, she would have been cured.

So I think that is an enormous way to lower cost: find them early; we don't have to pay for the lengthy treatments. And for that we do need continued research, continued focus on newer technologies.

Mr. ISSA. Mr. Chairman, I will put most of the rest of my questions in for the witnesses to answer, but could I ask just one more on the record?

Mr. CANNON. Certainly.

Mr. ISSA. Thank you, Mr. Chairman.

Dr. Karlan, you and I, as Californians, but you as a health care professional, have been in California during this entire period after we mandated a woman's right to get to an Ob-Gyn directly. Can you give me—because even though it is not in this law, but it is

an area of concern—how much has it accomplished? It was very controversial at the time.

General practitioners, among others, said, "Hey, we can handle this, we can handle the referral; we can prescreen." And, of course, the HMO—which used to be a nice word and now is pejorative normally—fought it, but it became law. How has that impacted in California, for the benefit of those who may be in States that don't have this?

Dr. KARLAN. The legislation that Mr. Issa is referring to, of course, is that every woman in the State of California has the right to see her obstetrician-gynecologist as her primary health care provider. And I will have to go back and look at actual numbers, because I don't know how it has enhanced the use of mammography screening, Pap smear screening, and early detection, because those would be the benchmarks that I would look at. We know that obstetrician-gynecologists are more cognizant of those screening practices.

I think when we look at the roll-out of Johanna's Law and making sure that we get the right information into women's hands before they have symptoms, I think that opportunity in California, that when you come in for your prenatal care there is information already out there, that while you are sitting there waiting in doctors' offices it is inevitable, that these are things, and whether it is a PSA loop, I mean, there are many ways people learn, whether it is visually, auditory, or the written word that we can use that opportunity by working with the American College of Ob-Gyn, the Society of Gynecologic Oncologists and its foundation, the Gynecologic Cancer Foundation can help put together the messaging that would be the ability to be accessed.

But I don't have actual benchmark numbers, to answer the question, at this time, but I will look into getting that for you.

Mr. CANNON. Thank you. The gentleman yields back.

Let me just wrap up, and after I go through a list of things, if any of the panel members want to comment, I would appreciate that.

It seems to me that we have come to the conclusion that there are some disruptive technologies. I have described them as protein decoding, cost declining dramatically, and as databases with the capability of making information available in either the structured form like the informatics kind of database or the peer-to-peer kinds of databases. And then, finally, those two things lead us to a point where scientists and MDs and other people can be freed to be innovators because they have more information available to innovate.

We have other things going on in the world today that I think are important as it relates. For instance, we have the availability of information. NIH just withdrew a rule that would require federally funded research to be available publicly. I suspect what we need to do there is—and the reason they did that is because the publishers of those journals had to pay the cost of preparation.

So what we probably need to do is increase the Federal funding for research to include the cost of publication so those publications can be made available. And then hopefully a Napster type micropayment system could be set up so that they can make money on

selling their information and people in America and worldwide have the ability to access that information.

In addition, we need a kind of patient information environment where a patient can make—and this is what the CDC is working on, and Secretary Leavitt at HHS—his information available, subject to certain rules, to certain types of people, M.D.s and scientists, so that it is a controlled environment. That is just a technological breakthrough that we need and we need to put in place. In fact, I mentioned there is a company in Utah that is doing that called NexLight.

I think, in addition to that, Dr. Karlan, you were talking about the gigabytes. You need the kind of computers to drive the issue so that you can come up to, even in the cases of an individual who may have a problem, to go through gigabytes of data to come up with the data points that may help him is well within our reach. The cost of supercomputing has plummeted, but we need to probably focus on a center for complexity studies that would provide that kind of availability.

Finally, we need public awareness so that people can identify their problems and then, in my view, in addition to that, drill down themselves to find out the kind of information that would be available in this world where we make information available so that an individual can find more and more about his or her particular problems.

And in that world of changes that have happened around us or that need to happen, it seems to me that the FDA needs to come up with new processes to accommodate how we do that. That means physicians need to have the ability to treat patients with best practices that they learn online; they need to be able to innovate and come up with, based upon their own analysis and based upon a context rich in information and rich in analysis, they need to be able to come up with their own innovations; and they have to be able to do that relatively quickly so that their individual patients can be treated as opposed to creating protocols and tests that were fine in an earlier time.

Because when you have an $800,000 to $1 million cost for a new drug, that means you have massive interests who all have a huge reason to keep the threshold high and to keep alternatives that may be cheaper, that may be more readily available, that may be innovated by a doctor with access to information. You want to keep those people out, you want to keep the thresholds up. And what that means is worse health for Americans, worse health for people all over the world, a stifling of creativity instead of an improved safety. And safety was the purpose of the FDA at a time when we were doing a lot of guessing.

And I think, Dr. Karlan, you were talking about following the chain of reactions that a protein causes. We know a lot about those chains, and in a complex environment where we have lots of information, we can have much better guessing. So the nature of what FDA does has to change. The nature of what the National Cancer Institute does has to change. The nature of what NIH does and the CDC does all have to change to accommodate these disruptive technologies.

I want to thank you all for being here. The suffering caused by cancer is phenomenal and personal, and I appreciate the roles that you all have played in this hearing today and in the cause of transforming our system so that we get the kind of treatments we deserve in America. Thank you all for being here.

The committee is now adjourned.

[Whereupon, at 2:10 p.m., the subcommittee was adjourned.]

[Additional information submitted for the hearing record follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

The Honorable Mark E. Souder
Chairman
Subcommittee on Criminal Justice,
Drug Policy and Human Resources
Committee on Government Reform
House of Representatives
Washington, D.C. 20515-6143

SEP 16 2005

Dear Mr. Chairman:

On September 7, 2005, Dr. Richard Pazdur, Director of the Office of Oncology Drug Products, Office of New Drugs, in the Food and Drug Administration's (FDA or the Agency) Center for Drug Evaluation and Research, testified at your subcommittee's hearing, "Women and Cancer-Where Are We in Prevention, Early Detection and Treatment of Gynecologic Cancers." At the hearing, you asked that FDA respond on the record to questions submitted by your staff by facsimile dated August 30, 2005. Below we have reproduced the questions followed by our response.

Question 1. Is there an effective vaccine available to prevent HPV infection or cervical cancer?

Response. FDA's Center for Biologics Evaluation and Research (CBER) currently is working with manufacturers to bring preventive vaccines to market to prevent cervical cancer. A vaccine to prevent cervical cancer is of great interest to both developing and developed countries. CBER convened an FDA Vaccines and Related Biological Products Advisory Committee meeting in November 2001 on endpoints for human papilloma virus (HPV) vaccine efficacy trials. CBER staff also have presented at World Health Organization meetings on HPV vaccine development, where the focus was cervical cancer-related indications.

There are several investigational new drug (IND) applications for prevention of HPV-related diseases. FDA cannot release information about products in the pre-approval process unless that information otherwise has been made public. The following information, however, has been made public. Two vaccines for prevention of HPV-related diseases are in Phase III clinical development. These two preventive vaccines are the Merck quadrivalent HPV vaccine (HPV Types 16, 18, 6, 11) and the GlaxoSmithKline (GSK) bivalent HPV vaccine (HPV Types 16, 18).

For further information, we suggest you contact these companies directly at:

GlaxoSmithKline
5 Moore Ddrive
Research Triangle Park, NC 277009
Phone: 1-888-825-5249

Merck & Co., Inc.
One Merck Drive
Post Office Box 100
Whitehouse Station, NJ 08880-0100
Phone: 908-423-1000

In addition, treatment of cervical cancer also is a very active field for clinical research. Several novel technologies currently are being applied for the treatment of this disease. CBER has a number of INDs under review for treatment of cervical cancer/dysplasia.

Question 2. Is there a "microbicide" available that can effectively prevent transmission of HPV?

Response. There are no prescriptions or OTC microbicides approved for prevention of HPV, HIV/AIDS, or other sexually transmitted diseases (STDs).

Question 3. Do condoms provide complete protection against HPV infection?

Response. FDA believes that condoms provide partial protection against acquisition of HPV infection based on recent HPV prevention studies and laboratory studies showing that latex condoms are a barrier to HPV. Although condoms provide only partial protection against HPV infection, there is ample scientific evidence that condom use is associated with a reduced risk of two important consequences of HPV infection, genital warts, and cervical cancer.

Question 4. The Centers for Disease Control and Prevention, National Institutes of Health and the American Cancer Society have all concluded that condoms do not provide effective protection against HPV infection. Does the FDA agree with this scientific consensus?

Response. None of those organizations has reached the definitive conclusion you suggest. For instance, the report from the 2000 workshop sponsored by the National Institutes of Health (NIH) states:

> For HPV, the Panel concluded that there was no epidemiologic evidence that condom use reduced the risk of HPV infection, but study results did suggest that condom use might afford some protection in reducing the risk of HPV-associated diseases, including warts in men and cervical neoplasia in women.

The NIH report also states that:

> The Panel stressed that the absence of definitive conclusions reflected inadequacies of the evidence available and should not be interpreted as proof of the adequacy or inadequacy of the condom to reduce the risk of STDs other than HIV transmission in men and women and gonorrhea in men. To definitely answer the remaining questions about condom effectiveness for preventing STD infections will require well-designed and ethically sound clinical studies.

In its 2004 Report to Congress, CDC states that "... the cumulative body of available scientific evidence suggests that condoms may provide some protection in preventing transmission of HPV infections but that protection is partial at best. The available scientific evidence is not sufficient to recommend condoms as a primary prevention strategy for the prevention of genital HPV infection. There is evidence that indicates that use of condoms may reduce the risk of cervical cancer." (pp 15-16).

Similarly, in a March 9, 2004, letter to FDA, the American Cancer Society (ACS) clarified misrepresentations regarding its position on condom effectiveness against HPV. Currently, the ACS website acknowledges that studies have not determined conclusively whether condom use may provide limited protection against HPV infection and indicates that while recent studies indicate that condoms do not provide complete protection against HPV infection, some studies have found that condom users are less likely to develop cervical cancer and precancerous cervical changes. (See *http://www.cancer.org/docroot/PED/content/PED_2_3X_Pap_Test.asp*, visited 9/14/05).

FDA's view on this question is explained in our responses to question 3 and 11.

> **Question 5. The FDA testimony for today states, "scientific studies on STDs characterized by genital ulcers, e.g., genital herpes and syphilis, are <u>inconclusive</u> as to whether the risks of these diseases is lowered for condom users." But then the FDA testimony states that "our current guidance recommends that the package insert for condoms contain the following statement: If used properly, latex condoms <u>will</u> help to reduce the risk of transmission of HIV infection (AIDS) and many other sexually transmitted diseases, including chlamydia infections, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis." Does that FDA guidance for condom labeling contradict the FDA's scientific studies?**

Response. We believe your question refers to the testimony given by Dr. Daniel Schultz of FDA's Center for Devices and Radiological Health (CDRH) in March 2004. Dr. Schultz testified that while scientific studies on STDs characterized by genital ulcers, e.g., genital herpes and syphilis, are inconclusive as to whether the risks of these diseases is lowered for condom users, our knowledge about the transmission vector for these diseases causes us to believe that the condom will provide some measure of protection when it covers the ulcer. As discussed in response to Question 6 below, FDA has developed a draft guidance document and proposed rule

that will offer new labeling recommendations for condoms to provide condom users with more information about the protection they should expect from condom use. This proposed guidance would replace the one referenced in your question.

Question 6. Public Law 106-554 directs the FDA to "reexamine existing condoms labels... to determine whether the labels are medically accurate regarding the overall effectiveness or lack of effectiveness in preventing sexually transmitted diseases, including HPV." As we have heard here today, the scientific consensus has concluded condoms do not provide effective protection against the transmission of HPV. When will the FDA require condom labels to reflect this lack of effectiveness against HPV infection, as required by law?

Response. P.L. 106-554 tasked FDA with examining condom labeling regarding the overall effectiveness or lack of effectiveness of condoms in preventing the transmission of STDs. Upon enactment, FDA immediately began developing an implementation plan to fulfill our obligations to evaluate comprehensively condom effectiveness in regard to all STDs, as directed by the public law (not just HPV). In the four years that elapsed since then, the Agency carried out this plan, which included:

- a survey of the current labeling on marketed condoms;
- a review of the Agency's current labeling guidance as well as policies that led up to it;
- a comprehensive and systematic review of the published literature (several hundred studies) and other clinical considerations;
- the summary report from the interagency (NIH, CDC, etc) workshop that was issued in 2001 and participation in a 2002 workshop;
- analysis of the possible effect new findings, regarding the risks of HIV transmission associated with use of nonoxynol-9 (N-9), would have on condoms with N-9;
- review and analysis of CDC's January 2004 Report to Congress: Genital HPV Infection;
- developing the regulatory method (draft guidance and proposed rule) to address changes to condom labels; and
- crafting a clear message to consumers regarding condom effectiveness for all STDs that would fit within the small confines of the condom label.

The draft guidance and proposed rule documents currently are under review at Office of Management and Budget.

Question 7. According to the American Cancer Society, "there is evidence that long-term oral contraceptive (OC) use increases the risk of cancer of the cervix. Some research suggests a relationship between using OCs for 5 or more years and an increase in the risk of cervical cancer. In one study the risk was increased four fold in women who used OCs longer than 10 years." Can you comment on this?

Response. What we know for certain is that the most important risk factor for the development of invasive cancer of the cervix is onset of sexual intercourse during puberty, when cervical metaplasia accelerates. We do not have definitive evidence that oral contraceptives increase the risk.

Question 8. CDC and others have mentioned that "microbicides" may offer protection against HPV and other STDs. What microbicides currently are available? Please explain the effectiveness of existing microbicides in protecting against HPV, HIV/AIDS and other STDs?

Response. There are no prescriptions or OTC microbicides approved for prevention of HPV, HIV/AIDS, or other STDs.

Question 9. Prostate cancer kills more than 30,000 American men every year. The company, Dendreon, has developed a prostate cancer "vaccine" called Provenge that stimulates the body's own immune system to fight the disease. The product is clearly safe and effective, and there are currently no other options for patients who fail to respond to standard chemotherapy. Yet due to FDA red tape, Dendreon can't even consider filing for approval of this product until 2005. Can you explain why this life saving medication is being held up from reaching patients?

Response. It is the responsibility of the manufacturer and/or developer to investigate a drug product and develop data from laboratory testing and clinical studies that are necessary to support an application for marketing the product. FDA is responsible for reviewing those data that are submitted in support of a product license, and determining whether they are adequate for granting approval for interstate sale. Applications are reviewed by the Agency for safety and effectiveness in as expeditious a manner as possible. FDA works with sponsors to allow the availability of promising new therapies to patients with life-threatening diseases, while following regulations to assure the safety of patients being treated with the investigative products. We respectfully must disagree with your characterization of those regulations as "FDA red tape." In addition, we respectfully must correct your statement that Provenge is "clearly safe and effective." Section 351 of the Public Health Service Act (42 United States Code 262) sets forth the standards for licensing a biological product. Until a manufacturer receives a biologics license from FDA based on the demonstration required by statute and regulation, it is not accurate to label that product "safe and effective."

The following information about Provenge is public, as Dendreon Corporation (the Company) has placed this information on its website. In its July 21, 2005, News Release, the Company indicated that a further analysis of survival data from a Phase III clinical study (D9902A) and a supplemental analysis that examined pooled survival data from two companion Phase III clinical studies (D9901 and D9902A) using Provenge to treat advanced prostate cancer is ongoing and will be submitted for presentation at an upcoming medical meeting. Provenge is being further evaluated in an ongoing Phase III study in asymptomatic, metastatic, androgen-independent prostate cancer (D9902B). It also is being evaluated in a Phase III trial, known as PROTECT or P-11, in men with early stage prostate cancer. Regarding the latter trial, Mitchell H. Gold, M.D., Dendreon's president and chief executive officer, is quoted in the Company's

June 21, 2005, News Release, "We anticipate that we will be able to complete the analysis of the trial and provide initial results during the first half of 2006." For further information, we suggest you contact the Company directly at: 3005 First Avenue, Seattle, Washington 98121; Phone: 206-256-4545-Ext-1500 Fax: 206.256.0571; e-mail: *ir@dendreon.com* *<mailto:ir@dendreon.com>*.

Please be assured that FDA continues to work with all sponsors of promising therapies for cancer and other life-threatening diseases to resolve issues so that patients can avail themselves of novel therapies. The Agency understands that nothing is more important than giving patients and their doctors new ways to fight serious and life-threatening illnesses and will continue to make review of products for serious and life-threatening diseases one of the Agency's top priorities.

Question 10. FDA requires products to undergo clinical trials to demonstrate safety and effectiveness for their intended purpose(s)? Have condoms ever undergone clinical trials for effectiveness in preventing the transmission of sexually transmitted diseases?

Response. Condoms were marketed in the U.S. for both contraceptive and prophylactic (prevention of transmission of STD) use prior to enactment of the Medical Device Amendments of 1976 (Public Law 94-295). Like all other pre-amendments devices, condoms were classified under the Federal Food, Drug, and Cosmetic Act after consideration by an expert panel of the information available at the time about their safety and effectiveness. Subsequently, the effectiveness of condoms in preventing STD transmission has been evaluated further both in laboratory (viral penetration assay studies) and in numerous clinical studies. These clinical studies have been reviewed by NIH (June 2000 Workshop "Scientific Evidence on Condom Effectiveness for Sexually Transmitted Disease (STD) Prevention"), Centers for Disease Control and Prevention (CDC) (Report to Congress "Prevention of Genital Human Papillomavirus Infection") and by FDA as part of proposed amendments to classification regulations for condoms (currently pending publication in the *Federal Register*).

Question 11. A meta-analysis of "the best available data describing the relationship between condoms HPV-related conditions" was published in the journal Sexually Transmitted Diseases in November 2002. This study found: "There was no consistent evidence of a protective effect of condom use on HPV DNA detection, and in some studies, condom use was associated with a slightly increased risk for these lesions." Could you speculate on why there was an increase in HPV DNA among those who used condoms? 13. Could it be because condom users may have had more partners wrongfully believing that they were being protected against HPV?

Response. This question refers to the meta-analysis published three years ago by Manhart and Koutsky in Sexually Transmitted Diseases, November 2002.[1] Of the twenty (20) clinical studies meeting all inclusion criteria specified by the authors, six studies, all among women, measured HPV DNA detection as the outcome. Three of these studies showed risk reduction from 10-80 percent, one with statistical significance. Three other cross-sectional studies reported odds ratios

[1] Manhart LE, Koutsky LA. Sex Transm Dis 2002; 29:725-735.

trending in the opposite direction with slightly increased risk for HPV DNA. In their discussion of these findings, Manhart & Koutsky noted that most of these studies had methodological flaws likely to mask the protective effect of condoms, e.g., many did not include measures of consistent condom use, and most failed to measure the temporal sequence of condom use and infection measurement needed to establish acquisition of disease (i.e., they did not determine whether or not subjects were infected before beginning condom use). It is interesting to note that the one study showing a statistically significant positive protective effect of condoms against HPV infection was the one that carefully measured these attributes.

We believe it is unlikely that assumptions regarding condom protection against HPV influenced behavior and thus played a role in the studies showing an increase in HPV DNA detection among condom users. Public awareness of HPV infection and its consequences was much less common when these studies were done (late 1980s-late 1990s) compared to HIV/AIDS awareness. There also is no apparent biologic reason why condom use would increase the risk of HPV infection. A more likely explanation is that the design of the three studies mentioned, as discussed above, did not adequately measure consistent condom use or the temporal sequence of condom use and STD status. These limitations can lead to an incorrect estimate of the association between condom use and HPV infection, most likely an underestimate (or ever finding a harmful effect). These and other epidemiological considerations that can bias results to indicate that condoms have no or little protective effect, or even harmful effect, have been well-described.[2] Optimal designs would collect information on consistent and correct condom use and would be able to determine whether HPV infection preceded or followed condom use.

Additionally, it is important to view these findings in the context of the clinical outcome of HPV infection. The same Manhart & Koutsky meta-analysis concluded that while condoms may not prevent HPV infection, they appear to protect against genital warts and cervical cancer, the two key sequellae of HPV infection. Clinical research in this area continues. Since that analysis was published in late 2002, many new studies have been reported. In its *Report to Congress: Genital HPV Infection*, CDC considered several more studies and also concluded that condom use protects against the most serious consequences of HPV infection.[3] And, at the recent international STD conference, researchers reported on a study, soon to be published, showing that among newly sexually active women, consistent condom use appears to reduce the risk of HPV infection[4] This study appears to address many of the methodologic limitations of earlier HPV condom effectiveness studies. This study recruited newly sexually active women, studied the temporal sequence of condom use and HPV infection, and measured correct and consistent condom use.

Question 12. As you know, as the number of sexual partners increase, the risk of HPV infection and cervical cancer increases. Has FDA conducted any studies analyzing the impact that condom promotion has had on number of sexual partners and STD acquisition over a lifetime?

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[2] See Devine OJ, Aral SO. Sex Transm Dis 2004; 31:588-595; Crosby R, Salazar LF, et al. Sex Transm Dis 2005; 32:513-515; Warner L, Macaluso M, Austin HD, et al. Am J Epidemiol 2005 ; 161 :765-773.

[3] Report to Congress: *Prevention of Genital Human Papillomavirus*. Centers for Disease Control and Prevention (January 2004)

[4] Winer RL, Hughes JP, Geng Q, et al. (in press)

Response. FDA has not conducted any such studies regarding condom promotion. FDA conducted outreach studies to test user comprehension of condom labeling to help ensure that important information on condom labels is easily understood.

Question 13. Is it true that the production methodology for the forthcoming HPV vaccine is expensive and the vaccine must be stored in a frozen state and that these factors create significant obstacles for vaccine delivery in developing countries?

Response. Questions regarding the expense of manufacturing would best be answered by the manufacturers, since FDA has no authority to collect information regarding production costs. Questions regarding vaccine storage for unapproved products also should be referred to the manufacturers, as FDA cannot publicly disclose information that is confidential commercial, trade secret or otherwise privileged under applicable law.

Question 14. Which test is more reliable to identify women at risk for cervical cancer, the PAP smear or HPV DNA screening?

Response. PAP smear testing is well recognized as the standard of care for screening for cervical cancer and precancerous diseases of the cervix. HPV testing has been approved by FDA for use in the triage of atypical PAP smears to help physicians determine what follow-up studies are needed. HPV DNA testing also has been approved for use as an adjunctive test to the PAP smear for screening for cervical disease in women over 30 years of age. The two in combination may be helpful in improving identification of at-risk patients.

Thank you for contacting us concerning this matter. If you have further questions, please let us know.

Sincerely,

Patrick Ronan

Patrick Ronan
Associate Commissioner
for Legislation

American College of Obstetricians and Gynecologists

"Women and Cancer: Where are we in Prevention, Early Detection, and Treatment of Gynecologic Cancers"

Subcommittee on Criminal Justice, Drug Policy, and Human Resources
House Committee on Government Reform

September 13, 2005

The American College of Obstetricians and Gynecologists represents 49,000 physicians and partners in women's health, who care for and treat women of all ages. As physicians dedicated to improving women's health care, ACOG is committed to decreasing the rate of gynecologic cancers. Early detection, and public and provider education of the risk factors and warning signs are critical to ensuring early treatment.

ACOG fully supports HR 1245, Johanna's Law, which would provide needed education, outreach and public service announcements to educate communities about gynecologic cancers.

Pap Tests for Cervical Cancer-A Public Health Success

Pap tests, or cervical cytology screenings, are the most effective way to determine the presence of abnormal cells in the cervix. The National Cancer Institute has stated that 12,800 cases of invasive cervical cancer were diagnosed in the United States in 1999. Half of these women had never had a cervical cytology test, and 63% had not had a cervical cytology test in 5 years. Many of these cases may have been prevented with better access to cervical cytology screenings.

ACOG is committed to identifying and preventing the human papillomavirus (HPV) infections that lead to cervical cancer. HPV is the name of a group of viruses with more than 100 different strains, of which approximately 30 are sexually transmitted. Only a small fraction of women with HPV are at high risk for cervical cancer, and cervical cytology screening can help identify those at highest risk. Although cervical cytology screening does not prevent genital HPV infection, it detects cellular changes caused by the virus, changes which can then be treated, when necessary, before they progress to cervical cancer.

THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS • WOMEN'S HEALTH CARE PHYSICIANS
409 12TH STREET SW WASHINGTON DC 20024-2188
MAILING ADDRESS: PO BOX 96920 WASHINGTON DC 20090-6920
Phone: 202/638-5577
Internet: http://www.acog.org

Recent advances in our knowledge of the development of cervical cancer as well as technological changes in cancer screening have led ACOG to revise our guidelines regarding cervical cytology testing. Human papillomavirus infections are common in young women, but in most, the immune system is effective in fighting the virus and preventing precancerous changes from occurring. Because most HPV infections resolve spontaneously and cervical cancer is exceedingly rare in adolescents, ACOG now recommends that cervical cancer screening begin approximately 3 years after first sexual intercourse—but no later than age 21 years. Women younger than 30 years of age should have a cervical cytology test each year. Women who are 30 or older, who are at low risk, and who have had 3 consecutive negative cervical cytology tests may be re-screened every 2-3 years. Women who are 30 or older may also choose to have an HPV test at the time of their cervical cytology test. If they receive negative results on both tests, they should be re screened no sooner than 3 years. ACOG strongly encourages annual gynecologic visits as a part of routine preventive health care.

Congress and the Administration have made great strides in ensuring more women have access to cervical cytology screenings. In 1990, Congress created the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) as part of the Breast and Cervical Cancer Mortality Prevention Act. Administered by the Centers for Disease Control and Prevention (CDC), this program helps low income, uninsured, and underserved women gain access to lifesaving screening programs for early detection of breast and cervical cancers. Between 1999 and 2003 alone, the program conducted nearly 1.5M cervical cytology screenings, and close to 17,000 cervical cancers or precancerous lesions were detected. These early detections allow women to be treated timely, preventing the progression of their cancer.

Access is Still A Problem

Despite improved screening rates due to the NBCCEDP, access to care is still problematic for some women; race, educational level, and age tend to predict access. African-American women have higher death rates from cervical cancer, and women with less than a high school education are less likely to have testing than women with more education. Cervical cancer has a peak incidence between the ages of 40 and 55, yet women in this age group are less likely to have been screened with cervical cytology testing than are younger women. Targeted outreach to these women and behavioral research on why they do not seek care could help decrease these alarming disparities.

Regular Gynecologic Screenings Are Key to Detecting Ovarian and Uterine Cancer

Ovarian and uterine cancers are the most lethal and common gynecologic cancers in the US. In addition to cervical cytology screening, obstetrician-gynecologists routinely look for abnormalities in the reproductive organs to detect uterine and ovarian cancers. Sometimes these cancers are diagnosed in their advanced stages because their symptoms (bloating, lower back pain, and diarrhea) are confused with other common ailments. Currently, it appears that the best was to detect early ovarian cancer is for both the patient and her clinician to have a high index of suspicion of the diagnosis in the symptomatic woman.

A study by the Gynecologic Cancer Foundation and Research! America found that 47% of women could not name one symptom of gynecologic cancers, 45% of women were not aware of personal risk factors that increased their chance of developing a gynecological cancer, and almost 60 % of women surveyed could not name one step they could take to decrease their personal risk of developing a gynecological cancer. Johanna's Law will increase both public and provider awareness of the risk factors and symptoms so gynecologic cancers can be detected and treated early.

We thank the Committee for addressing this important issue. We hope Congress will quickly pass HR 1245, Johanna's Law, to continue on the path of eradicating gynecologic cancers through increased awareness among the public and physicians-- leading to timely screening, and potentially saving thousands of women's lives.

September 7, 2005

Statement of the Ovarian Cancer National Alliance in Support of Johanna's Law

The Ovarian Cancer National Alliance supports the passage of H.R. 1245, "Johanna's Law: The Gynecologic Cancer Education and Awareness Act of 2005," as a vital component in the national strategy to conquer ovarian cancer through education, awareness and research, and commends the Subcommittee on Criminal Justice, Drug Policy and Human Resources for holding a hearing today to learn more about this urgently needed legislation.

Ovarian cancer is the deadliest of the gynecological cancers and the fourth leading cause of death by cancer for women. This year, approximately 22,220 women will be diagnosed and an estimated 16,210 will lose their lives to the disease. A federal awareness campaign created by the passage of Johanna's Law and a commitment to funding ovarian cancer research programs are major advancements in the fight against ovarian cancer.

Johanna's Law is an essential piece of a comprehensive legislative action plan, which must include a sustained federal commitment to fund key ovarian cancer research programs at the National Cancer Institute, the Centers for Disease Control and the Ovarian Cancer Research Program at the Department of Defense.

The Alliance continues to promote a grassroots advocacy campaign along with our partner, the Society of Gynecologic Oncologists, which includes educating, organizing and training activists to protect the funding for these ovarian cancer programs.

"Consistent federal investment in ovarian cancer research is imperative to making progress against ovarian cancer," said Sherry Salway Black, Alliance director. "Only when the commitment to funding awareness education and research becomes a national priority will we beat ovarian cancer."

Currently, only 25 percent of ovarian cancer cases in the U.S. are diagnosed in the beginning stages when it is 80 percent beatable. When diagnosed in advanced stages, the chance of five-year survival drops to 28 percent.

The Alliance will continue to partner with the Society of Gynecologic Oncologists and Congressional supporters, including the Subcommittee members gathered for the hearing today, to pass Johanna's Law and raise the voices of survivors for this important cause.

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The Ovarian Cancer National Alliance is an umbrella organization that unites the efforts of grassroots activists, women's health advocates, and health care professionals to bring national attention to ovarian cancer.

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Responses to Questions for the Record
Centers for Disease Control and Prevention

Q. CDC and the Association of Schools of Public Health members, like Emory University and Johns Hopkins University, have been instrumental in developing clinical practice guidelines and in collecting large amounts of data on disease and public health threats. CDC and the Public Health profession have helped develop evidence-based medicine and outcomes based study design.

1. Would CDC be interested in helping develop a comprehensive information system to help the medical profession better understand treatment protocols like we are having to implement right now in the areas devastated by the hurricane?

The CDC would be interested in helping develop a comprehensive information system to help the medical profession better understand treatment protocols. Such a system would build upon existing CDC efforts with professional organizations, many research partners, managed care organizations, hospitals and community health centers to assess how accepted standards of care are applied in clinical care settings. The proposed treatment protocol information system, coupled with other public health strategies targeting individuals, communities, schools and worksites, could have a significant impact on chronic diseases the leading causes of death in the United States. Chronic diseases are common, deadly, disabling, costly — and, most importantly, preventable.

- Chronic diseases are common: 133 million people live with at least one chronic disease, greatly increasing their risks of sickness, disability, and early death.
- Chronic diseases are deadly: 75% of all deaths are from chronic diseases.
- Chronic diseases are disabling: Chronic conditions cause major limitations in activity for 1 of every 10 Americans. Three chronic diseases — arthritis, heart disease, and diabetes — are the leading causes of activity limitations among working-age adults.
- Chronic diseases are costly: Nearly every dollar of Medicare spending is for people with chronic conditions.

Chronic diseases are preventable. Chronic diseases are not inevitable. Four aspects of good health also help prevent most chronic diseases: tobacco control, good nutrition, physical activity, and maintenance of normal weight. Furthermore, the better application of treatment guidelines/protocols can reduce risk factors for chronic disease. For example:

- Studies in the United States and abroad have found that better blood sugar control reduces the risk for eye disease, kidney disease, and nerve disease by 40% in people with type 1 or type 2-diabetes.
- Blood pressure control reduces the risk for heart disease and stroke among people with diabetes by 33%–50%. It also reduces the risk for eye, kidney, and nerve diseases by about 33%. Detecting and treating early diabetic kidney disease by lowering blood pressure can reduce the decline in kidney function by 30%–70%.

- Improved control of blood cholesterol levels can reduce cardiovascular complications by 20%–50%.
- A 12- to 13-point reduction in blood pressure can reduce heart attacks by 21%, strokes by 37%, and all deaths from cardiovascular disease by 25%.
- During 1999–2002, nearly 25% of U.S. adults had high cholesterol levels or were being treated with medication. Only 63% of those with high levels were aware of it.

Q. CDC's work in the environmental causes of cancer through the Agency for Toxic Substances and Disease Registry (ATSDR) and the environmental health lab's work in helping to change regulations to reduce cancer risks from things such as lead and mercury and second hand smoke, have helped in the battle against cancer. Environmental medicine and toxicology are practiced at CDC, but few physicians get trained in these areas.

2. Would CDC be willing to work with other agencies to develop a disease treatment and prevention database using evidence based medicine and outcomes based study protocols to determine the effectiveness of off-label use of drugs and devices, and further develop and train physicians in the use of environmental medicine and toxicology to help them treat patients for cancer and other diseases.

CDC's National Center for Environmental Health (NCEH) and the Agency for Toxic Substances and Disease Registry support the training of physicians in the use of environmental medicine and toxicology. Over the past 4 years, NCEH has hired several medical toxicologists to augment CDC's ability to train physicians in the use of environmental medicine and toxicology. Medical toxicology is a clinical specialty that includes the monitoring, prevention, evaluation and treatment of injury and illness due to occupational and environmental exposures and pharmaceutical agents, as well as unintentional and intentional poisoning in all age groups.

NCEH and ATSDR create educational documents for physicians to expand their knowledge in the area of toxicology. NCEH, for example, has conducted web casts and expansion of CDC's Chemical Emergency Preparedness and Response web site (http://www.bt.cdc.gov/chemical/). Four different types of educational materials have been created and posted on the Web site including the following:

1. More than 30 fact sheets for the public on specific chemicals
2. More than 15 toxic syndrome descriptions meant to aid the physician in the recognition of exposure to specific agents or categories of agents
3. More than 40 case definitions to aid physicians in the uniform reporting of chemical exposures and to direct appropriate resources
4. Three web casts were produced and posted on the website in 2004 and 2005 to aid physicians in the recognition of chemical exposures in their patients: (1) Recognition and Management of Ricin-Related Illness, (2) Recognition of Illness Associated with Chemical Exposure, and (3) Gastrointestinal Illness Related to Chemical Exposure.

ATSDR's Toxicological profiles, case studies in environmental medicine and guidelines for physicians and first responders in managing hazardous materials incidents are significant examples of these products and services. These and other informational resources and training curricula for health professionals could be effectively leveraged, expanded and enhanced in support of efforts to reduce cancer risks and other environmental related diseases. Evidence based medicine as well as outcome based study protocols have both been employed in the development and evaluation of these resources.

Responses to Questions for the Record
National Institutes of Health

Q1: NCI and the NIH are to be commended for the extensive databases they have developed regarding on-going clinical trials

1) Please describe each of the data bases available listing clinical trials that NIH is involved in.

The two clinical trial databases described in Question 1 are NCI's Physician Data Query (PDQ®) cancer clinical trials registry, which is part of NCI's PDQ comprehensive cancer information database and is accessible through NCI's Web site (www.cancer.gov), and the ClinicalTrials.gov registry, which is operated by the National Library of Medicine and is accessible through the ClincalTrials.gov Web site (http://clinicaltrials.gov).

PDQ

The PDQ registry is the older of the two databases and has its origins in the National Cancer Act of 1971, in which NCI was directed to "...establish and maintain an international cancer research data bank to collect, catalog, store, and disseminate insofar as feasible the results of cancer research undertaken in any country for the use of any person involved in cancer research in any country." In subsequent legislation, Congress reinforced its desire that NCI maintain an international cancer research databank, and it expanded the scope of NCI's information dissemination activities beyond researchers to include health professionals, patients and their families, and the general public. Specifically, the Institute was directed to provide physicians and the public with state-of-the-art information about the treatment of various forms of cancer, to identify cancer clinical trials that might benefit patients, and to disseminate the results of cancer research using information systems available to the public. In 1982, the international cancer research databank became known as the PDQ database.

The PDQ clinical trials registry has listings that date back as far as 1974. As of May 12, 2006, the registry included more than 3,700 trials that were open to patient accrual and 15,000 trials that were either closed to patient accrual or completed. The PDQ registry includes trials conducted in the United States and abroad. Although trial registration in PDQ has been encouraged, it has never been required.

To register a trial in PDQ, protocol documents can be submitted either electronically or in hard copy. Summaries of the protocol documents are then prepared for public display on the NCI Web site in both health professional and patient-oriented formats. The summaries are drafted by experienced staff using strict guidelines for information content and quality and are indexed using a controlled, hierarchical cancer terminology to enhance the accuracy of search and retrieval. On the NCI Web site, visitors can search for clinical trials on the basis of a number of parameters, including type of cancer, stage or subtype of disease, status of trial (open or closed), trial ID number, geographic

location, hospital or institution, intervention type (surgery, radiation therapy, etc.), drug name, phase of trial, physician name, lead organization name, and sponsor of trial.

One of the principal advantages of the PDQ registry for patients is the contextual environment in which it is accessed. The NCI Web site contains abundant educational information about clinical trials in general, as well as evidence-based information about cancer treatment, supportive care, genetics, screening, prevention, and complementary and alternative medicine. These information resources are cross-linked throughout the site.

The closed clinical trials in PDQ are a valuable resource for researchers who are seeking information about cancer clinical trials that have been conducted in the past. More than 4,600 of the protocol summaries in the PDQ registry have links to citations of published results listed in the National Library of Medicine's PubMed database or on the Web site of the American Society of Clinical Oncology.

PDQ accepts all cancer-related clinical research studies, including traditional phase I, phase II, phase III, and phase IV treatment, prevention, and screening studies, as well as ancillary tissue or laboratory studies. PDQ also includes cancer-related epidemiologic studies, genetics studies, and behavioral modification studies (e.g., studies of interventions for smoking cessation).

Information in the PDQ registry is kept current through a proactive update system. Trial coordinators and principal investigators are contacted at regular intervals to update information about the overall status of their trials (open or closed), the status at individual participating sites, the accuracy of the trial contact information, and to ensure that the descriptions of the trials remain accurate.

Finally, PDQ is the conduit by which NCI-sponsored clinical trials are included in the ClinicalTrials.gov registry (see below).

ClinicalTrials.gov

ClinicalTrials.gov is also an international registry. It includes trials of interventions for all diseases and conditions — not just cancer — being conducted and submitted by sponsors from across the globe. All studies in PDQ that involve the enrollment of human subjects are included in ClinicalTrials.gov. Currently, ClinicalTrials.gov is the largest clinical trials registry in the world.

Like PDQ, ClinicalTrials.gov was created as a result of federal legislation, namely the Food and Drug Administration Modernization Act (FDAMA) of 1997. Section 113 of FDAMA directed the DHHS Secretary, acting through the Director of NIH, to create, maintain, and operate a database of information about clinical trials of drugs and biologic products for the treatment of serious or life-threatening diseases and conditions that are conducted under an FDA Investigational New Drug (IND) Application. In response, the

NIH, acting through the National Library of Medicine and with input from the FDA and others, created the ClinicalTrials.gov registry. The registry was first made available to the public via the Internet on February 29, 2000. The final FDA guidance on trial registration requirements for ClinicalTrials.gov was issued on March 18, 2002. According to the guidance, all phase II, phase III, and phase IV trials of drugs or biologic products for the treatment of serious or life-threatening diseases or conditions that are conducted under an FDA IND must be registered within 21 days of the start of patient accrual. As noted above, ClinicalTrials.gov will accept other types of trials (e.g., phase I trials or phase II and higher trials of surgical or radiotherapy techniques), but only drug and biologic product trials conducted under an FDA IND are required by statute.

As of May 12, 2006, ClinicalTrials.gov contained more than 12,600 trials that were open to patient accrual and 15,000 trials that were closed to patient accrual or were completed. Approximately 38 percent of the open trials and 37 percent of the closed/completed trials were cancer trials.

ClinicalTrials.gov provides trial information in one format only. It does not include separate health professional and patient-oriented trial summaries. Trial registrants, who supply the information used to create the public trial summary displays, are asked to use language that is accessible to a non-expert or lay audience.

To list a trial in ClinicalTrials.gov, registrants must first apply for a Protocol Registration System (PRS) account. The PRS is a Web-based data entry system. Required elements for trial registration include, among others, a brief title, a brief summary, the phase of the study, the type of study (interventional or observational), the design of the study (randomized, controlled, measured clinical endpoints, etc.), the disease or condition, the name of the intervention, eligibility criteria for the study, gender or age restrictions, the study's recruitment status (open or closed), study contact information, the study's sponsor, and the study's identification number(s). Because the PRS uses open-text fields for several of the required elements, the amount of information supplied about individual trials can vary significantly.

For NIH-sponsored trials, ClinicalTrials.gov has asked that a single registrant be designated for each institute or center that conducts or sponsors clinical research. As indicated previously, PDQ is the designated registrant for NCI-sponsored trials. PDQ exports clinical trial information to ClinicalTrials.gov electronically on a regular basis, and computer programs are used to extract the information needed for the PRS data fields automatically. In creating a single, public summary display for the trials obtained from PDQ, ClinicalTrials.gov uses information from both the PDQ patient-oriented summary and the corresponding health professional summary.

Visitors to ClinicalTrials.gov can search for clinical trials on the basis of disease or condition, experimental treatment, geographic location, age restriction, phase of study, study sponsor, study identification number, or visitor-defined search terms.

Cancer Trial Listings: PDQ versus ClinicalTrials.gov

Shortly after the launch of the ClinicalTrials.gov registry, cancer advocates began to encourage NCI and the National Library of Medicine to work together to ensure that the cancer trial listings in PDQ and ClinicalTrials.gov are equivalent. The advocates felt strongly that, regardless of which registry people used, they should be able to find the same cancer trials. In response to this request, NCI and the National Library of Medicine established a program of regular, reciprocal data exchanges. Cancer trials registered in PDQ are registered in ClinicalTrials.gov and vice versa.

As noted above, PDQ submits NCI-sponsored trials to ClinicalTrials.gov. In addition, PDQ registers trials sponsored by the National Cancer Institute of Canada, the European Organization for the Treatment of Cancer, and other international organizations and institutions in ClinicalTrials.gov. ClinicalTrials.gov submits primarily pharmaceutical company cancer trials registered under the requirements of FDAMA to PDQ.

Because of differences in the business models of the two registries (i.e., differences in the way the data are processed and prepared for public display), the cancer trials in the two databases at any given moment in time may not be exactly equivalent, but that is the goal.

Recent events influencing the comprehensiveness of clinical trial listings in PDQ and ClinicalTrials.gov

On July 1, 2005, the International Committee of Medical Journal Editors (ICMJE) implemented formal requirements aimed at more complete registration of clinical trials in publicly accessible registries. The primary goal of the ICMJE was to increase the level of transparency regarding the worldwide clinical trial enterprise, but an added benefit was a substantial increase the number of clinical trial options for patients and their doctors to consider.

The ICMJE requirements specified that, as of July 1, 2005, all new phase II or higher trials that have at least one prospectively assigned comparison group must be registered in a publicly accessible registry before the start of patient accrual if the investigators want to have their trial results considered for publication in a peer-reviewed biomedical journal. The ICMJE also set a registration deadline of September 13, 2005 for ongoing trials that began recruiting participants prior to July 1, 2005. Any research study "...that prospectively assigns human subjects to intervention and comparison groups to study cause-and-effect relationships between a medical intervention and a health outcome" must be registered. The ICMJE defined "medical intervention" as "...drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like." Therefore, the ICMJE specified that trials not previously covered by FDAMA must now be registered.

When the ICMJE requirements were first announced, ClinicalTrials.gov was specifically identified as the only registry the editors were aware of at that time that met all of their requirements.

One consequence of the implementation of these requirements was that both PDQ and ClinicalTrials.gov experienced a massive influx of new trials during the summer and early autumn months of 2005. The new "steady state" of trial registrations in both registries appears to be about two- to three-times higher than before the requirements were implemented.

During the time the ICMJE requirements were under development, the World Health Organization (WHO) initiated discussion of a global approach to clinical trial registration that would address the problems of incomplete registration and an absence of uniform standards for registration. Based on recommendations presented to the 115th WHO Executive Board in January 2005 and to the 58th World Health Assembly in May 2005, the WHO International Clinical Trials Registry Platform (ICTRP) was created. The ICTRP began operations in August 2005.

The goals of the ICTRP are 1) to set international norms and standards for trial registration and reporting, 2) to ensure that all clinical trials are registered and, therefore, publicly declared and identifiable, and 3) to ensure that a minimum set of results will be reported and made publicly available in some format for all trials.

The ICTRP defined a set of 20 required elements for a trial to be fully registered. The ICMJE then modified its registration requirement elements to harmonize them with the ICTRP's.

2) During the hearing you mentioned a centralized Internet database that physicians and/or patients can refer to that outlines current treatment protocols for a given medical condition. Please describe it and its location.

This question appears to refer to the ClinicalTrials.gov registry, which is maintained and operated by the National Library of Medicine (part of the National Institutes of Health). The ClinicalTrials.gov registry was described above in the response to Question 1, part 1.