

**NIH: MOVING RESEARCH FROM THE BENCH TO
THE BEDSIDE**

HEARING
BEFORE THE
SUBCOMMITTEE ON HEALTH
OF THE
COMMITTEE ON ENERGY AND
COMMERCE
HOUSE OF REPRESENTATIVES
ONE HUNDRED EIGHTH CONGRESS

FIRST SESSION

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THURSDAY, JULY 10, 2003

HOUSE OF REPRESENTATIVES,
COMMITTEE ON ENERGY AND COMMERCE,
SUBCOMMITTEE ON HEALTH,
Washington, DC.

The subcommittee met, pursuant to notice, at 10 a.m., in room 2123, Rayburn House Office Building, Hon. Michael Bilirakis (chairman) presiding.

Members present: Representatives Bilirakis, Burr, Whitfield, Norwood, Wilson, Buyer, Brown, Eshoo, Stupak, Green, Strickland, Capps, and DeGette.

Staff present: Cheryl Jaeger, majority professional staff; Jeremy Allen, health policy coordinator; Eugenia Edwards, legislative clerk; John Ford, minority counsel; and Jessica McNiece, minority staff assistant.

Mr. BILIRAKIS. I call this hearing to order.

I would like to start by thanking our witnesses for taking the time to join us today. Are our witnesses in the room? They may not be.

I am sure that these two panels of experts will help members of the subcommittee better understand the dynamic and successful relationship between taxpayer-supported Federal research and private industry, and how this relationship ensures that Americans have access to cutting edge biomedical technology.

I am going to hold for a minute or 2. Please take your seats as soon as you can.

We have a journal vote coming up, and that is why we are trying to rush through these opening statements. So please help us out by getting settled.

Can we shut those doors, please?

As everyone here today is aware, we recently completed our effort to double the budget of the National Institutes of Health. I often say that while we are not famous for following through on our promises up here at Washington, this is one case where I think Congress really came through for the American people. However, it is our job to ensure that we get the most out of this massive investment of resources.

Today's hearing is another in a series of hearings that will examine different aspects of NIH, and we will focus today on how private industry's partnership with the Federal Government helps move new discoveries from the bench to the bedside. After all, what good is the bench without it getting to the bedside?

As we will no doubt discuss today, the 1980 Bayh-Dole Act laid the foundation for our current system of technology transfer. Prior to Bayh-Dole, the Federal Government held the patent rights to new technologies that were developed using Federal funds. This greatly discouraged private sector innovation and the translation of these discoveries into useful products.

Bayh-Dole changed all of that by permitting entities such as universities and small businesses that develop new technologies using Federal funds to retain title to these technologies. In addition, Bayh-Dole allowed Federal agencies to license inventions that are developed through intramural research.

While we will spend the majority of this hearing learning more about technology transfer and its role in speeding new therapies to patients, it is safe to say that Bayh-Dole created a highly successful model that helps fuel our research-driven biotechnology and pharmaceutical industries. As we will hear from our witnesses, the technology developed using Federal resources is often far from any potential commercial uses.

Considering the substantial investment needed to turn these discoveries into therapies, it just makes sense for the Federal Government to partner with private entities willing to incur the necessary risk to bring new products to market.

I am glad that we have a variety of perspectives on this important issue before us. I think that after today every member of the subcommittee will have a much better understanding of the relationship between the Federal Government, the research community, and the private sector.

And, again, I would like to thank our witnesses for being with us today.

And with that, I would now yield to the gentleman from Ohio for an opening statement, and we might be able to go through two or three opening statements, and then, of course, we will have to recess for the vote, and then return.

Mr. Brown.

Mr. BROWN. Thank you, Mr. Chairman. I think Ms. Capps and Mr. Stupak both want to forego their opening statements, so they can do longer questions. So perhaps we can get through that.

I want to welcome our witnesses and look forward to hearing their testimony, and thank the chair for calling this hearing on this very important issue. Each year for the last 5 years NIH has been allocated several billion dollars to support basic research in biomedical science. In doing so, the Federal Government is investing taxpayer dollars in the future of health care, improving health care through promoting scientific curiosity and discovery.

Universities, hospitals, and institutes in my own State of Ohio have accepted the challenge, as they have elsewhere, in using public dollars to promote discoveries that some day will improve the health of not just Ohioans but people in nation after nation around the world.

Case Western Reserve University School of Medicine is among the 20 top recipients of NIH research funding among the Nation's medical schools. Just yesterday Ohio State was awarded a grant as part of a public-private partnership initiated by the Friends of Cancer Research, yet today House Republicans are asking my Demo-

cratic colleagues on the floor to—asking all of us to vote on an appropriation bill for the Department of Health and Human Services that jeopardizes the progress we have made.

This bill falls short of what is needed merely to keep up with inflation and research costs, which NIH estimates at 3.3 percent for fiscal year 2004. As is everything else around here, all important public functions like that have been cut in order to make room for a tax cut that goes overwhelmingly to the most privileged people in our society.

I will vote against this bill on the floor, because Federal funding of biomedical research is a worthy investment. Questions about Congress' commitment to NIH research underscore the importance of understanding, in both qualitative and quantitative terms, the government's return on its investment in biomedical research.

The reason for today's hearing—and, as I said, I thank the chair for this—is to talk about how basic research investments are realized as a public health benefit. This process is a complex system of many parts, each critical, each contributing to the success of the whole. For this process to work, it must never forget that this process has a face—the face of a patient who 1 day can benefit from cancer vaccines or from stem cell research or from a novel diagnostic technique.

Policy tools like patents, the Bayh-Dole Act, the Stevenson-Wydler Act, and incentives for commercialization, are important links in the bench to bedside chain, but they are ineffective if, at the end of the day, a patient cannot afford or does not have access to treatment. They are ineffective if they discourage rather than nurture research formally in the domain of open scientific discourse.

Congress has long recognized that the value of an idea is in using it. Bayh-Dole allows universities to patent and license discoveries made in the course of government-sponsored research. But growing concerns about the prohibitive costs of prescription drugs and their effect on the health care system overall has renewed debate over the licensing of inventions.

There are also concerns that some of the incentives can hinder rather than accelerate research. In this context, our witnesses' views on key issues are extremely important. Among others that Chairman Bilirakis raised, those issues include whether American taxpayers should accept an "ends justifies the means" approach to justify the outrageous costs of prescription drugs when they have already subsidized the research on those drugs on the front end and seeing drug prices significantly lower in other nations, as well as whether and to what extent patents may actually be hindering what our constitution explicitly states is the intention of patents—promoting science and the useful arts.

I look forward, Mr. Chairman, to an enlightening discussion. I thank you for calling this hearing.

Mr. BILIRAKIS. The chair was going to recognize Mr. Buyer. Let us see, Mr. Stupak.

Mr. STUPAK. I waive opening statement.

Mr. BILIRAKIS. Thank you.

Ms. Capps.

Ms. CAPPS. I waive an opening.

Mr. BILIRAKIS. No? All right.
Well, that ends opening statements.
[Additional statements submitted for the record follow:]

PREPARED STATEMENT OF HON. BARBARA CUBIN, A REPRESENTATIVE IN CONGRESS
FROM THE STATE OF WYOMING

Thank you, and good morning.
There is no denying the fact that America sets the standard in medical research. We are the ones constantly pushing the envelope to find that ultimate diagnosis—that cure we know is out there.

It is what makes research at NIH virtually undisputed in this country and around the world.

Year in and year out, Congress devotes billions of dollars to this agency, believing it to be not only worthwhile but honorable.

I often question what it is exactly that makes us so determined to conquer the diseases of the human mind and body. Is it financial gain? Is it notoriety? Is it arrogance? I don't think so.

The answer to this question comes down to a common experience that each of us will face during our lifetime.

It is that moment when we walk hand-in-hand with a sick loved-one; when we listen as the doctor tells them, "I'm sorry there is nothing else we can do"; when we feel powerless to the disease that is taking our family member away.

That is when I as an individual and we collectively as a country put our frustration to good use and say we will find a cure. That is all the reason we need.

There is no single motivating factor greater than personal experience. I know that first-hand and, the reality of the human condition is such that, you will likely know it too—if not today, then someday.

With each dollar we channel toward medical research, we improve the quality of someone's life—perhaps for as little as a day, but maybe for years to come. That is what makes all the difference, and that is why we do it.

I commend NIH for its steadfast ability to take something from the drawing board and turning that into the miracle drugs and treatments we have today. The full extent of how they do that is not clear to me, and that is why I would like to learn more about it.

I look forward to hearing from our witnesses, and appreciate you holding this hearing today, Mr. Chairman. I yield back the remainder of my time.

PREPARED STATEMENT OF HON. W.J. "BILLY" TAUZIN, CHAIRMAN, COMMITTEE ON
ENERGY AND COMMERCE

Thank you, Mr. Chairman, for holding this timely hearing today.

The National Institutes of Health serves one primary purpose: to generate knowledge that can be used to protect the public health. Through NIH research investments, scientists are making huge strides in the fight to better diagnose, treat, and ultimately prevent and cure disease. Because the NIH shares the results of its research to the broader scientific community and the public, creative minds are presented a unique opportunity to translate this information into tangible products and therapies that improve the quality of life.

What began as a single laboratory in a military hospital has grown to an amazing institution. NIH research programs now operate in almost all parts of the United States and internationally. NIH research programs also involve more than 16,000 scientists on NIH intramural research campuses alone—truly an amazing amount of manpower dedicated toward such important purposes.

What is even more impressive, besides the sheer size of the National Institutes of Health, is the real world impact the research findings at NIH ultimately have on patients. The volume of information generated by NIH is enormous. I am pleased that we will hear testimony today from one of the most prominent "librarians" in the world, the Director of the National Library of Medicine, Dr. Lindberg. This is a person who effectively catalogs some of the most important information generated by the NIH.

As new communication mediums unfold, such as the Internet, it is critical that our research resources are made as widely accessible as possible. I applaud Dr. Lindberg for his dedication to ensuring the National Library of Medicine rises to this challenge. It certainly is not an easy task to constantly reorganize entire databases so that researchers can readily access the most recent scientific findings. But the Library of Medicine is doing just that.

Generating knowledge for public health is the primary purpose of the research undertaken at the NIH. We want to ensure that the private sector applies the knowledge gleaned from NIH research so that we can discover newer and safer ways to treat patients.

Today, we will hear testimony from the Director of the Office of Technology Transfer at the NIH about the technology transfer policies in place that create incentives for private sector investments. We will have the opportunity to learn more about how technology transfer policies impact industry, universities, and patients. These are risky ventures where failures are many and successes few. But, every success story represents a win for patients. We may not translate all basic research into commercialized products, but when we do the American public benefits. That's part of the dichotomy of technology transfer.

Finally, I am glad the Committee is recognizing a new collaborative project underway at the Department of Health and Human Services between two agencies with distinct missions, the NIH and the Food and Drug Administration. Often we speak of the need to create more "public-private partnerships." Equally important is the goal of ensuring collaboration between agencies whose work compliments each other. I am excited about the new interagency agreement being developed by the National Cancer Institute and the FDA to help speed the approval of cancer therapies and improve the post market surveillance of products. If this collaboration works, it will become a model for future interagency agreements. I am encouraged by the potential of this project.

Mr. Chairman, I look forward to learning more about the critical technology transfer policies that are being utilized by the NIH. As our Committee continues its oversight over this important agency, there can be no more critical challenge than for us to promote policies that move the maximum amount of research from the laboratory bench to the patient's bedside. We have invested a great deal of resources in the NIH in recent years. Now it's time to ensure that taxpayers and America's patients are getting a good return on that investment.

Thank you and I yield back the balance of my time.

PREPARED STATEMENT OF HON. GENE GREEN, A REPRESENTATIVE IN CONGRESS FROM
THE STATE OF TEXAS

Thank you, Mr. Chairman, for holding this hearing on research at the National Institutes of Health (NIH).

For the past five years, the Congress has provided unprecedented increases in funding for biomedical research within the NIH.

I have been a strong proponent of these increases, as I have been able to witness firsthand some of the miraculous medical breakthroughs occurring at Baylor College of Medicine in my home town of Houston, Texas, as well as at facilities across this country.

And while I certainly support additional increases—certainly larger increases than the meager 2.5 percent increase in this year's Labor HHS appropriations bill—I think it's fair for us to spend some time investigating how NIH spends its money, whether we are getting a "good rate of return" on this investment, and whether there are things we should be doing differently to ensure that this research benefits all taxpayers.

The issue of technology transfer is a complex one, but I think it is an important one for us to look at.

The technology transfer process ensures that the groundbreaking research being done at NIH reaches patients when they need it.

I am interested in learning more, however, about whether this process hinders the development of some areas of scientific research that are perhaps not as commercially profitable.

For example, I know that a constituent of mine suffers from scoliosis, and is frustrated by the lack of research being done at NIH to find better treatments or a cure for this condition.

I know her frustration is compounded when she hears about research into drugs like Viagra—which certainly earn the pharmaceutical industry a lot of money.

Now I don't know whether Viagra was developed through the NIH, but I would like to know how NIH goes about determining where resources are allocated, and whether there is more that we can or should be doing to encourage research for conditions such as scoliosis.

This is certainly an important issue, and I look forward to learning more about it.

With that, Mr. Chairman, I yield back the balance of my time.

PREPARED STATEMENT OF HON. JOHN D. DINGELL, A REPRESENTATIVE IN CONGRESS
FROM THE STATE OF MICHIGAN

Mr. Chairman, thank you for scheduling this hearing. The laws, policies, and practices that govern the process of technology transfer are one of the keys to improving public health. The National Institutes of Health (NIH) will spend approximately \$28 billion this year on biomedical research. Other government programs will also make multibillion dollar contributions to this kind of research. This will be augmented by nearly \$30 billion in research and development expenditures by the pharmaceutical industry. Philanthropies and individuals will also make significant contributions to biomedical research.

In order for this level of support to be sustained or enhanced, the translation of basic research into useful therapies needs to occur at an acceptable pace. We have an excellent array of witnesses who will inform us of what is working well, and what could be improved, in our biomedical research and development technology transfer programs.

The Bayh-Dole and the Stevenson-Wydler Acts were passed in 1980 to address the need to convert federal investments in basic research into useful innovations that improve public health. The ensuing years have shown that these programs, augmented by others, have led to some notable successes. Bayh-Dole is one of the key reasons we have a robust biotechnology industry. Training programs for scientists and medical personnel, as well as advancement of knowledge, have flourished at universities in every state. We have many new therapies that are enabling persons with serious and life threatening diseases to live longer, suffer less, and enjoy life to a greater extent. These activities and products provide thousands of jobs and stimulate our economy.

This compels me to mention some matters that could adversely affect some of the good things we will hear from today's witnesses. NIH is doing a good job, yet the budget provides a meager increase for its programs. In addition to my concerns with the budget, I am especially disturbed by the so called "strategic human capital management" initiative and the "competitive sourcing program." These twin blunders are already having a corrosive effect on NIH morale and should be shelved immediately. The NIH has a unique role in public health. I, for one, do not want to see it run just like a business. The NIH funds research that the private sector would never support. This is important for finding effective therapies for many diseases and conditions that are not profitable. NIH also supports large scale biomedical science, such as the human genome project. In sum, the private sector and the government play vital, yet distinct roles, and they should not be effectively consolidated into one.

Mr. BILIRAKIS. We are going to take a break. As soon as we get back, we will get right into the witnesses. Thank you very much for your patience.

[Brief recess.]

Mr. BILIRAKIS. The chair apologizes. You are also very important people, and we treat you this way, but that is the way things are.

The first panel consists of Dr. Donald A.B. Lindberg, who is Director of the National Library of Medicine with NIH; Dr. Mark Rohrbaugh, Director of the Office of Technology Transfer from the Office of the Director of National Institutes of Health; Dr. Anna D. Barker, Deputy Director for Strategic Scientific Initiatives with the National Cancer Institute with NIH; and Dr. Theresa Mullin, Associate Commissioner, Office of Planning and Evaluation for the Food and Drug Administration.

Welcome, again, to all of you. Thank you so much for being here.

I will set the clock at 5 minutes. But obviously, if you are on a roll in terms of making your point, I will let you go for a little while longer. Obviously, your written submittal is part of the record, so we would hope that you would sort of complement and supplement that.

Having said that, if we can all be in order here, we will recognize Dr. Lindberg. Please proceed, sir.

STATEMENTS OF DONALD A.B. LINDBERG, DIRECTOR, NATIONAL LIBRARY OF MEDICINE, NIH; MARK L. ROHRBAUGH, DIRECTOR, OFFICE OF TECHNOLOGY TRANSFER, OFFICE OF THE DIRECTOR, NIH; ANNA D. BARKER, DEPUTY DIRECTOR FOR STRATEGIC SCIENTIFIC INITIATIVES, NATIONAL CANCER INSTITUTE, NIH; AND THERESA MULLIN, ASSOCIATE COMMISSIONER, OFFICE OF PLANNING AND EVALUATION, FOOD AND DRUG ADMINISTRATION

Mr. LINDBERG. Thank you, Mr. Chairman, for this opportunity to brief you and your colleagues about the National Library of Medicine. The role of the Library is important to the Nation's health, and this is due in large part to the strong support we have received from the Congress historically.

Progress in health care is a cyclical process, much as the title of your hearing implies. It starts with a problem recognized by a medical practitioner. This leads to experiments or experimental observations. Scientists describe the results in what we now call the peer-reviewed scientific literature. This informs the next cycle of experiments, which in turn are read by clinicians to use in patient care, and by patients to inform their participation in treatments and cures.

The National Library of Medicine—NLM—collects about 27,000 scientific periodicals from across the world, and includes about 5,000 of the very best in the printed Index Medicus and the online Medline file. The print version started in 1879; the computer version effectively in 1965. NLM is the biggest medical library in the world, again, due to the encouragement and support of the U.S. Congress, plus gifts of many historical holdings by scholars. The Library is a major scientific and medical resource in the U.S. and abroad.

Let me give a measure of the information available to physicians. Medline holds the descriptions of over 14 million scientific reports. Each year we add 500,000 new ones. Clearly, no doctor or scientist can possibly know all that is described in this library.

Consider the case of a conscientious medical practitioner. Let us imagine the doctor faithfully reads every night before going to bed two articles from the specialty journals he or she buys. May one imagine, then, that the doctor has by this method kept up with progress? Really, no. By the end of such a year, this good doctor will have fallen 648 years behind on reading the new publications. So in reality what good doctors do is search the NLM files—without charge and available night and day on the Internet—and read the best one or two articles for the particular patient problem of the moment.

We can tell you countless examples of getting a tough diagnosis made through this system, of selecting the best new drug for treatment, and even of coming to understand new terms and ideas through reading the right paper at the right time.

Special files cover complementary and alternative medicine, space medicine, bioethics, AIDS, and toxicology. There is also a version of this knowledge that is aimed at patients, families, and the public. We call this MedlinePlus. This is organized into about 600 health topics, including genetics information for the public.

An additional important computer resource for linking laboratory discoveries to clinical practice is ClinicalTrials.gov. Here one can find out over 7,700 clinical trials in over 75,000 American communities, including the purpose of the trial, the enrollment requirements, and the telephone number of the investigator who can take on new patients.

The system began in 1998. It was created by NLM with initially the participation and support of all NIH Institutes, and subsequently inclusion, too, of trials supported by the major pharmaceutical manufacturers. The stimulus for creation of this system was congressional; namely, the 1997 FDA Modernization Act, which required that FDA, NIH, and NLM make some such system available for serious and life-threatening diseases.

Mr. Chairman and members, so far I have described three major NLM computer-based information systems that provide the fundamental infrastructure that connects doctors, scientists, and patients with worthwhile writings and publications on human health. This has worked well for, really, about 160 years, but now a new science challenges us—the Human Genome Project. This and similar genomic studies on literally thousands of animals, plants, and microorganisms make our traditional books to some extent inadequate.

The human genome alone contains billions of nucleotide bases, tens of thousands of genes, hundreds of thousands of biological proteins to do the work of the genes. I am sure my colleague Francis Collins discussed this with you in earlier hearings before the committee, and doubtless more skillfully than I.

The simple point I want to make now is that genomic information simply is not readable from printed books. It is accessible only through a computer system that can present the right portions of the data along with the desired relationships.

This is comparable to the child looking at a drop of pond water. The life of the teeming protozoa and bacteria is visible to today's schoolchild just as it was to Leuwenhoek centuries ago only through the lens of a microscope. At NLM, that microscope to modern medicine is the National Center for Biotechnology Information—NCBI.

NCBI was authorized by the Congress in 1989. It has the responsibility to collect, annotate, and provide creative access to all the human genome data from the U.S. and abroad, as well as much else. The spectacular new anticancer drug Gleevec, for example, came directly from clever use of these data by scientists in academia and at Novartis Labs.

Taking together all of the NLM computer knowledge sources I have mentioned, these are used online more than a million times a day, 500 million uses per year.

I apologize for describing only the outline of these systems, in order to stay within my time. I will submit a more detailed description for the record. And, of course, if you wish, I would be happy to go into more detail or do my best to answer any questions.

Thank you for the privilege of appearing before you.

[The prepared statement of Donald A.B. Lindberg follows:]

PREPARED STATEMENT OF DONALD A.B. LINDBERG, DIRECTOR, NATIONAL LIBRARY OF MEDICINE, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Thank you, Mr. Chairman, for this opportunity to brief you and the Subcommittee about the National Library of Medicine, which is part of the National Institutes of Health within the Department of Health and Human Services. The role of the Library is central to the Nation's health, and this is due in large part to the strong support we have received in the Congress.

Progress in health care is a cyclical process, much as the title of your hearing implies. It starts with a problem recognized by a medical practitioner. This leads to experiments or experimental observations. Scientists describe the results in what we now call the peer-reviewed scientific literature. This informs the next cycle of experiments, which in turn are read by clinicians to use in patient care and by patients to inform their participation in the treatments and cures.

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There is also a version of this knowledge that is aimed at patients, families, and the public. We call this MedlinePlus. This is organized into about 600 Health Topics.

An additional important computer resource for linking laboratory discoveries to clinical practice is ClinicalTrials.gov. Here one can find out about over 7700 clinical trials in over 75,000 American communities, including the purpose of the trial, the enrollment requirements, and the telephone number of the investigator who can take new patients. The system began in 1998. It was created by NLM with initially the participation and support of all NIH Institutes, and subsequently inclusion too of trials supported by the major pharmaceutical manufacturers. The stimulus for creation of this system was the 1997 FDA Modernization Act, which authorized FDA, NIH, and NLM to make some such system for all serious or life threatening disorders.

Mr. Chairman and members of the Subcommittee, so far I have described three major NLM computer-based information systems that provide the fundamental infrastructure that connects doctors, scientists, and patients with worthwhile writings and publications on human health. This has worked well for more than 100 years, but now new science challenges us: the Human Genome Project. This and similar genomic studies on literally thousands of animals, plants, and micro-organisms make our traditional books to some extent inadequate. The human genome alone contains billions of nucleotide bases, tens of thousands of genes, hundreds of thousands of biological proteins to do the work of the genes. I am sure my colleague Francis Collins from NIH's National Human Genome Research Institute discussed this with you during the May 22, 2003, hearing before this Subcommittee—and doubtless more skillfully than I. The simple point I want to make now is that the genomic information simply is not readable from printed books. It is accessible only through a computer system that can answer questions and present the right portions of the data along with the desired relationships. This is comparable to the child looking at a drop of pond water. The life of the teeming protozoa and bacteria is visible to today's schoolchild just as it was to Leuwenhoek centuries ago only through the lens of a microscope. At NLM, that microscope to modern medicine is the National Center for Biotechnology Information (NCBI), which was authorized by Congress in 1989. It has the responsibility to collect, annotate, and provide creative access to all the human genome data from the U.S. and abroad—as well as much

else. The spectacular new anti-cancer drug Gleevec, for example, came directly from clever use of these data by scientists in academia and at Novartis Labs.

Taking together all of the NLM computer knowledge sources I have mentioned, these are used on-line more than one million times each day, 500 million uses per year!

I apologize for describing only the outline of these systems, in order to stay within my time. I am submitting for the record a more detailed description of these services. If you wish, I would happily go into more detail now or do my best to answer any questions.

ADDITIONAL MATERIAL FOR THE RECORD

The National Library of Medicine has a number of databases and services that are involved in biomedical research, health care delivery, and information for the public. Three of the most important are PubMed/MEDLINE, MEDLINEplus, and ClinicalTrials.gov.

PubMed/MEDLINE

The “literature” is the touchstone of progress in medical research and practice. In the health sciences, the standard reference source since 1879 has been NLM’s published bibliography, *Index Medicus*. For the past 30 years it has been supplemented by MEDLINE, an online database derived from the *Index Medicus*. MEDLINE (and its backfiles) is a constantly growing online resource that at last count contained more than 14 million references and abstracts to articles from about 5,000 medical journals. When it appeared in 1971, it was truly a pioneering effort in information technology, and it is today the most authoritative entry point into an ever-expanding biomedical literature. The MEDLINE files extend from the nineteen fifties to the present, and the Library is now adding data from even earlier years. PubMed/MEDLINE is by far the most widely used medical information database in the world. Each day the 14 million records are queried more than 1.3 million times by 220,000 unique users. This is roughly a half *billion* searches per year.

The sophisticated yet easy-to-use access system for searching MEDLINE on the Web is called PubMed. Since the launch of PubMed in 1997, continual improvements have been introduced, and today it offers a high degree of flexibility. For example, there are now Web links to almost 4,000 of the journals represented in MEDLINE, allowing users to have access to the full text of articles referenced in the database. In addition, NLM has introduced CAM on PubMed, which provides the public with access to citations from the MEDLINE database regarding complementary and alternative medicine.

An increasingly popular service on the Web for the scientist and health professional is an extension of PubMed known as PubMedCentral. This is a digital archive of life sciences journal literature, created by NLM’s National Center for Biotechnology Information (NCBI). Publishers electronically send peer-reviewed research articles, essays, and editorials to be included in PubMedCentral. A journal may deposit material as soon as it is published, or it may delay release for a specified period of time. NLM undertakes to guarantee free access to the material; copyright remains with the publisher or the author. There are at present more than 50 journals in PubMedCentral, with more soon to come online.

MEDLINEplus

The National Library of Medicine, in 1998, introduced an information service directed at the general public—MEDLINEplus. MEDLINEplus is a source of authoritative, full-text health information from the NIH institutes and a variety of non-Federal sources. The main features of MEDLINEplus: more than 600 “health topics,” from Abdominal Pain to Yeast Infections, detailed and consumer-friendly information about 9,000 brand name and generic and over-the-counter drugs, an illustrated medical encyclopedia and medical dictionaries, directories of hospitals and health professionals, a daily health news feed from the major print media, and 150 interactive and simply presented tutorials (with audio and video) about diseases and medical procedures. With one click in MEDLINEplus, one can even do a search using PubMed/MEDLINE to retrieve references and abstracts (and in some cases, full text) of biomedical journal articles. The most recent usage figures for MEDLINEplus attest to its growing popularity among the public and health professionals. In June 2003 there were more than two million unique visitors who viewed almost twenty million MEDLINEplus pages.

The Library has learned that many health professionals are finding MEDLINEplus to be an excellent source of information. They use it to keep current on medical subjects outside of their specialty. Others are referring their patients to MEDLINEplus for up-to-date and authoritative information about their health con-

ditions. One reason physicians feel comfortable in doing this is that they trust the imprimatur of the National Institutes of Health and the National Library of Medicine. They know that highly trained NLM information specialists follow strict guidelines in selecting Web pages that are appropriate to the audience level, well-organized, easy to use, educational in nature, and not selling a product or service. NLM receives a constant stream of testimonials from both the public and health professionals about how useful—clear and comprehensive—the system is.

Like MEDLINE, MEDLINEplus is a constantly evolving system. Links are checked daily and new health topics added weekly. In the days following September 11, entries on anthrax, smallpox, and other bioterrorism-related subjects were quickly compiled and for a while were even more heavily accessed than cancer information. The latest improvement is MEDLINEplus en Español, introduced in September 2002. It provides hundreds of links to health information in Spanish and is being constantly expanded. The next major improvement in MEDLINEplus will be to link users to local resources—city, county, state, and regional agencies and support groups. In this regard, a successful prototype of a statewide system has been developed with NLM support and introduced in North Carolina.

ClinicalTrials.gov

The MEDLINEplus health topics have links to a database of ongoing and planned scientific studies—ClinicalTrials.gov. Trials are conducted when there is no proven treatment for a specific disease, or to test which treatment works best for a particular disease of condition. ClinicalTrials.gov is a registry of some 7,700 protocol records sponsored by NIH and other Federal agencies, the pharmaceutical industry, and nonprofit organizations in over 75,000 locations, mostly in the United States and Canada, but also in some 70 other countries. The stimulus that brought the FDA, NIH, and NLM together to create ClinicalTrials.gov was the 1997 FDA Modernization Act. NLM designed the system and coordinates all input from the National Institutes of Health and, through the FDA, from industry.

ClinicalTrials.gov includes a statement of purpose for each study, together with the recruiting status, the criteria for patient participation in the trial, the location of the trial, and specific contact information. The site is used extensively by patients and health professionals, and hosts over 8,000 visitors daily. NLM has worked with the Food and Drug Administration in crafting FDA's "Guidance for Industry: Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions." Within six months following its release, ClinicalTrials.gov received over 400 protocols from pharmaceutical industry sponsors.

Human Genome Information

The National Center for Biotechnology Information, a component of the NLM authorized by the Congress in 1989, designs and develops databases to store genomic sequence information and creates automated systems for managing and analyzing knowledge about molecular biology and genetics. With the release of the "working draft" of the human genome, the global research focus is turning from analysis of specific genes or gene regions to whole genomes, which refers to all of the genes found in cells and tissues. To accommodate this shift in research focus, NCBI has developed a suite of resources to support the comprehensive analysis of the human genome and is thus a key component of the NIH Human Genome Project.

One of the principal resources is the GenBank database, a publicly available, annotated, collection of all known DNA sequences. The NCBI is responsible for all phases of GenBank production, support, and distribution, including timely and accurate processing of sequence records and biological review of both new sequence entries and updates to existing entries. GenBank is growing rapidly with contributions received from scientists around the world and now contains more than 15 million sequences and more than 14 billion base pairs from over 100,000 species; it is accessed on the web 200,000 times each day by some 50,000 researchers.

Scientists use not only the sequence data stored in GenBank, but avail themselves of the sophisticated computational tools developed by NCBI intramural investigators, such as the BLAST suite of programs for conducting comparative sequence analysis. Entrez is NCBI's integrated database search and retrieval system. It allows users to search enormous amounts of sequence and literature information with techniques that are fast and easy to use. Using this system, one can access NCBI's nucleotide, protein, mapping, taxonomy, genome, structure, and population studies databases, as well as PubMed, the retrieval system for biomedical literature.

Continued progress in our understanding of the relation between genes and disease requires that our information-handling capabilities keep pace with the voluminous data being generated by scientists. The assembled and annotated human genome sequence is allowing researchers to identify disease genes, decipher biological

mechanisms underlying disease, and design and develop therapeutic strategies for treating and preventing disease.

Mr. BILIRAKIS. Thank you very much, Dr. Lindberg. And, of course, there will be questions, and so you will have that opportunity.

Dr. Rohrbaugh, please proceed, sir.

STATEMENT OF MARK L. ROHRBAUGH

Mr. ROHRBAUGH. Chairman Bilirakis and members of the subcommittee, I am pleased to present to you a synopsis of NIH technology transfer activities both within the National Institutes of Health and at institutions receiving NIH funds.

First, I would like to speak to the NIH mission, which is to uncover new knowledge that will lead to better health for everyone. In furtherance of this mission, we conduct our technology transfer activities with the following goals in mind—to expand fundamental knowledge about the nature and behavior of living systems; to improve and develop strategies for the diagnosis, treatment, and prevention of disease; and to communicate the results of research to the scientific community and the public at large with the goal of improving public health.

One of the greatest challenges to realizing the promise of the NIH mission is the ability to translate basic research findings into drugs and therapies for patients. Translating a new drug discovery from the laboratory to an initial clinical evaluation in patients requires navigation of a multi-step review process involving several critical implementation issues over the course of 6 to 10 years.

This “bench to bedside” pathway often begins with the transfer of an early stage technology developed in the course of federally funded research to a private sector partner. While this is but one step in a lengthy and expensive process, it is often the step that jump starts the development of a new therapeutic product.

The overwhelming majority of the NIH budget—over 80 percent—is devoted to the support of scientists at approximately 1,700 organizations. This is what is known as our extramural program. A much smaller portion of our budget—slightly less than 10 percent—supports research and training conducted by the Federal scientists at NIH facilities. This is known as our intramural research program. I believe it is important to make this distinction while discussing technology transfer activities, because these two areas are governed by different legislative authorities.

In its broadest sense, technology transfer is the movement of information and technologies from research findings to practical application, whether for further research purposes or commercial products. At the NIH, we transfer technology through publications of research results, exchange of data, sharing materials, public-private partnerships, as well as the patenting and licensing of technologies.

The NIH Office of Technology Transfer administers over 1,500 active licenses and approximately 2,400 patents and patent applications. In fiscal year 2002, we received more than \$51 million in royalties from licensees. This accounts for about two-thirds of the royalties collected by all Federal laboratories combined.

About 200 products have reached the market that include technologies licensed from the NIH; 17 of these are vaccines and therapeutics. We view these products as the best and ultimate measure of our success in facilitating the transfer of technologies that the private sector develops into products that benefit the public health.

This leads me to a brief discussion of the Bayh-Dole Act of 1980, which applies to recipients of Federal funds. As you mentioned, Mr. Chairman, the Act provides incentives to move federally funded inventions to the private sector where they benefit the public. With a few exceptions, the legislation does not prescribe methods to be used in the licensing of these inventions, but the institutions must agree to pursue practical application of inventions, and to provide the U.S. Government with a royalty-free right to use the inventions for government purposes.

That Federal Government right does not extend from the federally funded technology to the final product, except in those rare cases where the technology is the final product. Moreover, this government right applies only to the patent—that is, the intellectual property—not to the materials themselves that constitute the physical embodiment of the invention. In most cases, a federally funded technology is combined with other intellectual property or know-how, often proprietary to a company, to develop the final product.

NIH-funded technology is usually at the earliest stage of development and requires much further investment to bring the technology to the marketplace. Thus, technology transfer is a high-risk venture, and few inventions ultimately result in products that reach the marketplace, yet the NIH has been fortunate in having a number of its technologies licensed and incorporated into methods of making, administering, or as components of new products.

In summary, the field of technology transfer facilitates the movement of research findings to promote further research or to develop them further into products of use to the public. It is through our statutory framework, unique institutions, and public-private partnerships that the Nation has created the most envied research enterprise in the world.

I can assure you, Mr. Chairman, and members of the subcommittee, that the NIH is committed to its mission of improvement of public health and will utilize all of the mechanisms it has to achieve this mission.

I thank you for the opportunity to come before you today, and I welcome any questions you may have.

[The prepared statement of Mark L. Rohrbaugh follows:]

PREPARED STATEMENT OF MARK L. ROHRBAUGH, DIRECTOR, OFFICE OF TECHNOLOGY TRANSFER, OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Chairman Bilirakis and Members of the Subcommittee, I am pleased to present to you a synopsis of NIH technology transfer activities both within the National Institutes of Health (NIH) and at institutions receiving NIH funds. I would also like to refer the Subcommittee to a report developed by the NIH, with input from patient advocacy groups, academia, and industry, on ensuring that the taxpayers' interests are protected. This report, titled "A Plan to Ensure Taxpayers' Interests are Protected," was submitted to the Senate Appropriations Committee in July 2001 and provides excellent background information on the nature of Government-funded research and drug discovery, the history of Federal agency technology transfer legislation, including the Bayh-Dole Act, and the ways in which the NIH ensures that the American taxpayers benefit from our technology transfer activities.

First, I would like to speak to the NIH mission, which is to uncover new knowledge that will lead to better health for everyone. In furtherance of this mission, we conduct our technology transfer activities with the following goals in mind: (1) to expand fundamental knowledge about the nature and behavior of living systems; (2) to improve and develop strategies for the diagnosis, treatment, and prevention of disease; and (3) to communicate the results of research to the scientific community and the public at large with the goal of improving public health.

One of the greatest challenges to realizing the promise of the NIH mission is the ability to translate basic research findings into drugs and therapies for patients. Translating a new discovery from the laboratory to an initial clinical evaluation in patients requires navigation of a multi-step review process involving several critical implementation issues over the course of six to ten years. These include issues relating to preclinical efficacy evaluation, drug production, preclinical safety assessment, regulatory documentation and approval, protocol design and approval, and a range of logistical issues regarding execution of the trial itself. This “bench to bedside” pathway often begins with the transfer of an early-stage technology developed in the course of federally-funded research to a private-sector partner. While this is but one step in a lengthy and expensive process, it is often the step that “jump-starts” the development of a new therapeutic product.

Our success in meeting the goals of our technology transfer activities depends on the ability to disseminate and share research findings with the research community and, when possible, to transfer findings into research and diagnostic tools and devices, and to assist in the development of therapeutic drugs and vaccines. Despite the lengthy and expensive process to bring research findings to use by the research community and the public, the NIH and federally-funded institutions have been able to bring new technologies forward to enhance the research enterprise and public health. This is due in part to the enactment of legislation to overcome a number of the issues that hampered research and development and the licensing of federally funded technologies for further development into products. Prior to the passage of the Bayh-Dole Act in 1980, many inventions arising out of government research sat on the shelf and were never commercialized into products to treat patients. Since 1980, these incentives have paved the way for the development of many new drugs, vaccines, and medical devices. These activities have also stimulated economic development and the creation of new jobs in the United States. My remarks will provide you with several examples of NIH technologies that have been of benefit to public health, and other speakers will be able to enumerate the successes they have been able to produce with Federal research funds.

The overwhelming majority of the NIH budget, over 80%, is devoted to the support of more than 200,000 scientists and their collaborators in the extramural research community who are affiliated with approximately 1700 organizations, including universities, medical schools, hospitals, and other non-profit and for-profit research facilities located in all 50 states, the District of Columbia, Puerto Rico, Guam, the Virgin Islands, and points abroad. This is what is known as our extramural program. A much smaller portion of our budget, slightly less than 10%, supports research and training conducted by Federal scientists at NIH facilities. This is known as our intramural research program. I believe it is important to make this distinction when discussing technology transfer activities, because these two areas are governed by different legislative authorities.

In its broadest sense, technology transfer is the movement of information and technologies from research findings to practical application, whether for further research purposes or commercial products. At the NIH we transfer technology through publications of research results, exchange of data, sharing of materials, public-private partnerships, as well as patenting and licensing technologies. Technologies licensed from the NIH include the HIV Test Kit, marketed by several companies including Abbott; Videx (ddI), marketed by Bristol-Myers Squibb for the treatment of HIV/AIDS; Vitravene, marketed by Isis Pharmaceuticals for the treatment of cytomegalovirus infections of the eye and the first product of its class; Zenapax, manufactured by Hoffman La Roche for the treatment of non-Hodgkin’s lymphoma and the first radioimmunotherapy to be approved; and Fludara, marked by Berlex as a treatment for chronic lymphocytic leukemia (CLL).

I direct the central technology transfer office at the NIH, which is located in the NIH’s Office of the Director. Our responsibilities can be viewed as twofold. First, we are responsible for the identification, evaluation, protection, marketing, and licensing of technologies arising out of NIH laboratories to achieve the agency’s mission. As a part of that activity, we monitor our licensees’ progress and collect royalties from licensed technologies. Secondly, we provide policy direction to the agency and to scientists and administrators receiving NIH funding. We also represent the Department of Health and Human Services on technology transfer matters. Other

technology transfer transactions, such as the negotiation of agreements to transfer materials and collaborations with private institutions, are conducted by technology transfer staff who are employed by the individual Institutes and Centers at NIH.

The activities of the Office of Technology Transfer are carried out by a well-qualified staff and supported by contractors, including 11 patent law firms. Members of our professional staff generally have at least one advanced degree, such as Ph.D., J.D., or M.B.A., and many have more than one advanced degree. Our staff administers over 1500 active licenses and approximately 2,400 patents/patent applications. In Fiscal Year 2002, we had 331 Employee Invention Disclosures, 173 patent applications filed in the United States, and 88 patents issued, and we executed 231 license agreements.

While we have these metrics as outputs of our activity, we have initiated through the GPRA process the development of a new metric to measure the ultimate outcomes of our activities. We have developed a system of case studies for technologies developed at the NIH and licensed to private sector partners for further development and commercialization. To date, we have completed two case studies: Havrix, the first vaccine against Hepatitis A; and Synagis, a therapeutic for a lower respiratory tract infection in infants and small children. This new metric provides a more complete view of the technology transfer process by providing a time line for the development of a technology into a final product, a description of the respective roles of the NIH and its private sector partner, and the impact of that new product on public health. It is that final measure that, we believe, provides the best indicator of success, since it addresses the NIH mission to improve public health. We expect to have three additional studies on our web site by the end of the calendar year, and we will be contracting for support to accelerate this process for all of products and materials that have reached the market utilizing at least in part technologies licensed from the NIH.

NIH intramural research technology transfer activities, as is the case for all federal research and development technology transfer activities, are governed by the Stevenson Wylder Act, the Federal Technology Transfer Act, and subsequent legislation. The original legislation was enacted in 1980 as part of an economic stimulation package for the U.S. economy. The legislation calls for the Federal laboratories to review their research findings to determine if they constitute new inventions, whether patent protection should be sought, and finally to use mechanisms such as licensing to move these new technologies to the private sector for further development and commercialization.

Our license agreements provide rights to use NIH technologies in return for royalty fees and, in the case of commercialization licenses, a commitment to bring the technology to the market. Fees are assessed usually on an annual basis throughout the term of the license or when certain milestones are reached. When a product reaches the market, our licenses call for a negotiated percentage of sales to be paid to the NIH. We have been able to generate strong returns from licensing activities. In Fiscal Year 2002, NIH generated \$51M in royalty income. That amount represented about two-thirds of the royalty income generated by all the Federal laboratories combined. Over the past 9 years, we have generated over \$325M in royalty income. By law, we pay a prescribed portion of royalty income to inventors, and the remainder of royalty income is used for technology transfer activities and for further research.

Our licensing policies, including the manner in which we grant licenses and structure the terms of those agreements, are also designed to promote the overall mission of the NIH. Exclusive licenses, which constitute a small portion of our total license portfolio, are granted when necessary as an incentive for a company to invest in the high-risk, long-term commercial development of a particular technology. While our statutory authorities for licensing inventions prescribe the conditions under which we can grant exclusive licenses, we go a step further in ensuring that exclusive licenses encourage the broadest development of new technologies for the public good. For example, the scope of a license to a single technology with broad applicability is usually limited to include only those aspects of the technology the company intends to develop and demonstrates the capability to develop. Thus, multiple aspects of a single technology may be exclusively licensed to multiple parties. For example, a technology for treating a variety of cancers might be licensed to one company for lung cancer therapeutics and to another for liver and pancreatic cancer therapeutics. In addition, we require licensees to provide a plan to ensure the rapid development of the technology. Our monitoring group has post-licensure responsibilities to ensure that the company reasonably complies with these terms.

This leads me to a brief discussion of the Bayh-Dole Act, which applies to recipients of Federal funds. This 1980 Act brought about a major change in governmental operations by permitting institutions receiving Federal funding for research and de-

velopment, as grantees and contractors, to retain title to any invention developed with the use of Federal funds. Prior to this time, title to these inventions generally reverted to the U.S. Government, where they rarely were moved to the private sector and thus did not benefit the public.

In return for the right to hold title to inventions developed with Federal funding, institutions agree to pursue practical application of those inventions and to provide the U.S. Government with a royalty-free right to use the invention for Government purposes. That Federal Government right does not extend from the federally-funded technology to the final product, except in those rare cases where the technology is a final product. Moreover, this Government license right applies to only the patent, that is, the intellectual property, not the tangible property that constitutes the physical embodiment of the invention.

The legislation did not prescribe methods to be used in the licensing of those inventions, with a few exceptions. Institutions electing title are required to give preference to small, U.S. businesses in licensing their technologies; exclusive licensees are required to manufacture their product substantially within the US when a product is to be used or sold in the US; licensing terms should not encumber future research and discovery; and non-profit organizations must obtain Government approval to assign title to third parties.

In most instances, NIH-funded technology, both in our intramural and extramural activities, is at the very early stage of development and requires much further research and development to bring the technology to the marketplace. The discovery may be a basic research finding without any animal testing or human clinical trials, a method for making or using a material, or a material that is only a part of the total technology that must be brought together to create a new product. As early stage technologies, they are highly risky projects for anyone to pursue and require a great deal of time and money to bring them to fruition. The closer a technology is to the marketplace, the lower the risk and cost to the licensee, and the more valuable the technology from a royalty standpoint.

However, in both academia and Federal laboratories, technology transfer is a high-risk venture, and few inventions ultimately result in products that reach the marketplace. The NIH has been fortunate in having a number of its technologies licensed and incorporated into the process of manufacturing, administering, or as one of the ingredients in making new prescription drugs, therapeutics, and vaccines. In most cases, a federally-funded technology is combined with other intellectual property or know how, often proprietary to a company, to develop a final product.

Due to the regulatory requirements on technologies that involve products used in humans, the development of biomedical technologies may take from 7 to 10 years to reach the market, if it ever reaches the market due to a high failure rate. This makes the biomedical technology development process expensive and risky.

The NIH has been quite successful in its pursuit of technology transfer activities and is viewed by many as one of the premier biomedical technology transfer operations in the world. We are pleased to report that NIH technologies have been licensed as part of the development of 17 prescription drugs and vaccines approved by the FDA. Again, we have not developed the final products; our technology is only a part of the process for making or administering the product or ingredients incorporated in the product. Overall, about 200 products are sold utilizing, at least in part, technologies licensed from the NIH.

I would also like to bring to your attention our biomedical research resources policy, known as our Research Tools policy. It is an important part of NIH's role to serve as a provider of technical assistance to NIH and recipient institution scientists and administrators. This policy arose from concerns in the scientific community that there appeared to be reluctance on the part of some institutions and researchers to share unique research tools at all or at least under reasonable terms. These tools include cells lines, strains of mice, reagents, monoclonal antibodies, and in some instances software. In response to the concern, the NIH asked a subgroup of the Advisory Committee of the Director to conduct a review. Their review found that these concerns were well founded and consequently recommended that the NIH develop guidelines for the research community to follow in combating the problem.

In 1999, NIH issued a document entitled, "Sharing of Biomedical Research Resources, Principles and Guidelines for Recipients of NIH Research Grants and Contracts." The policy applies to research tools developed with NIH funds and calls for the sharing of these tools among non-profit organizations with minimal terms and impediments. In the passage of the Technology Transfer Commercialization Act of 1999, P.L. 106-404, language was added in support of the tools guidelines when they amended the Bayh-Dole Act's purpose. The language was changed to state that inventions made under Federal funding are to be brought to practical application in

a manner to promote free competition and enterprise *without unduly encumbering future research and discovery.*

This policy is now a term and condition of NIH grants, and the latest information we have gathered indicates that this policy has significantly improved the sharing of materials between non-profit institutions, has improved sharing between non-profit institutions and for-profit entities, and reportedly has also improved the sharing by for-profits with non-profit entities. We continue to monitor this area to ensure that our recipients are complying with the intent of the policy.

While my comments have centered mostly on licensing activities, I have mentioned other technology transfer mechanisms including public-private partnerships, such as Cooperative Research and Development Agreements (CRADAs) and Clinical Trial Agreements. I would be pleased to provide information on these mechanisms if the Subcommittee so desires.

In summary, the field of technology transfer combines legal, business, and scientific skills to bring about the movement of research findings to promote further research or to develop them further into products of use to the public. It is through our statutory framework, unique institutions, and public-private partnerships that the Nation has created the most envied research enterprise in the world. I can assure you, Mr. Chairman and members of this Subcommittee, that the NIH is committed to its mission of improvement of public health and will utilize all of the mechanisms it has to achieve that mission. I thank you for the opportunity to come before you today and I welcome any questions you may have.

Mr. BILIRAKIS. Thank you very much, Doctor.
Dr. Barker?

STATEMENT OF ANNA BARKER

Ms. BARKER. Good morning. Thank you, Mr. Chairman and members, for the opportunity to be here today to discuss a new task force that the NCI has established with the Food and Drug Administration. I have the privilege of co-chairing that task force, along with Dr. Mullin, who will speak after me.

Before highlighting the mission and work of this task force, I would like to focus just briefly on the stunning advances in biomedical research over the past few years that recently led our Director at the National Cancer Institute, Andy von Eschenbach, to challenge the cancer community with a goal, and that goal is to eliminate suffering and death due to cancer and to do it by 2015.

That is a daunting and challenging goal for all of us. Why do we believe that that is a feasible goal, even though it is a major challenge? The reason is that progress in research over the past few years has led to unimagined advances across the entire research continuum of discovery, development, and delivery. As a result, we have reached an inflection point in research, meaning that progress from this point forward can be unprecedented and nearly unimagined.

The sequencing of the human genome, which you heard about from Francis Collins recently, and associated progress in new areas such as genomics and proteomics, are allowing us to dissect out the genetic changes and mechanisms that actually produce cancer. We now understand that cancer is a process—a process with multiple opportunities to develop new, more effective interventions to detect, treat, and prevent this disease.

The development of targeted therapies and preventives for cancer is really within our grasp. For the first time in our national effort to conquer this devastating disease, we have proof of concept. What do I mean by that? With new targeted drugs, such as Gleevec that you just heard about from Dr. Lindberg, we are on the threshold, we believe, of a paradigm shift in the way we treat cancer. This

new approach is based on targeting specifically molecular defects in tumor cells, and we believe this will allow us to move from a model of toxic, moderately effective agents, to highly efficacious drugs with minimal toxicity.

Genomics and proteomics, combined with progress in bioinformatics, immunology, nanotechnology—and I could go on—other areas of science, also offer us the ability to detect cancer early before it metastasizes, and to adopt rational approaches, finally, for preventing the disease.

To achieve this goal of eliminating suffering and death from cancer, we must match the extraordinary advances in basic science fueled, in large measure, by the doubling of the NIH research budget over the last 5 years. We must also make progress in translating that research into patients and delivering those agents to people in need.

To optimize and hopefully accelerate efforts to translate these advances from the laboratory into the clinic, we have undertaken a range of new initiatives. Our new partnership with the FDA is one of those initiatives. There are others.

NCI has a long history of working with the FDA to deliver safe, more effective drugs to patients as soon as possible. For example, a currently ongoing program at the NCI and the FDA in clinical proteomics is allowing our agencies to jointly provide the foundation for the new development of proteomics-based diagnostic technologies.

These new revolutionary technologies developed through the clinical proteomics program have generated protein fingerprints, or patterns, that may provide early warnings of cancer and offer new ways to measure drug side effects. This collaboration has yielded the identification of more than 130 proteins in cancers of the breast, ovary, and prostate, the change in types and amounts as the cells in these tissues grow abnormally, and they can be detected.

NCI and FDA staff will continue to develop this particular program and use it as a foundation, along with others, to build initiatives in other areas, such as diagnostic imaging and molecular targeting.

Although it is early in the work of this taskforce, Dr. Mullin and I and our colleagues have just begun. We have identified several areas of common interest across this continuum of research, including the development of a formal interagency agreement, which will allow us to do several things, common bioinformatics platforms, and joint programs to further optimize the processes that we undertake to develop drugs, including science-based models for endpoints to assess clinical benefit patients.

And, finally, joint training programs and appointments for staff—although I don't have time during my opening comments to discuss each of these activities, we anticipate that each of these focus areas will be valued in our joint efforts. For example, a common bioinformatics platform will be key to improving the reporting of data across the continuum of drugs and device discovery and development, especially in areas such as reporting of clinical trials.

This is a key step in evaluating the safety and efficacy of new drugs and technologies in patient populations. Since both agencies

have significant strengths in these areas, we are exploring ways to leverage both of our capabilities.

The task force will also examine science-based strategies that could enable the development of standard approaches for evaluating potential biomarkers of clinical benefit. Some of these biomarkers and technologies may some day serve as surrogate endpoints for the conventional measures that we usually use to measure clinical benefit and clinical trials.

Finally, all of these initiatives will benefit from staff training and joint appointments of staff and fellows, who will have training rotation at both agencies. The task force is currently assessing existing programs that offer opportunities for joint training and appointments, as well as determining needs for efforts in areas such as new technologies.

In conclusion, the goal of this task force is to ensure that the NCI and the FDA work together more effectively than ever before for the benefit of cancer patients and their families. With over 1.4 million Americans expected to be diagnosed with cancer this year, and 560,000 people expected to die from this disease—1,500 people today—NCI is committed to meeting the challenge of eliminating suffering and death from this tragic disease.

We anticipate that this new alliance with the FDA will facilitate a seamless continuum across discovery, development, and delivery of new cancer drugs and devices that will be needed to achieve our goal.

Our Director, Dr. von Eschenbach, features on the cover of our plan for 2004 made the following statement, “When I look into the eyes of a patient losing the battle with cancer, I say to myself it just doesn’t have to be this way.” We are committed to ensuring that it just doesn’t have to be this way.

Thank you again for this opportunity to discuss this new initiative. We are excited about this new collaboration with the FDA. And I would be happy to answer any questions when we get to the question period.

Thank you very much.

[The prepared statement of Anna Barker follows:]

PREPARED STATEMENT OF ANNA BARKER, DEPUTY DIRECTOR FOR STRATEGIC SCIENTIFIC INITIATIVES, NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Good morning, I am Dr. Anna Barker, Deputy Director for Strategic Scientific Initiatives for the National Cancer Institute (NCI) of the National Institutes of Health within the Department of Health and Human Services, and Co-chair of the NCI/FDA Oncology Task Force.

Thank you, Mr. Chairman and distinguished members of the Subcommittee, for the opportunity to be with you this morning to discuss the National Cancer Institute’s recent announcement of the formation of joint Task Force with the Food and Drug Administration (FDA). The mission of the Task Force is to work together to explore areas of mutual interest and responsibility that could better inform and optimize the development and review processes for new cancer drugs and technologies. The scope of this Task Force includes several areas of common interest including the extension of current collaborations and the development of: 1) a formal inter-agency agreement; 2) bioinformatics platforms; 3) joint programs to further optimize each agency’s research and regulatory processes; 4) science-based models for endpoints to assess clinical benefit in patients; and 5) joint training programs and appointments for staff. NCI is committed to meeting the challenge of eliminating suffering and death due to cancer by 2015; and we anticipate that this collaboration

with the FDA will help to achieve that goal by providing safe, more efficacious cancer drugs to patients sooner.

With over 1.4 million Americans diagnosed with cancer each year, NCI recognizes the need for a closer collaboration with the FDA in order to best serve patients' needs. NCI's goal, in furthering all of its collaborations with the FDA, is to work jointly to improve communication and outcomes in key areas of cancer drugs, especially targeted agents and diagnostics development. This alliance with the FDA will focus on the development of a seamless continuum between discovery, development, and delivery of new cancer drugs and devices.

Exponential growth in biomedical research and the explosion of enabling technologies have resulted in a "new science" of oncology. Since there is still a great deal that we must learn about cancer, we must continue to support the biomedical research that drives this engine of discovery. In parallel, it is critical that we translate our understanding of cancer beyond the cell into the individual and into specific populations. The sequencing of the human genome and our sustained investment in all areas of biomedical research have led to an ever-increasing fundamental understanding of cancer as a disease process. This foundation of knowledge now provides us with multiple opportunities to intervene at various steps of this process through the development of new drugs and technologies to detect, prevent, and treat cancer. We must capitalize on this 21st century "inflection point" in cancer research, accelerate the translation of knowledge into new interventions for cancer patients, and ensure that they are delivered to all who are in need.

The collaboration between the NCI and the FDA will be formalized through an interagency agreement. Interagency agreements between government agencies allow and facilitate the exchange of services, supplies, advice, counsel, and funds. NCI has several successful Interagency Agreements already in place with the FDA, including the Cooperative Center for Biologics Evaluation and Review-NCI Microarray Program for the Quality Assurance of Cancer Therapies and other Biological Products, and the FDA-NCI Clinical Proteomics Program. The clinical proteomics initiative has allowed our agencies to jointly provide the foundation for the development of proteomics-based diagnostics technology.

Proteomics is the study of the proteins that are produced by cells to carry out the specific tasks that underlie most of our life processes. New technologies that were developed through the Clinical Proteomics Program have generated protein fingerprints that may provide early warnings of cancer and offer new ways to measure drug side effects. This collaboration has yielded the identification of more than 130 proteins in cancers of the breast, ovary, and esophagus that change in types and amounts as the cells in these tissues grow abnormally. The assessment of these patterns may provide new means of diagnosing and treating cancers earlier. Most recently, this collaboration has produced a new technique that may allow physicians to monitor patients' responses to molecularly targeted drugs. In one study, researchers successfully identified specific proteins that may be useful in monitoring patients treated for breast and ovarian cancer. This approach could assist physicians in monitoring patients on therapy to determine if a particular drug is working effectively. The NCI-FDA proteomics team has developed new tools for visualizing and analyzing protein patterns that reduces the risk of error, increases productivity, and provides an efficient method to analyze large sets of protein data. NCI and FDA staff will continue to develop this clinical proteomics collaboration and use it as a foundation to build initiatives in other areas, such as diagnostic imaging and molecular targeting.

The FDA-NCI Task Force will also explore opportunities to facilitate the sharing of information technologies and tools that may further optimize the drug and device development process. To this end, the Task Force has established a working subgroup to examine the potential of creating an overarching and inclusive bioinformatics structure that is capable of capturing and integrating data from pre-clinical, pre-approval, and post-approval research across all the sectors involved in the cancer drug development and delivery process. Bioinformatics is a key linkage across the discovery, development, and delivery continuum—and common data platforms for communication will be key to future progress. A new NCI initiative, the NCI Cancer Bioinformatics Grid (CaBIG), which will be piloted in a selected number of NCI cancer centers and programs this year, will provide tools and expertise to support the achievement of this goal.

Common bioinformatics platforms will serve to facilitate the performance and reporting of clinical trials—a key step in evaluating the safety and efficacy of new drugs and technologies in patient populations. The Task Force also plans to identify opportunities to optimize other interfaces that occur across the continuum of drug and device development and delivery. An additional focus of the group's efforts to optimize the work of all sectors is the further development of biomarkers; which

have the potential to optimize and accelerate both the discovery and development of new targeted cancer drugs for treatment—and to improve diagnostics for early detection of cancer.

The group will mutually examine science-based strategies that could enable the development of standard approaches for evaluating potential biomarkers of clinical benefit. Some of these biomarkers and technologies may someday serve as surrogate endpoints for the conventional measures of clinical benefit currently being used to assess new agents and technologies. NCI and FDA will explore ways to develop the science required for the development of evidence-based standards and approaches to evaluate these endpoints. A portion of this effort will also be dedicated to further study of standards and processes that could facilitate the development of safe agents for cancer prevention, especially chemoprevention.

Finally, all of these initiatives will benefit from staff training and joint appointments of staff and fellows, who will have training rotations at both agencies. The Task Force is currently assessing existing programs that offer opportunities for joint training and appointments as well as determining opportunities for new efforts in areas such as new technologies.

In conclusion, the goal of this Task Force is to ensure that the NCI and FDA work together more effectively than ever before—for the benefit of cancer patients and their families. We have a tremendous opportunity to optimize and hopefully to accelerate the development process for new cancer drugs and diagnostics. Bridging the gaps between research and regulatory processes benefits everyone involved, especially cancer patients. Building on past collaborative efforts with FDA, and working toward the development of a seamless continuum between the discovery, development and delivery of safe and effective drugs, will help the NCI achieve its goal of eliminating suffering and death due to cancer by 2015.

Thank you again for this opportunity to discuss NCI's new collaboration with FDA to optimize and accelerate the development of safe and more effective drugs and technologies to detect, prevent, and treat cancer. I will be happy to answer any questions that the Subcommittee may have.

Mr. BILIRAKIS. Thank you very much, Dr. Barker.
Dr. Mullin?

STATEMENT OF THERESA M. MULLIN

Ms. MULLIN. Good morning, Mr. Chairman, Ranking Member Brown, and members of the subcommittee. I am Theresa Mullin, the Assistant Commissioner for Planning at the U.S. Food and Drug Administration.

And since January of 2003, I have been directing FDA's development of a new strategic plan, have played the lead role in coordinating the Agency's new initiative to "Improve Innovation in Medical Technology Beyond 2002." And I am co-chairing with Dr. Barker the Interagency Oncology Task Force, and we appreciate the opportunity to testify with NCI about our collaborative efforts to facilitate drug development.

Today, I would like to provide FDA's perspective on why we are entering into this collaboration and what we hope to achieve.

FDA's primary role is to ensure the safety and effectiveness of drug products through pre-market drug review and post-marketing safety. Today I will focus on our role in the pre-market phase.

There are several phases to drug development, and FDA interacts with product sponsors all along the way. This enables the sponsor to focus research on studies of compounds that are likely to lead to approval. And after completing and analyzing their research, sponsors, including NCI-funded researchers, file an application with FDA. The application provides evidence from clinical trials to demonstrate that a product is safe and effective for its intended use.

By setting clear standards for the evidence that we need in order to approve a product, we can take the guesswork out of the process.

Under the prescription drug user fee program, FDA is committed to goals for fast review and action on submitted applications. For example, we are committed to completing the review and acting on 90 percent of submitted priority applications within 6 months.

In 2002, FDA continued to meet those review goals, but the number of approvals for truly new drugs is now at the lowest level we have seen in about 10 years. This is directly related to the decline in the number of applications submitted to FDA for new drugs, new molecular entities, and biologic licensing applications. But this is a worldwide phenomena right now.

This chart you see over here with the bars shows you the trends in filed applications and those approved. The line shows the number of filed applications, and this is just looking at new molecular entities. That is the really new drug applications and biologic licensing applications, and the bars show the number of approvals for those kinds of products. And you can see that there really is a pattern that follows. What we get submitted to us is what we can work with for approvals.

But we think that this is temporary, because at the same time that that is occurring the government and industry are spending significantly increased amounts of funds on research and development, and there are a lot of complex and innovative new products in development, as Dr. Barker was describing and others have described. And so we see this as an opportunity for FDA and NCI to move more products to applications.

In January of this year, FDA launched an initiative to improve innovation in medical technology, and that focuses on trying to maximize our efficiency in reviewing and communicating with sponsors, and also trying to put out the best guidance possible for sponsors to speed development all along the pipeline.

My second chart shows the drug development pipeline, and the lettering in orange—it is too small for you to read I think from where you are sitting, but it describes some of the problems that sponsors may face in trying to develop products all along the way. And below that we have in green, which I am afraid you also can't see, what FDA—the kinds of actions that FDA is trying to take all along the way to help products move as quickly as possible.

And as part of that initiative, we will be clarifying regulatory pathways for some emerging technologies, for example, cell and gene therapies. And we are developing guidance to help specify the clinical endpoints for clinical trial design, and so that we can get the best quality applications possible submitted, and that allows us to avoid delays in approval and helps reduce development costs.

Our collaboration with NCI and the interagency task force is really a great fit to what we are trying to do in this more general way and allow us to expand and strengthen our work in trying to develop new cancer drugs and helping with speeding the drug—development of cancer products.

The NCI/FDA collaboration will provide FDA reviewers with some exposure—additional exposure to state-of-the-art technologies, and that will give them a better understanding of those technologies for products in development. By the same token, NCI researchers could benefit from hands-on experience with the FDA review process to understand better the kinds of evidence of safety

and effectiveness that are looked for for quick approval of new products.

Although the interagency task force is at its early stages, we are considering several areas—I will be brief here, because Dr. Barker has described them—but joint training and fellowships, development of markers of clinical benefit, including surrogate endpoints, information technology infrastructure to better collect and share data, and improve the development process.

We look forward to collaborating with NCI in building on the Institute’s cancer bioinformatics infrastructure to streamline data collection, for example, integrating data analysis for preclinical, preapproval, and postapproval research. This spans all of the sectors in development and delivery of new cancer therapies, and we are hopeful that that collaboration will ultimately help reduce the reporting burden for clinical investigators and improve the quality of the data.

The Tufts Center for the Study of Drug Development has noted that faster development times and quicker decisions to terminate unsuccessful compounds and higher success rates provide industry with substantial savings in drug development. But NCI is also engaged in development and, clearly, they should also benefit from those opportunities. So the discussions of our task force will probably yield additional ideas for streamlining the process.

In conclusion, FDA’s safety and effectiveness standards are viewed by many as the gold standard, and FDA is recognized as a world leader in both quality and speed of regulatory review. We believe that FDA and NCI’s new interagency oncology task force will further our goals in providing new drugs for patients who need them as swiftly and cost effectively as possible.

I am happy to answer any questions you have.

[The prepared statement of Theresa M. Mullin follows:]

PREPARED STATEMENT OF THERESA M. MULLIN, ASSISTANT COMMISSIONER FOR PLANNING, FOOD AND DRUG ADMINISTRATION

INTRODUCTION

Mr. Chairman, Ranking Member Brown and Members of the Subcommittee, I am Theresa Mullin, Assistant Commissioner for Planning at the U.S. Food and Drug Administration (FDA or the Agency). I advise and assist the Commissioner concerning the performance of FDA planning, evaluation and economic analysis activities. Since the beginning of January 2003, I have been directing FDA’s development of a new strategic plan and have played a lead role in coordinating the Agency’s new initiative to “Improve Innovation in Medical Technology Beyond 2002.” I am also Co-Chair of the National Cancer Institute (NCI)/FDA Interagency Oncology Task Force, which involves senior staff from both agencies.

We appreciate the opportunity to testify with NCI about our collaborative efforts to facilitate cancer drug development. As you may know, we are at the very beginning of this new initiative, but this is a goal that both agencies have shared. Today I will provide FDA’s perspective as to why we are entering into this collaboration and what we hope to achieve.

FDA’S DRUG DEVELOPMENT PROCESS

FDA’s primary mission is to protect and promote the public health. One way we do this is by promptly and efficiently reviewing investigational new drug applications (INDs) for clinical studies within 30 days of submission by the product sponsor. In addition, FDA reviews new drug applications (NDAs) and biologics license applications (BLAs) and does so on an expedited basis for applications with priority status, such as those for new cancer drugs. We also monitor 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.

There are several phases to drug development, and FDA makes itself available to interact with product sponsors during this process (see Attachment A, Drug Development Pipeline). Meetings requested by the sponsor provide an important venue for communication. 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 1,000 such meetings with sponsors each year. Meetings with FDA can help sponsors to clarify research questions that need to be addressed, identify earlier the unsuccessful compounds, and focus research on studies of compounds that are likely to lead to approval. The Tufts Center for the Study of Drug Development has cited earlier consultation between FDA and sponsors as a key factor in reducing drug development time. Tufts estimates that shifting 5 percent of all clinical failures from Phase III/regulatory review to Phase I would reduce out-of-pocket clinical costs by up to \$20 million.

Upon completing and analyzing their research, sponsors, including NCI-funded researchers, send us applications providing evidence from clinical trials to demonstrate that a product is safe and effective for its intended use. We assemble a team of physicians, statisticians, chemists, biologists, microbiologists, pharmacologists, and other scientists to review the sponsor's data and proposed labeling for the drug. By setting clear standards for the evidence we need to approve a product, we try to take the guesswork out of the process and help medical researchers bring new products to American consumers more rapidly.

Once a drug is approved for sale in the United States, our consumer protection mission continues. We monitor the use of marketed drugs for unexpected health risks. If new, unanticipated risks are detected after approval, we take steps to inform the public and change how a drug is used or even remove a drug from the market. We also monitor manufacturing changes to make sure they will not adversely affect safety or efficacy. We evaluate reports about suspected problems from manufacturers, health care professionals and consumers.

As the pharmaceutical industry has become increasingly global, we are involved in international negotiations with other nations to harmonize standards for drug quality and the data needed to approve a new drug. This harmonization can assist in reducing the number of redundant tests manufacturers do and help ensure drug quality for consumers at home and abroad.

CURRENT STATUS OF FDA NEW DRUG APPROVALS

By the end of 2002, FDA was able to meet all of the review goals for NDAs and BLAs established under the Prescription Drug User Fee Act. We evaluated many new drugs that offered important treatment options for Americans. Thanks to the enormous growth in research investments, more complex and innovative products are in development. We see this situation as one of great opportunity, and FDA is doing its part to help sponsors capitalize on the opportunities presented. However, we are concerned that the number of approvals for truly new drugs is at the lowest level in a decade, and this is directly related to the decline in the number of new applications for drugs and biologics being submitted to the Agency for approval. This trend is illustrated in the bar chart depicted in Attachment B. This pattern is occurring at the same time that the government is allocating significantly more resources to promote research, and the pharmaceutical industry has increased spending on research and development to more than \$30 billion per year.

FDA MEDICAL TECHNOLOGY INITIATIVE

In January of this year, FDA launched an initiative to improve the development and availability of innovative medical products. We recognize that early communication with sponsors is essential to achieve the Agency's goal to further reduce delays and avoidable product development costs, and also to improve the quality of new product applications. With the complex new technologies in development, FDA sees an opportunity to reduce the uncertainty for product innovators, including small companies with limited experience bringing a medical technology to commercial development. We are working to clarify regulatory pathways for emerging technologies, by, for example, working to further characterize, and define the dosing for new products like cellular and gene therapies. Also, we think it would help sponsors for FDA to update current guidance and provide new ones that specify clinical endpoints, including surrogate endpoints, such as tumor shrinkage, that will provide good evidence of safety and effectiveness for new treatments for particular diseases.

FDA hopes to facilitate the development of new technology by addressing and clarifying regulatory uncertainty and by increasing the predictability of product development. Some of the steps FDA is taking under its new initiative to more quickly facilitate the drug development process are listed in Attachment A.

In addition to doing what we can to help sponsors improve the quality of their data and submitted applications, the Agency is also taking steps to further improve its application review process by identifying and addressing the causes of avoidable delays in new drug review. This month we expect to publish a request for proposals to conduct both a retrospective analysis and a prospective evaluation of our review process and to provide us with ideas for possible process improvements based on comments from both FDA staff and drug sponsors.

NCI-FDA COLLABORATION

FDA is committed to finding better ways to get safe and effective treatments to patients with life-threatening diseases as quickly as possible. FDA's participation in the NCI-FDA Oncology Task Force is consistent with the Agency's initiative to improve the development and availability of innovative medical products. FDA's role is to help ensure the safety and effectiveness of drug products through the pre-market drug review process and through post-marketing programs. Through basic and clinical biomedical research and training, NCI conducts and supports programs to understand the causes of cancer; prevent, detect, diagnose, treat, and control cancer; and disseminate information to the practitioner, patient, and public. NCI's clinical research for new drug development is also subject to FDA regulation and oversight.

The NCI-FDA collaboration will provide FDA with exposure to state-of-the-art technology that will enable the Agency to have a better understanding of new products in development. Similarly, NCI will benefit from hands on experience with FDA's review process that will help it to conduct and oversee research to provide evidence of safety and effectiveness, resulting in faster development of approvable products. We are hopeful that our collaborative efforts will result in better communication between reviewers and researchers, which we believe is essential to improving the development and availability of innovative medical products. Though the Task Force is in its early stages, we are considering several areas of collaboration including: joint training and fellowships; developing markers of clinical benefit, including surrogate endpoints; information technology infrastructure to better collect and share data; and ways to improve the drug development process.

Joint Training and Fellowships

Staff capabilities can be enhanced through collaborative training, joint rotations, and joint appointments. We hope that bridging gaps between research and regulatory processes will make the drug development process more efficient. As noted above, early effective communication between researchers and reviewers is critical in product development. Cancer drugs are typically designated by FDA as priority review products and are eligible to be designated as "Fast Track" products. Beginning in fiscal year 2004, FDA will be piloting two programs to provide earlier FDA review and feedback for "Fast Track" products while they are still in development.

While a primary goal of the NCI/FDA collaboration is to provide cross-fertilization between the two agencies, the Task Force will also explore the possibility of a nationwide program to rotate fellows through FDA and NCI who have completed their training in medical oncology.

Developing Markers of Clinical Benefits

The Medical Technology Initiative that FDA announced last January included a series of collaborative discussions with the American Society of Clinical Oncology to identify appropriate endpoints for clinical trial design for cancer therapies, by type of cancer and stage of disease. NCI is also involved in this process. These identified endpoints will be published in guidance documents. Such guidance documents, developed in collaboration with other government and academic organizations, the pharmaceutical industry, health practitioners and patients, can help sponsors structure claims, offer proven standardized approaches to evaluating efficacy, and give insights into safety testing. In NCI-FDA's Interagency Task Force discussions to date, there has been interest in further extending this work and in further identification of clinically valid surrogate endpoints.

NCI and FDA will also continue their current collaboration involving proteomics, the discovery of protein markers in the blood that can be used to detect and monitor disease course and drug response. In addition, FDA's Center for Biologic Evaluation and Research is currently collaborating with NCI on a Microarray Program for the Quality Assurance of Cancer Therapies including therapeutic cancer vaccines and other cellular and gene therapy biological products. The Microarray Program has

provided a foundation for the identification of new molecular targets, understanding of the mechanism of action of targeted cancer therapeutics, and characterization of complex therapeutic cancer vaccines. As potency and identity of these cancer vaccines is difficult to assign, the genomics (study of genes)-based technology provides a novel approach to achieving this goal.

Information Technology Infrastructure

FDA looks forward to collaborating with NCI building on its cancer bioinformatics infrastructure to streamline data collection, integration and analysis for pre-clinical, pre-approval, and post-approval research across all of the sectors involved in the development and delivery of cancer therapies. We are hopeful that this collaboration may ultimately reduce the reporting burden for clinical investigators and improve the quality of reported data. Some proposals being considered are: creation of a shared repository for clinical investigator Curricula Vitae (CVs) to keep current and to eliminate the requirement of repeated submissions of such CVs. Another proposal being explored is for development of templates for INDs and clinical trial protocols to simplify the process of creating and submitting these documents and improve the quality of submissions. NCI grantees may also be product sponsors that FDA regulates. Given this dual role, there may be duplicative reporting requirements that we may be able to streamline through this collaborative effort.

Improving the Drug Development Process

Tufts Center for the Study of Drug Development has noted that faster development times, quicker decisions to terminate unsuccessful compounds, and higher success rates would enable industry innovators to reap substantial savings in the cost of new drug development. NCI is the sponsor of many cancer studies regulated by FDA. They too can benefit from faster development times, quicker decisions to terminate unsuccessful products, and higher success rates.

CONCLUSION

The safety and effectiveness standards for drug review and approval in the U.S. are viewed by many as the “gold standard.” FDA is the recognized world leader in both the quality and speed of regulatory review. The scientists at FDA constantly strive to maintain these high standards and we believe that the new NCI-FDA Interagency Oncology Task Force will further our goals of providing new life-saving drugs to patients who need them as swiftly and cost-effectively as possible.

I am happy to answer any questions you may have.

Mr. BILIRAKIS. Thank you very much, Dr. Mullin.

I hear your testimony, and all I can think of is wow. Yet at the same time, think back—I lost my sole surviving brother this last April to lung cancer, and, you know, it makes me wonder. You know, all of these good things are taking place, but he wasn’t helped.

Let me ask Drs. Barker and Mullin very quickly, is the task force—has the task force been created—and it sounds like gangbusters to me, so I commend you for it. But was it created because the feeling was that there is just a lack of proper coordination among NCI and FDA? What would you say there?

Ms. MULLIN. I will speak first, if Dr. Barker—

Mr. BILIRAKIS. Yes, very quickly.

Ms. MULLIN. I think we actually see that we have a lot of good success, that it looks like a great opportunity to build on what we have got already. There are a number of collaborations going on, and we want to take it up to the next level, I think, and do it more broadly. We see a lot of synergy.

Mr. BILIRAKIS. Should the same thing be done regarding other diseases, other institutes, etcetera?

Ms. MULLIN. I think so, and I know our Commissioner, Dr. McClellan, is reaching out. And we are looking for opportunities to do this.

Mr. BILIRAKIS. Is he? Great.

Ms. MULLIN. Yes.

Mr. BILIRAKIS. Okay. Dr. Barker, is there anything you wanted to add?

Ms. BARKER. I would just add, actually, I think it is more opportunity than anything else. In the cancer arena especially, we have a pipeline of a hundred, maybe thousands of opportunities for new drugs and diagnostics. And I think we want to do everything we can to help the FDA by bringing our science forward in ways that can inform these processes.

And it helps that I think that within 24 hours actually of Dr. McClellan's appointment, Dr. von Eschenbach was in his office offering him the opportunity to work with him. Dr. McClellan was enthusiastic about this, and the task force just grew out of that almost immediately. So I think we are all committed to this.

Mr. BILIRAKIS. That is terrific, and I do think it should be considered for other diseases.

Dr. Lindberg, are you aware of any research materials produced largely in part by federally funded projects that are not made publicly available? And if they are, if that is the case, why aren't they?

Mr. LINDBERG. I don't, but there is a variety of mechanisms involved. NLM really deals with the published scientific literature, and generally speaking there is not a great amount of delay in bringing forward those announcements.

In addition to the literature itself, of course, this sometimes involves materials—organisms or tissues or whatever—as an integral part of the research. And NIH has taken the formal position of stating that it wants to encourage the ready availability of both kinds of results of research funded by public funds as quickly as possible.

Mr. BILIRAKIS. Well, you illustrate in your written testimony how health care providers are able to access journal articles on Medline in order to get up-to-the-minute information, etcetera. Obviously, it is an undeniable benefit. But I am curious about what type of doctors have been able to take most advantage of this service. Are the patterns of utilization different between doctors who practice in urban areas versus those who practice in rural or frontier communities?

And, of course, I would ask: does the Library have the capability to track this type of information? Otherwise, you wouldn't be able to answer my question, right?

Mr. LINDBERG. We are concerned about all of those things. Historically, actually, the Library has taken the point of view that it would pay for the communication costs, even before there was Internet, so that there was exact parity whether you practice in a rural area or a metropolitan area, because the communication costs were absorbed in what were earlier the charges for the search.

We do, however, worry more about the availability of computers and Internet connections on the part of the public, because we think probably only half of the people really have that access. And so we have initiated a string of experiments with public libraries, because they are more numerous and they are more likely to be at a community level, asking ourselves whether the public would bring medical questions to the library, what are the nature of the questions, how good are the answers, how can we help.

And in all cases, we found that it is actually a very good strategy. People do bring questions to the libraries. In many cases, they get very, very good answers, and what worried me was, how can we help? Because I was afraid that they were going to say that we would like you to provide \$10 interlibrary loans to 100 million people.

But, in fact, the answer was that the public library people would like instruction from the medical people on how to do these sort of searches, and that, of course, is readily available. So that is a somewhat long-winded answer to your good question.

Mr. BILIRAKIS. Well, you have indicated a possible lack of computers, but could a country doctor, for instance, pick up the telephone and call the Library of Medicine and—

Mr. LINDBERG. Oh, absolutely.

Mr. BILIRAKIS. [continuing] get the information that they might need?

Mr. LINDBERG. Yes, sir. Happens all the time.

Mr. BILIRAKIS. It happens all the time.

Mr. LINDBERG. Yes.

Mr. BILIRAKIS. So my son who is an internist—I don't know, how long has he been out of medical school now? Ten years I—anyhow, he would know that the Library of Medicine is available for this type of information?

Mr. LINDBERG. I am pretty certain that he would. We get about a million calls a day.

Mr. BILIRAKIS. I guess I will have to ask him that. You do, a million calls a day?

Mr. LINDBERG. Yes.

Mr. BILIRAKIS. Wow.

Mr. LINDBERG. And of that, about 30 percent actually are non-doctors, non-scientists, ergo members of the public. Of course, we know we can all wear more than one hat. But basically about a third of the use of the Library is now the public, and we are very happy about that.

Mr. BILIRAKIS. Okay. Thank you. Thank you very much.

Mr. Brown?

Mr. BROWN. Thank you, Mr. Chairman.

I would like to ask all four panelists one sort of central—at least central in my mind—question. I would start with the technology transfer of Taxol, which has been a very successful—for the public and successful for Bristol-Meyers and successful for the government—drug.

I think that the facts generally are well known—the GAO report of earlier this summer. NIH invested \$484 million on discovering/developing Taxol, most of that from the National Cancer Institute. Some of that money was to begin the clinical trials. Bristol-Meyers told GAO, although GAO seems to look at this number with a bit of skepticism, that once they were given the drug to produce and market they spent somewhere in the vicinity of a billion dollars, including their clinical trial costs.

The government began the clinical trials. Bristol-Meyers, during that period, provided—supplied the drug, \$90 million or so worth of the drug it cost them, and then, as I said, they told—Bristol-

Meyers has told GAO they spent about a billion dollars total on the clinical trials.

Bristol-Meyers made \$9 billion in profits. For several years running, they made a billion dollars a year. But overall, from 1993 to 2002, they made \$9 billion. NIH negotiated a royalty rate of five-tenths of 1 percent, which resulted in the government getting back \$35 million in royalties.

I would add also that of the \$9 billion in profits in those 10 years, a significant amount of that came from the government—Medicare, I assume, and hospital costs, because Medicare, as we know, doesn't have a drug benefit. Medicare paid Bristol-Meyers \$687 million over the period 1994 to 1999. I don't have the numbers for the entire 10 years.

So, in other words, we have a drug that taxpayers put basically a half a billion dollars in—very quantifiable, very proven number of dollars. We have a drug that was almost given to a company, who has done a good job of developing it, further developing and marketing. They claim a billion dollars; that number is probably high. But even if it were a billion, Medicare paid \$600 million of that. So of \$600 million, it was—they made \$9 billion in profits. Government gets a paltry \$35 million.

My question is: is that fair? Is that a good system that way? And my more specific question is: should we consider a larger but still modest return—royalty rate for the government, considering what the government put in and what Bristol-Meyers has reaped?

Now, understanding this doesn't happen every time, but when it does, if Bristol-Meyers or any biotech firm or drug company makes this kind of money, these kinds of huge profits off a blockbuster drug, when the government has done almost all, if not all, of the basic research and really discovered this product, is there something we should do differently from the way we do it now?

Mr. LINDBERG. I don't think I can offer you any wisdom on that topic. Sorry. I am just not an expert in it.

Mr. BROWN. What about as a taxpayer?

Mr. LINDBERG. Well, what I am remember is the people in the street claiming that we are going to strip the planet of yew trees because of Taxol. And I was grateful that the synthetic chemists were able to make it in a lab. I think it is a great outcome, and I don't know—I really don't know the answer to your question, what is a fair return. I simply don't.

Mr. BROWN. Dr. Rohrbaugh?

Mr. ROHRBAUGH. Well, at the time that the National Cancer Institute started working with Bristol-Meyers-Squibb, they were looking for partners to move forward an important—what they perceived as an important, potentially therapeutic, chemotherapeutic drug. And it has been quite a success with over a million people treated, primarily women, for ovarian and breast cancer and now lung cancer.

It is a generic compound that is being combined with a number of other therapies by many different companies in treating now more than a million people. So from the perspective of our mission to benefit the public health, this has been a great success.

With respect to the return, the only mechanism we have to receive a return is to license inventions made by government sci-

entists. And the only invention here that was made by a government scientist was a method of administering the drug, and this method was not required for FDA approval, it is not in the packaging insert, it is not in the instructions.

It was only a small part of the total package, so to speak, of the drug that went forward. And we licensed that technology to Bristol-Meyers-Squibb for a reasonable amount, considering the technology that we had licensed. But ultimately, our mission is to benefit public health, and this has been a great success.

Mr. BILIRAKIS. Dr. Barker? All right, yes. Very quickly, if you can go—Dr. Barker?

Ms. BARKER. It is a complex question, and I am not wise enough to answer it in terms of the return on investment issues. But I am able to tell you that Taxol is a revolutionary drug in terms of the treatment of ovarian and breast cancer specifically, and now lung cancer.

I have a personal story in that regard, actually. My mother, who was suffering from breast cancer at that point, was one of the first people on a clinical trial, and probably gained an additional 2 years of life because of that drug.

So from our standpoint in the National Cancer Institute, this was an extremely successful venture in terms of this particular drug. So I think for us it was a success story.

Ms. MULLIN. Mr. Brown, I don't think I have a good answer to your question. It is a really difficult one. I think, prospectively, it is hard to know how things will work out often when you are developing a product, and in hindsight things may look different as well.

Mr. BILIRAKIS. Mr. Buyer for 8 minutes.

Mr. BUYER. I don't villainize drug companies, so the answer is not a difficult one. What is excluded, I think, out of the proposition that Mr. Brown has given to you in that question is that if we, as the government—i.e., you are going to take public dollars and make this investment—we believe that in the end we are going to improve the quality of life of our society.

And from that, there are tremendous benefits, both that are tangible and intangible, whether it is quality of life and productivity, and is it meaningful to have a mother for a child. I mean, the list goes on and on and on. So get out the pen and paper, Mr. Brown, and try to calculate all those other things. That is what I would ask.

But, you know, it is a lot more fun in politics to villainize somebody or something out there. That is the politics of it, and that is what is unfortunate, and it just turns my stomach. I applaud your answers.

I do have a question that is outside of the scope perhaps of the hearing. It was sort of stimulated as I was listening to your testimonies. The more you want to collaborate, that is all wonderful. The access to the Library, that is all wonderful. What was stimulated in my thinking—and I don't know the answer to this question that I am about to ask—is about your information technology enterprise architecture.

So you can talk about how you want to collaborate and talk to each other, but if under HHS, and you have got NIH and CDC and HRQ and FDA, can you all talk to each other in an architect enter-

prise? And then, you have got institutes below each of them—let me just ask the two doctors. Here we have got Center for—we have got the Cancer Institute and FDA. Can you all talk to each other? Can you send e-mail? Can everybody talk to everybody within—

Ms. MULLIN. Everybody is on the same network. Yes, we can pull up names on our, you know, Outlook and every—

Mr. BUYER. So everyone within HHS—

Ms. MULLIN. Yes.

Mr. BUYER. [continuing] is all on the same enterprise architecture, there are no little cultures out there that are—that you can't access.

Ms. MULLIN. We certainly have a lot of things in common at this point, common platforms.

Mr. BUYER. That is great.

Ms. BARKER. I think the challenge for us in science actually is the explosion of data from genomics and proteomics in areas of science that has evolved very quickly has prompted us specifically at the Cancer Institute to create a grid to connect our cancer researchers, specifically the physicians with the scientists.

And so that is a challenge that we are actually rolling out this year, a new information grid that is—but it is totally connected to everything else we just talked about. So we are actually in pretty good shape, I think.

Mr. BUYER. So between your hardware, your storage, and your servers, and your software, it is all compatible, and you all can talk to each other, and there are no problems?

Ms. MULLIN. I think that that is a major initiative and goal for our department, and in following the President's management agenda. But I know that HHS is working very diligently to—we have a lot of things in common. We are working to have everything possible that makes sense to have common and interconnected.

Mr. BUYER. Working toward that goal. So we are not there yet.

Ms. MULLIN. I think there are some—

Mr. BUYER. Dr. Lindberg, do you have anything you can add to that?

Mr. LINDBERG. Well, I think just at the level of communicating I don't think there is any problem whatsoever. But I would attribute that as much to the Internet as I would to our own department. Now, whether there is reason to communicate, that is, of course, an administrative matter.

But I have been delighted. I have been in government only since 1984, but I have been delighted to see how many good people there are in each of the agencies, and how easily they do work together. I think it is a myth to say that they don't work together when there is reason to.

Mr. BUYER. I am not proposing that there is even a myth. I just wanted to make sure, if you want to corroborate, that you have got the architecture to actually do it. So what I discovered in our work with other departments and agencies, you would be shocked to find out who has got what funding stream, and somebody goes out and buys whatever they want, and finds out that they can't talk to each other.

Thank you. I yield back.

Mr. BILIRAKIS. The chair appreciates that.

Mr. Stupak for 8 minutes.

Mr. STUPAK. Thank you, Mr. Chairman.

Let me just follow up a little bit on what Mr. Brown was saying. He used Taxol, but just about any of these drugs that the government helped to develop, a lot of us feel that the return we are getting is inadequate.

Taxol, if you use Mr. Brown's numbers, the government put forth \$500 million and royalties—to date it has been \$35 million. A lot of people believe that we should at least go a dollar for a dollar, get our return on the money. Do you think that would stifle research if we did that? Does anyone care to answer that?

Mr. ROHRBAUGH. In the late 1980's, early 1990's, we had a reasonable pricing clause in our agreements. And there was concern by the mid-1990's that this was causing companies not to even consider collaborating with us. We held—

Mr. STUPAK. What is reasonable reimbursement? You said you had a reasonable reimbursement clause. Can you define that for me?

Mr. ROHRBAUGH. That is part of the problem.

Mr. STUPAK. You can't define it.

Mr. ROHRBAUGH. It is difficult to define, but all we had was the clause that said that the price would be reasonable.

Mr. STUPAK. So you moved from reasonable to what?

Mr. ROHRBAUGH. And in 1994, we held two public hearings with members of the public constituency groups, etcetera, who determined that the clause inhibited the formation of potentially beneficial scientific collaborations without providing an offsetting benefit to the public. And some question whether we had—

Mr. STUPAK. Okay. I don't mean to rush you, but I want to get through a lot of questions, and I don't want to take 8 minutes on trying to get this one answer. What is the standard now?

Mr. ROHRBAUGH. There is no—

Mr. STUPAK. It was reasonable. It is gone now. What is it now?

Mr. ROHRBAUGH. There is no control in our license agreements over the pricing of—

Mr. STUPAK. So each is negotiated.

Mr. ROHRBAUGH. We negotiate a standard licensing agreement based on the technology we are licensing, and industry tells us if the government has control over its costs, they would not work with us. And, therefore, these drugs would not reach the market. So I think our choice is: does the government—

Mr. STUPAK. How would you have control over their costs? When they spend \$2 on advertising for every dollar on research, that is the problem some of us have—they spend twice as much on advertising as they do on research and development, and government seems to be supplementing it. And we are getting five-tenths of 1 percent return?

Mr. ROHRBAUGH. Our mission at the NIH is to facilitate the development of new information and new products that are brought to the market by the private sector with a great deal of time and investment by the private sector.

Mr. STUPAK. I don't disagree, but if you have a reimbursement program, a lot of us feel it should be reasonable. By that, I mean at least a little bit more than five-tenths of 1 percent.

Let me move on to something else. Dr. Mullin, you indicate in your testimony that FDA is there to make sure that we have safety and effectiveness of a drug is—is paramount in your mission statement. We have done hearings on the ImClone and Herbitex. And while the drug was being developed in the initial application to see if it was going to be a beneficial cancer drug, there was a lot of hype in that drug through USA Today, Business News, even 60 Minutes.

FDA testified they were appalled at the statements or claims being made. Should not the FDA then step in, when these drugs are being promoted and hyped, while they are still in the initial stages of development, and say, wait a minute, folks. If you are concerned about safety and effectiveness of a drug, that the hype you just saw on USA Today or 60 Minutes shouldn't—don't you have a responsibility to step out and say that is not true, that is not what the tests are showing?

Ms. MULLIN. I am afraid, Mr. Stupak, that I can't—I don't know the legal constraints on the agency with respect to what we can say when a product is still under IND.

Mr. STUPAK. Sure. But under IND, when they are making claims that can't possibly be true, to protect your mission, to continue to be the gold standard, as you like to be referred to, don't you have a responsibility as the FDA to say these claims are not going to the effectiveness or the safety of a drug, it is in IND as you call it? Don't you have a responsibility to let the public know that this isn't true? Because, as we saw, we had all kinds of investor fraud and everything else associated with that.

Ms. MULLIN. I would like to be able to follow up with you and with the people who are most familiar with that drug and that issue, so I can give you an accurate answer on that, if that is all right.

Mr. STUPAK. Okay. You further go on and testify that drugs are being approved now 90 percent within the 6 months underneath PDUFA. During this 6-month period, have you been able to get all of the information you requested from the drug companies?

Ms. MULLIN. I think maybe I was—I didn't say it clearly enough on what that meant. FDA won't approve a product until all of our questions are answered, but we—what we will commit to is a complete review and a letter and an action. The action might be a letter that says this is not approvable, or it is approvable, but the following questions must be satisfactorily addressed.

So it doesn't mean an approval within 6 months, unless the application does answer all of the questions and there is adequate demonstration of safety and effectiveness. So I didn't mean to imply that we approve them and guarantee anything of that kind. We will approve a product when it is shown that it is safe and effective, and we are satisfied that we have that—the evidence that is necessary.

Mr. STUPAK. Well, if we are concerned about the safety and effectiveness, and some of us are concerned at how quickly some of these drugs are being approved, when we take a look at it underneath this new system we have had in place we have had more drugs withdrawn in the last few years than you did in the whole

history of the FDA, because they have been approved so quickly they had to be later withdrawn.

And the answer we usually get with the FDA is, well, if it is 3 or 4 percent that have to be withdrawn, that is what it was before. Even though we are approving more drugs quicker now, we are still withdrawing about 3 or 4 percent of more drugs, which would result in about 1,200 tests.

Is quickness the standard you are using? Or what is the—are you under a legislative timeframe to do it in 6 months? Or is it really safety and effectiveness that should be the goal here?

Ms. MULLIN. Well, the review process—there is a legislative timeframe, although we have—which is 180 days. But we work with and are committed to trying to meet the PDUFA commitments that are not legislative but that FDA has committed to, and that is just for review.

We don't have particular timeframes for withdrawal, and what those statistics that you are referring to mean is on average. And what we looked at in the 3 to 4 percent that you describe is the average over a longer term in terms of withdrawal rates for approved products.

And one of the things that you are seeing is a great—a much greater uptake of new products once they are approved, and there is a much greater use of new products within—

Mr. STUPAK. Greater drugs are being approved, but a greater number are being withdrawn when you just look at the raw numbers.

Ms. MULLIN. Greater numbers—

Mr. STUPAK. Later being withdrawn.

Ms. MULLIN. Well, actually, and the rate of withdrawal has not gone up and—

Mr. STUPAK. No, it has not gone up. But you have got more drugs, you are withdrawing more drugs. So how is that an improvement upon the safety factor, is what I am asking.

Ms. MULLIN. Well—

Mr. STUPAK. Let me ask you this. My time is almost up. You said on page 4, once a drug is approved for sale in the United States, our consumer protection mission continues. We monitor for the use of marketed drugs for unexpected health risk, and we take steps to inform the public.

Other than a public health advisory to doctors or to prescribing physicians through MedWatch, how do you inform the public? And what mechanism is in place to do post-marketing review once a drug is approved for sale?

Ms. MULLIN. Post-marketing review—what we—as part of the prescription drug user fee reauthorization last year, we have actually established—we have enlarged our post-marketing safety and oversight and have additional funds now to do that activity.

One of the things FDA is currently doing through, as I have mentioned, our strategic action plan that we are developing is to try to get, work with others who collect data to get the largest capability to do active surveillance that we can, Mr. Stupak, because we know that drugs are—they are used according to labeling, and they are also used in a way that is not always according to the labeling.

And it is very important that we get the earliest and best information that we can to understand what the problem is, if there is a problem on a product. We need to analyze whether it is the product or how it is being used—

Mr. STUPAK. Right, realize all of that, but—

Ms. MULLIN. [continuing] to work that out. So we have—

Mr. STUPAK. But there is no scheme in place, like 6 months later review it, a year later—

Mr. NORWOOD [presiding]. Mr. Stupak, your time has expired. Let her finish answering the question, please.

Mr. STUPAK. Sure. Well, I was just trying to get to the meat of it.

Mr. NORWOOD. I know. I understand.

Ms. MULLIN. What we are doing—if I just—one quick thing on that. We have this program in place now for risk management in the post-market period, the first 2 to 3 years when if we are going to see something unexpected, that we didn't pick up on in clinical trials, we are doing a lot more active work, and over the next 5 years expect to spend about \$70 million on post-market safety, which is so much better than we have been able to do in the past.

So I think we will be very vigilant in those first few years, because that is when a lot of the safety problems happen, and we pick up on them.

Mr. STUPAK. And then, my other question was: how do you inform—

Mr. NORWOOD. Mr. Stupak?

Mr. STUPAK. [continuing] the public—can she just answer—

Mr. NORWOOD. Your time has expired, and it has expired a good bit.

Mr. STUPAK. Other than MedWatch, do you do anything else to inform the public?

Mr. NORWOOD. Ma'am, don't answer the question, please.

Your time has expired.

I want to remind myself that when the yellow light comes on, it means your time is almost up. When the red light comes on, it means your time is up, and it gives all members an equal opportunity to question the witnesses.

Mr. Whitfield, you are now recognized for 5 minutes.

Mr. WHITFIELD. Mr. Chairman, thank you very much.

I suppose this question would go to Dr. Mullin. But of the approvals that you give for new medicines, would you have an idea what percent of those would be coming from what I would refer to as small, maybe startup companies, versus companies like Merck, Bristol-Meyers, the large, large drug companies?

Ms. MULLIN. You know, I don't have that number on the top of my head, but we do keep track of that information, and I can get that information to you.

Mr. WHITFIELD. Do you have any idea at all?

Ms. MULLIN. I am going to hazard a guess that it is at least 20 percent, but I think higher than that from small companies.

Mr. WHITFIELD. Twenty percent? And I suppose this would go to Dr. Barker or someone else, but are there funding mechanisms in the government that helps bridge this R&D phase of drug develop-

ment and assist small companies to bring a drug through the FDA clinical trials for a new drug application?

Ms. BARKER. The National Cancer Institute has several of these mechanisms, including, of course, the SBIR and STTR awards, which many small companies use to develop drugs, and that is probably one of the most I think effective mechanisms. Those are partnerships generally with universities and small companies.

We also have at the NCI two other programs for technology development—one called the unconventional innovation program—UIP—the second one is called the IMAT program. Both of those programs actually are good vehicles for small companies to actually bring their drug forward. Small companies often don't know going into these kinds of development activities how much they are going to cost.

So we are actually looking more closely at that at the NCI, because we do have a lot of interesting cancer, as you might imagine, in the biotechnology companies. And many of these small companies just don't succeed, and we are looking for mechanisms to capture some of that technology or to lend some different kinds of assistance, maybe through some of our university relationships. It is an issue we are very interested in.

Mr. WHITFIELD. The very first two you mentioned, one was SBIR, and what was the other one?

Ms. BARKER. STTR. One is more of a technology-focused grant for diagnostics and other kinds of technologies.

Mr. WHITFIELD. And do you have any idea how many dollars are available for those programs each year?

Ms. BARKER. In the case of the SBIR program, it is in proportion actually to the amount of dollars that you receive as a Federal agency. And I don't exactly—I don't have that number right at hand. I can certainly get it for you.

Mr. WHITFIELD. Okay. Thank you.

This I guess would be going back to FDA again, but I notice in your testimony you refer to at some point priority approval and standard approval.

Ms. MULLIN. Right.

Mr. WHITFIELD. Would you explain to me how you determine what is a priority and what is a standard?

Ms. MULLIN. FDA determines whether an application will be priority or standard. And the priority applications are ones for treatment or therapies that represent a new approach to diagnostic treatment, and just—so it is something that offers an approach or a therapy that hasn't—that doesn't already exist. So, for example, it is the first of a kind in an area for diagnostic or treatment.

Mr. WHITFIELD. And you mentioned also new drug applications and biologic license applications.

Ms. MULLIN. Yes.

Mr. WHITFIELD. Would either one of those include—or would it be separate—a new drug delivery technique, for example?

Ms. MULLIN. A new drug delivery system, for example, might involve a device component and a biologic or device and a drug combination, and those—we refer to those as combination products, and they may be classified as a device and be in what is called a PMA. It will be jointly reviewed by a device center and the center

that would handle, say, the drug component of it or the biologics component of it.

We actually have a new Office of Combination Products to facilitate and make sure those reviews occur in a very timely fashion.

Mr. WHITFIELD. But if the drug delivery system consisted only of some new chemical mechanism or, for example, a system that would disguise the drug being used so that your own immune system would not attack it, would that be considered a device, or would that be a drug delivery system or—

Ms. MULLIN. I don't think I can answer that, I am sorry to say. And, actually, it can be kind of complex sometimes to figure out what the—where the home of it or where the review will be primarily done. And there are increasing numbers of products that are combination products that are very effective.

Mr. WHITFIELD. Thank you, Mr. Chairman.

Mr. NORWOOD. Thank you, Mr. Whitfield.

Ms. Capps, you are now recognized for 8 minutes.

Ms. CAPPs. Thank you, Mr. Chairman.

I thank you for your presence here today, this panel, and for the committee for organizing it.

I was not here when the goal of doubling the funding for NIH was started, but one of my proudest moments was to see that goal realized. And we will be needing to leave to speak on the floor because of our funding appropriation that we are dealing with today, which includes NIH funding. And I am dismayed that we have actually gone backward the very next year by flatlining the budget.

I really so support what you all do, that umbrella of NIH that includes each of your particular positions. I think the fact that Congress took this on, to double the funding, speaks to the value that the American people place in what you do. And that is, well, for some folks, and me included, research is to be valued for its own sake.

I was married to an academician for over 30 years, and that whole life means a lot to me. And I think you get such wonderful unintended results sometimes from trips to the moon or wherever people decide—what people decide to do with their intellect. So I would value it for its own sake.

But now we see clearly—and I have the experience of having a daughter in the battle of her life for a year with lung cancer, and I know what clinical trials are about. And so to the extent that we see close up the impact of what you are about, it makes this a very significant arena for our deliberation as Members of Congress as well.

We are raw, some of us, from having gone through the Medicare modernization, including prescription medication debate right here a few weeks ago, and then 2 weeks ago on the floor. And so that is why there is feeling about the high cost.

And I want to use this little time to explore the relationship between what you do, valuable as it is in itself, and then the close relationship that exists in the private sector which allows—to the degree that that is an ingredient that is essential to having that really make a difference in people's lives.

And so I don't even know where I am going to address this, but I am going to start with the fact that Bayh-Dole was initiated with

a relationship with universities, and I know our second panel is going to get us more there. And I am not going to go so far as to say, how can we get more of a return on some of these very lucrative byproducts, because I don't know that you can anticipate that in advance. And you wouldn't want that to be the issue.

But I was taken with a comment—I think, Dr. Rohrbaugh, you mentioned a method by which a standard agreement is negotiated. And maybe that is a good starting point, to hear from you, and ways that perhaps with our leadership we should develop—or should we revisit Bayh-Dole, or should we—what advice can you give someone like me? Start with that. Very open, I am sorry.

Mr. ROHRBAUGH. Well, Bayh-Dole applies to the recipients of Federal funds.

Ms. CAPPS. Yes.

Mr. ROHRBAUGH. There is the Stevenson-Wydler Act and amendments to the Federal Technology Transfer Act that apply to Federal agencies and direct our activities in technology transfer.

We license technologies at a very early stage. We often don't have much more, if we are fortunate than a proof of principle often before that point of time. So industry takes on a great risk in having very early stage risky technology that may not prove to be a benefit, may fail, most of them fail in the process of development. That is just the way things work.

Ms. CAPPS. Yes.

Mr. ROHRBAUGH. And we license our technologies that are invented by government employees under standard licensing agreements, with terms that are negotiated based on the value of the technology, the stage of the technology, and its overall value. And what we license ultimately is typically a small part, or only one part, of the final product.

Even if we have a chemical entity that becomes ultimately a drug developed by a company, the company may—usually provides an awful lot of other important proprietary technology in formulating it, in encapsulating it, in developing it, in finding ways to make it better and cheaper and bringing it to market.

So ours is only a small part of the final product, then, typically.

Ms. CAPPS. I am not saying that you don't need to defend the private sector. I am just concerned that there—from some of your remarks that I heard earlier, it seems like they are holding hostage to some degree, that they won't—if you go too far down the road, they are not—and limit the amount that they can make or do any kind of things that impinge on that, that they won't have a relationship with you. What is that like?

Mr. ROHRBAUGH. Industry and investors in industry are reluctant to—the investors are reluctant to invest, and companies are reluctant to take on technologies at a very early stage, as our technologies are, if we have some control over the final price of the product. It is too far downstream. They have to invest so much money into it. Ours is a small part of the final product. They just will not work with us under those conditions.

Ms. CAPPS. I will wait until the second panel to get into more that the university might have a different relationship with you in terms of that partnership. But I will—I don't want to—I am looking at the clock, and, Dr. Barker, I do want to get in one question

about the National Cancer Institute and the mapping of clinical trials. And maybe that isn't even what you came prepared to discuss, but that is certainly a very big interest to many people.

Ms. BARKER. Could you clarify your question?

Ms. CAPPS. To make it easier for—and it wouldn't just be cancer, but that is certainly an area where life-saving depends—can often be seen as getting into a trial. And how can we make that work more efficiently for—

Ms. BARKER. I know you are very familiar with this process.

Ms. CAPPS. Yes.

Ms. BARKER. As you know, also, we only have about 3 percent of patients go on clinical trials who have cancer, and that is a very complex—there is a whole series of complex reasons why that is true.

We have undertaken a lot of activities at the NCI, ranging from new communications tools to actually new bioinformatics systems, to ease the burden of actually putting people on clinical trials in the communities, increased funding basically for the cooperative groups to actually make them more competitive in terms of actually really enhancing opportunities to put people on clinical trials.

And clinical trials actually is a major initiative across the National Institutes of Health is part one of Dr. Zuhini's road maps this year.

Ms. CAPPS. Okay.

Ms. BARKER. So we have an enormous number of initiatives, especially in the National Cancer Institute, to actually increase accrual and to make it simpler for patients to access, know about the trials, and ultimately be enrolled, and for physicians to actually have enough resources to put patients on clinical trials.

Ms. CAPPS. So this is an area—and I know my time is up, but this is an area that funding could really be useful in—that there would be a real impact on consumers.

Ms. BARKER. Well, I think the doubling of the NIH budget has actually allowed us to do an enormous number of things in clinical trials. And certainly, going forward, that would be beneficial to continue to improve this for cancer specifically, but I think for other diseases as well.

Ms. CAPPS. Thank you.

Mr. BILIRAKIS. Dr. Norwood for 5 minutes.

Mr. NORWOOD. Thank you very much, Mr. Chairman. I am enjoying this immensely and having a lot of my questions answered by others' questions. So I would like to take my 5 minutes and yield it to Mr. Stupak and let him finish his line of questioning.

Mr. STUPAK. I thank the gentleman for yielding and appreciate the courtesy, because I was trying to ask Dr. Mullin, in the information we have—and I asked you about, how do you notify the public, then, about the effectiveness of a drug or the safety of a drug, because they say you issue public health advisories to doctors, which are commonly called Dear Doctor Letters, or else there is the MedWatch.

How does the public know about the safety of a drug? If you have a question, how do you communicate that to the public, I guess is what I am asking.

Ms. MULLIN. Mr. Stupak, if FDA has a question or—

Mr. STUPAK. Well, the FDA has found something wrong, so that is when you do a Dear Doctor. You have to notify the prescribing physicians that you have to watch for this or do something like this.

Ms. MULLIN. Right.

Mr. STUPAK. How do you inform the public? Because you said in your statement, again on page 4, if new, unanticipated risks are detected after approval, we take steps to inform the public and change how a drug is used or even remove it from the market. So I am asking, how do you inform the public?

Ms. MULLIN. Actually, as part of this planning effort that I have described this year, we are identifying a number of partners through—both public and private to try to both get the data—as I mentioned before, we see information technology as one key to trying to get a more complete picture as quickly as possible. We are going to be partnering with grantees for the AHRQ, with the CDC networks—

Mr. STUPAK. Okay. But there is no mechanism like launching some kind of program to inform the public?

Ms. MULLIN. Well, on the other part of that—

Mr. STUPAK. It is still being developed?

Ms. MULLIN. Yes. And we are trying to partner with—well, as you know, the list of MedWatch partners, there are various practitioner groups and specialties, and we are basically going to be disseminating information through as many conduits as we can to health care professionals.

Mr. STUPAK. Yes, health care professionals. But I am asking the general public. So we, the patients, and eventually the victims when a drug goes wrong, how do we know to watch for things?

Ms. MULLIN. Well, we are also looking for ways to get better information to the media and better ways, which is a very effective way to reach patients and refer them to their physician. And we actually have been pretty successful in that mode of having people become aware through the media, and then people ask their doctor or can visit FDA's website, or get more information at that point as they need to.

Mr. BILIRAKIS. Has the gentleman—the advising of the provider, of the medical doctor, are you satisfied in terms of how that is done?

Mr. STUPAK. The question was to the public. Advising the medical doctor doesn't help the patient or the families, if the problem—

Mr. BILIRAKIS. Well, I was just—

Mr. STUPAK. [continuing] to clarify—

Mr. BILIRAKIS. [continuing] the doctor ought to know.

Mr. STUPAK. Sure. They should, yes. The key word is “should.”

Mr. BILIRAKIS. Are you satisfied as to how that is done? I don't know whether that—

Mr. STUPAK. Oh, no. I am satisfied that they notify the physicians.

Mr. BILIRAKIS. All right.

Mr. STUPAK. But how do you get it—her statement was to the public. I am just trying to say, how do we get it to the public?

Ms. MULLIN. Well, and I think that is—we absolutely agree with that, and we have the patient safety initiative going on at FDA to identify every mechanism possible to reach people, to do it through media, we think every venue, every channel you can go to to try to reach people as quickly as possible.

Mr. STUPAK. Let me ask you this. If you are going to have to change a label because of a safety concern on a drug, do you have that labeling that is found on a drug product, does that have to be changed within so many days or months or years, wherever it is going to be?

Ms. MULLIN. I know there is a timeframe for it, Mr. Stupak, but I don't know what it is. I can get that information.

Mr. STUPAK. If you would, I would appreciate it.

With that, I will yield back to Dr. Norwood. Appreciate your courtesy, Dr. Norwood, for letting me follow up on that question.

Mr. NORWOOD. Thank you. Thank you very much.

Mr. Chairman, I will just get in one quick one, since I have got a minute left. I am a big fan of NIH. I am very pleased with the work that you do, and I presume that I understand it right when you do basic science, you do research. It comes out basically through the National Library. That is where people actually pick up on that. Is that—do I understand that right?

Mr. LINDBERG. I think that is right. I think I could add something to the question Mr. Stupak asked, actually, because there is a phenomenon we call clinical alerts. Now, when Medline searches are done, and they are done a million times a day, we have a banner in certain cases that announces a piece of emergency information.

So, for example, when the women's health trial, the estrogen-progestin trial, when it reached a point where they could conclude early that it should be stopped, the arm of the combined drugs, that was a clinical alert. That was announced, and the decision was made by the director of the relevant Institute, in that case Heart/Lung.

Now that was an alarm. That said stop doing it, because you are endangering people. But in happier circumstances, a trial will be terminated early because of a very good result. So, for instance, the use of massive doses of corticosteroids for acute spinal cord injury, was tested in 20 academic centers and NIH, and it ended early because they were so effective.

So that was a clinical alert that announced that we don't want anyone on the control side of that one anymore. We want everybody getting the treatment. So we do have at least that mechanism, and it relates to drugs but not directly. It more relates to clinical trials.

We fought very hard to get it in, because the—in some of the better journals—the New England Journal of Medicine, for instance—there had been a rule that if you are going to announce these results before it is published, we won't take your paper.

So in order to put through this particular scheme, we convened a meeting at National Library of Medicine in which the editors of New England Journal and JAMA and certain other major papers all agreed that this should happen, these clinical alerts should be permitted, and it would not bother anybody's acceptance or non-ac-

ceptance of the paper. So I am just suggesting that this is yet one other mechanism which we do use.

Mr. BILIRAKIS. Ms. Eshoo for 5 minutes.

Ms. ESHOO. I didn't make an opening statement, Mr. Chairman.

Mr. BILIRAKIS. Under the rules, you have to be here in order to waive the opening.

Ms. ESHOO. Oh, all right. I am sorry.

Well, I would like to welcome the panelists here, and say—repeat what I always say when anyone from the NIH comes before us, that it represents I think to our country the National Institutes of Hope. And I think really that is why you are here today to talk about the undertakings that are a part of that mission of hope, and I salute you for the work that you do and what it is producing for the people of our country, and certainly for the world.

You are the gold standard, and we want to keep you that way. I think the investments that have been made are amongst absolutely the best that the Congress has ever made. Absolutely amongst the best. And so I want to start out with that, because I have enormous respect for each one of you and the work that you do, and the work that has come out of the—our National Institutes.

I would like to just say something about some of the conversation that took place earlier in the committee's hearing. I don't know how many members know that earlier this week—I think it was Monday—that a GAO report found that the Federal Government, while it has been licensing agreements for only four of the top 100 drugs dispensed by the DoD, that there are only four.

I think that the case is not as large as maybe it was referenced, and I think that members should avail themselves to this GAO report, because even though it is being charged, you know, this whole case that the Federal Government is paying X number of dollars, getting very little out of it. I would say that it is important to read the report, because there are four drugs. There are only 4 out of 100 that are actually dispensed by the DoD.

The Federal Government contributes 1.6 percent in terms of bio-research. So while we are a player, and a very important one—and I think that we should be doing more, most frankly—but because, again, I think this is amongst the most important and the greatest impact return for the investment dollars, it is 1.6 percent.

It reminds me of constituents at town hall meetings that believe that 25 percent of the Federal budget represents foreign aid, and it is widely exaggerated. There are those that don't support any dollars for foreign aid, but I don't think that we should lose sight of the context here. And as we don't lose sight of the context, we will, I think, more fully appreciate what 1.6 percent is bringing back to us.

To any of the witnesses, how often has the NIH turned over fully completed drug products to a drug or biotechnology company? Has that ever happened?

Mr. ROHRBAUGH. I am not aware of any.

Ms. ESHOO. Anyone on the panel aware of any? That is what I thought, but I think that it is a question that is worth asking.

Dr. Rohrbaugh, you mentioned that the reasonable pricing clause had a detrimental effect on public-private partnerships. Can you elaborate on that? And do you have statistics showing that?

Mr. ROHRBAUGH. Those conclusions were made based on public hearings that were held in 1994. I don't have all of the statistics, but the report that I would be happy to refer to you is on the website from those committees. And they did conclude that it was having a chilling effect on the interest of industry to work with the National Institutes of Health collaboratively and in licensing technologies.

Ms. ESHOO. And it is now a decade later, since that report. Do you believe that what—

Mr. ROHRBAUGH. Yes, it has had a positive effect. And since then from the standpoint of our statistics, our licenses, our royalty income, all of the measures of our tech transfer activities are higher, much higher than they were at that time. And new and better drugs are being developed from our partners, who invest their time and money in these early stage technologies.

Ms. ESHOO. I thank you all again, and I think that you are really a great source of pride to our country in terms of what you do. I am so impressed with what the Library is doing. I thought that the national "do not call list" had a lot of hits, but I think that you are right up there, and that speaks, excuse the expression, volumes about what you have and what you do. Thank you very, very much.

Mr. BILIRAKIS. The chair thanks the gentlelady, and you certainly made a point that I tried to make, and that is—it is a wild thing to me that they do so much. And what is available—if only the people—the patients, and particularly the medical providers are aware of all that is available to them. And that is something that concerns me. I don't know whether it should or shouldn't.

Let us see. Mr. Burr is recognized for 5 minutes.

Mr. BURR. I thank the chairman. I won't take 5 minutes.

I would like to pose two questions probably to Dr. Rohrbaugh and Dr. Barker. The first one is: what do you see the future of combination products playing in the delivery of health care in this country? And the second question would be: as we look at the plus-up that Congress has made in the NIH budget over the last several years, and hopefully a plus-up that will continue, how much of those extra dollars have been used for extramural research?

Ms. BARKER. As you know, the majority of our work at the NIH is in the extramural community, and certainly that is true at the National Cancer Institute. So most of those dollars have gone to the extramural community.

In terms of your first question, it is intriguing that you are—I think everyone is beginning to see that the future of medicine actually is going to be in genomics. And as we know more about genomics, we are beginning to understand that these molecular defects are very rarely due to a single defect. It is going to be multiple defects.

So we are challenged to address that issue. And at the National Cancer Institute especially, we are looking at all kinds of ways to do that, all the way from computational biology and systems biology to be able to use approaches to predict what that should look like, to very specific kinds of models and animals to actually effectively predict that before we can go into humans.

And the future, of course, is even more interesting because areas like nanotechnology, where we will be able to very specifically de-

liver multiple ligands or signatures within cells, also sits there. And we are just beginning to exploit that for cancer. And as you go forward, you are going to be able to see how you are going to be able to combine imaging, for example, with therapeutics.

So the future is just—what I said in my opening comments is so true. It is just unimagined what we can accomplish in the next probably as few as 5 years, and even at 10 years I think we will look back and wonder how we were so naive in terms of our approaches to therapy and diagnostics and prevention today.

So I think you are right on in terms of the issues of combinations. That is where the world is going to go, especially for us in cancer.

Mr. BURR. Well, my hope is that you devote some time to spend not only with FDA but possibly with CMS as it relates to understanding the world of combination products. My greatest fear is that we make tremendous progress at NIH and through the extramural programs, and then we hit this permanent red light that deals with the approval process that we continue to—we improve and we have improved.

But the combination product decisions are much tougher down the road than what we have had up until this point, and I believe it has been even tougher to try to determine a reimbursement scheme as it relates to those products. And many times our great work is only for naught if, in fact, we can't get it to the patient.

Ms. BARKER. I would agree with that.

Mr. BURR. Thank you.

Anything to add?

Mr. ROHRBAUGH. No, I don't.

Mr. BURR. Great. Thank you, Mr. Chairman. I yield back.

Mr. BILIRAKIS. The chair thanks the gentleman.

Mr. Allen to inquire.

Mr. ALLEN. Thank you, Mr. Chairman, and thank you, in particular, for allowing me to participate in this hearing today. Though a member of the committee, I am not a member of this particular subcommittee, and a lot of good work is done in this subcommittee.

I want to thank all of the panelists for being here today. This is a very helpful and informative hearing.

Dr. Mullin, I would like to begin with you. I have introduced a bill in June called the Prescription Drug Comparative Effectiveness Act of 2003. It is a bipartisan bill. It would fund studies of comparative effectiveness and cost effectiveness of prescription drugs that are used to treat particular diseases or conditions, specifically those which involve high amounts of expenditures for Medicare and Medicaid.

The bill authorizes \$50 million for NIH and \$25 million for the Agency for Health Care Research and Quality to carry out these studies on comparative effectiveness and cost effectiveness.

And, Mr. Chairman, with your approval, I would like to offer for inclusion in the record an editorial in the July issue of *Clinical Therapeutics*, which explains the bill.

Mr. BILIRAKIS. Without objection, that will be the case.

Mr. ALLEN. The FDA—it is assumed under the legislation that the FDA would cooperate with NIH and AHRQ in doing this, deal-

ing with this issue. I assume you haven't had a chance to review the bill.

Ms. MULLIN. Right, I haven't.

Mr. ALLEN. But I wondered if you could comment briefly on the value of having better information and how drugs that treat a particular disease or condition should be compared to other drugs that treat the same disease or condition, and ultimately, of course, you know, the question of relative cost effectiveness. You are probably familiar with what Oregon has done in this—along these lines.

Ms. MULLIN. Well, I especially can speak to the different—looking at weighing the therapeutic benefit of one versus another in the review process. I am not a reviewer, but I know very well that they make those decisions about approval of a new product with all of the other options in mind, what is already out there available to patients.

And FDA has a trove of information and experience, and because of where we are in the process we see everything. We see all of the detailed clinical data, and so I—and we will be, I am sure, collaborating. I know we have conversations with AHRQ already underway, you know, and we want to share what we know more.

And there is a summary that is always provided at the end of a review process when a drug is approved that talks about that product and this clinical—and within the armamentarium of what is available to treat patients with the condition. So I think we see that as an opportunity.

Mr. ALLEN. Well, thank you for that. Of course, this goes beyond the FDA's traditional mission of safety and efficacy, but it is an important area.

Dr. Rohrbaugh, we have a—you were talking earlier about the conversations you have with industry when something that has been developed at NIH is ready to go out and be further developed for the market. We have a staff memorandum here that says that in July 2001, NIH submitted to Congress a plan to assure taxpayers' interests are protected, and talked about greater transparency.

And it said you would modify your existing extramural policy manuals to assure that grantees and contractors report to the agency the name, trademark, or other appropriate identifiers of a therapeutic drug that embodies technology used by NIH, that you would make that information available on a web-based data base that—anyway, I just wondered if you could clarify just where that process is. I mean, is that kind of information now being developed, and is it available on a data base that could be used by the public?

Mr. ROHRBAUGH. It is. What we have done for the intramural program, the program that I oversee, is list on our website all 17 FDA approved technologies, drugs, therapeutics, vaccines, that include, at least in part, technologies licensed from the NIH.

With respect to our recipient—the recipients of Federal funds, that was handled by the Office of Extramural Research, and they have implemented that program. And on their website, I believe there was only one reported drug last year. I don't know if any have been reported this year.

Mr. ALLEN. But there should be more as we go forward?

Mr. ROHRBAUGH. Yes.

Mr. ALLEN. Yes. Well, it is important, I think, just because if we are going to understand this process, we need to know how much of the value—or how much of the research that went into a particular drug was publicly funded, and then we can discuss the policy implications of that later.

Mr. ROHRBAUGH. Exactly.

Mr. ALLEN. Thank you.

Thank you very much, Mr. Chairman.

Mr. BILIRAKIS. And I thank the gentleman.

Yes, we are going to go into our second panel now, but I want to thank you all. You were just tremendous, as usual. We will have questions in writing to you as per the way it is usually done. We would appreciate timely responses to them.

And, you know, the second panel has sat through the audience and listened to you. And then, of course, you are all busy people, so you will probably be leaving. And that is why I told the staffer, hey, I want one panel, everybody to be here together to hear each other, and what not.

But I would hope that if you can't stay for the second panel you would maybe ask someone from your particular, you know, office to stay in your place and take notes, and what not, because I think it is—I know you are concerned. I mean, you are certainly interested in the comments that will be made by the second panel.

Thank you so very much. Thanks.

The second panel consists of Dr. Phyllis Gardner, Senior Associate Dean for Education and Student Affairs, Stanford University; Dr. Andrew Neighbour, Associate Vice Chancellor for Research, University of California Los Angeles; Dr. Jonathan Soderstrom, Managing Director of the Office of Cooperative Research, Yale University; and Dr. Ellen V. Sigal, Chairperson, Friends of Cancer Research located here in Washington, DC.

If you will take your seats, please. Again, your written statement is a part of the record, and we would hope that you would complement and supplement it orally. We will set the clock at 5 minutes, and I would appreciate it if you could stay as close to that as you can, but certainly I won't cut you off if you are on a roll regarding a particular point.

Okay. Let us start off with Dr. Gardner. Thank you very—thank you all for being here and for your patience and, you know, waiting and having to wait while we have votes and that sort of thing. But anyhow, Dr. Gardner, please proceed.

STATEMENTS OF PHYLLIS GARDNER, SENIOR ASSOCIATE DEAN FOR EDUCATION AND STUDENT AFFAIRS, STANFORD UNIVERSITY; ANDREW NEIGHBOUR, ASSOCIATE VICE CHANCELLOR FOR RESEARCH, UNIVERSITY OF CALIFORNIA LOS ANGELES; E. JONATHAN SODERSTROM, MANAGING DIRECTOR, OFFICE OF COOPERATIVE RESEARCH, YALE UNIVERSITY; AND ELLEN V. SIGAL, CHAIRPERSON, FRIENDS OF CANCER RESEARCH

Ms. GARDNER. Chairman Bilirakis and members of the committee, I am pleased to testify before you today regarding technology transfer issues as they relate to the biotechnology industry. Thank you for your continued leadership in the area of health care.

I am here today representing Biotechnology Industry Organization, or BIO. BIO represents more than 1,000 biotechnology companies, academic institutions, and State biotechnology centers. BIO members develop medical and pharmaceutical products as well as agricultural, industrial, and environmental products.

My testimony is based on my own experience in both the academic and private sector. I have been a tenured associate professor in the departments of molecular pharmacology and medicine since 1984 at Stanford University. I am a former Senior Associate Dean for Education and Student Affairs.

In addition, in the past 10 years, I was associated with ALZA Corporation—a pharmaceutical company acquired by Johnson & Johnson—as the vice president and head of their Technology Institute. I have been on biotechnology company boards. I have served on the boards of private and public biotechnology companies, I have founded companies, and I have advised venture capital firms as a partner and advisor.

I want to emphasize three important points today, and ask that my written testimony be submitted for the record.

Point one, the biotechnology industry differs significantly from large pharmaceutical companies. There are over 1,400 biotechnology companies in the U.S. In contrast to large pharmaceutical companies, many biotech companies are small, not publicly traded, and have not achieved profitability yet. While large pharmaceutical companies tend to pursue blockbuster drugs with market potentials of a billion dollars or more, many biotechnology companies pursue products with much lower market potentials, including orphan drugs.

The biotechnology industry is the most research and development industry in the world. In 2002, the industry spent \$20.5 billion on R&D focused on new targets and highly innovative therapies. No industry spends more on R&D per employee. No industry faces a lengthier or more complex regulatory process to bring products to market. And you all know the statement—a biotech company typically spends 15 years and hundreds of millions of dollars to complete testing and secure product approval.

Point two, the Federal Government funding plays a small but important role in biotech R&D. As Congresswoman Eshoo pointed out, only 1.6 percent of the industry's R&D funding in 2002 originated from the Federal Government. Thus, public support for biotechnology and the far greater dollars is key to the success of the industry. Federal R&D programs must be flexible enough not to stifle the private sector investment that is so critical for bringing products to market.

Point three, partnerships between the Federal Government and private sector foster innovation and improve health. Passage of the Bayh-Dole Act, which has been discussed much today, and the Federal Technology Transfer Act, established vehicles, including licensing and the cooperative research and development agreement, or CRADAs, for tech transfer from the public to the private sector.

Prior to these laws, Federal agencies rarely relinquished ownership of federally funded inventions, and valuable technology was left languishing on the shelves of research institutions.

In addition to CRADAs and licensing, biotechnology companies also rely on direct financial support from the government through small business innovation research programs—the SBIRs—and advanced technology programs, or the ATPs. The SBIR program is a competitive three-phase government-funded program. It is used overwhelmingly by seed stage companies for startup and early development stages of product development.

The advanced technology program, by contrast to supporting product development, it supports enabling technologies essential for the development of new products, processes, and services across diverse application areas. Both of these vehicles support seed stage companies in critical early phases. This early support is critical to support the large private investment for subsequent development and commercialization. They are particularly important in down markets when VC and other sources of private funding divert to later stage, less risky companies.

BIO does suggest one change in SBIRs, or one change to the Small Business Administration—that is, that they redefine the definition of size of small business and equity ownership, so that it will not preclude venture capital backed funding for small business—the venture capital backed companies from being funded.

In conclusion, BIO supports the various vehicles that Congress has authorized for transferring valuable technology from the public to the private sector. Given the significant technological breakthroughs achieved in medical and health fields, BIO believes that Federal dollars invested in biotechnology research have yielded significant benefits generally for the health of the Nation and specifically for the Federal Treasury.

Thank you, again, for your support of biotechnology's efforts to contribute and advance the health of the United States. I would be pleased to respond to questions from the committee.

Thank you.

[The prepared statement of Phyllis Gardner follows:]

PREPARED STATEMENT OF PHYLLIS GARDNER, ASSOCIATE PROFESSOR OF MEDICINE, STANFORD UNIVERSITY, ON BEHALF OF THE BIOTECHNOLOGY INDUSTRY ORGANIZATION

Chairman Bilirakis and Members of the Committee, I am pleased to testify before you today regarding technology transfer issues as they relate to the biotechnology industry. I would like to thank the Committee for its continued leadership on issues related to Americans' health. I am here today representing the Biotechnology Industry Organization (BIO). BIO's membership includes more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in all 50 U.S. states. BIO members are involved in the research and development of health-care, agricultural, industrial and environmental biotechnology products.

My comments today are based on my years of experience on biomedical research in both the academic and private sectors. I have been a tenured associate professor in the departments of molecular pharmacology and medicine at Stanford University since 1984. I am also the former Senior Associate Dean for Education and Student Affairs.

In the past ten years, I have also been associated with ALZA Corporation—a leading drug delivery and pharmaceutical company, recently acquired by Johnson & Johnson—serving as Vice President of Research and Head of the ALZA Technology Institute. In addition, I am or have been a member of the board of directors of several public and private biotech companies, including Aerogen, Inc., Aronex, Inc. (acquired by Antigenics, Inc.), BioMarin Pharmaceuticals, Pharmacyclics, iMEDD Pharmaceuticals, Health Hero Network and Elim Biopharmaceuticals, Inc. I have also served on a number of advisory committees to the National Institute of Health.

In addition, I serve as an adjunct partner of Essex Woodlands Health Ventures, a BIO member, and am an advisor to Draupnir, LLC, a private equity firm.

THE PRIVATE SECTOR ANNUALLY FUNDS BILLIONS OF DOLLARS OF RESEARCH AND DEVELOPMENT IN THE BIOTECHNOLOGY FIELD

The biotechnology industry is the most research and development intensive and capital-focused industry in the world. R&D in the biotechnology world is robust, focusing on new targets and highly innovative therapies. No industry spends more on research and development per employee and no industry faces a lengthier or more complex regulatory process to bring products to market than the biotechnology industry. There are over 1,400 biotechnology companies in the United States, of which about 25 percent are publicly traded. The revenue of these companies was about \$35 billion in 2001 with a market capitalization of \$206 billion in mid-2003. This research-intensive industry spent \$20.5 billion on R&D in 2002¹, with the top five companies spending an average of \$133,000 per employee on R&D. Biotechnology companies rely heavily on public-private partnerships in their R&D initiatives. Importantly, however, only approximately 1.6 percent of the industry's R&D funding in 2002 originated from government sources.²

Biotechnology companies range from very small, private companies with few employees to larger public ones such as Amgen and Genentech. Generally, however, biotechnology companies are either privately held or have much lower market capitalization than the large pharmaceutical companies and very few have yet achieved profitability. While large pharmaceutical companies tend to pursue development of "blockbuster" drugs with market potentials of \$1 billion or more, many biotechnology companies will pursue products with lower market potentials, including those products whose projected revenues may only be 10% or so of the acceptable market potential for a large pharmaceutical enterprise.

Biotechnology companies use living organisms to make their medicines rather than the chemicals used by pharmaceutical companies. As well as—entailing very complicated R&D efforts, this also requires enormously complex manufacturing capabilities. The manufacturing facilities, whose role is to define the biotech medicine, are subject to strict FDA licensing requirements. In addition, both the facilities and the medicine itself are very tightly regulated.

The biotechnology industry is also a dynamic one. The industry supports 437,000 U. S. jobs, including approximately 200,000 jobs directly in the industry, in sectors as varied as agriculture, industrial products and pharmaceuticals. As a whole, the industry is not yet profitable, but biotechnology companies make tax payments of about \$10 billion per year, including income, corporate and other federal, state and local taxes.

Moreover, unlike the pharmaceutical industry, the vast majority of biotech companies spend more than 50 percent of their operating expenses on research and development. This is necessary given the huge investments required to bring a product through the discovery and lead optimization phase, preclinical testing, and then clinical trials required to gain market approval. With the consolidation in the pharmaceutical industry and the risk-averse culture of many of the largest companies, the bulk of early stage research and early clinical development is now performed by the biotech industry, especially in areas focusing on newer targets and featuring the most innovative therapeutics approaches.

It is the early stages of drug development that are most vulnerable to perturbations in the capital markets. While it has been relatively easy for entrepreneurs to obtain seed financing, it is the follow-on financing, the second and third rounds of venture investment required to fund companies beyond "proof of concept", that is often the most difficult. Through the first six months of 2003, follow-on venture financing has represented only twenty five percent of the total venture financings. The total amount of venture financing raised during this period is down twenty seven percent from the same period in 2002. The same challenges also confront smaller cap public companies that have a difficult time raising capital through secondary offerings with depressed stock prices. It is this critical link in the drug development value chain that could be jeopardized if investors become concerned about the government seeking additional compensation for participation in early stage "proof of concept" research.

¹ Source: Ernst & Young, "Resilience: America's Biotechnology Report 2003"

² Source: BioWorld Online, "2002 Grants and Awards to Biotech Companies," April 7, 2003. Grants and awards to biotechnology companies from federal government agencies totaled \$326.1 million in 2002.

THE BAYH-DOLE ACT HAS BEEN AN EFFECTIVE ENABLER FOR TECHNOLOGY TO BE TRANSFERRED FROM FEDERAL AGENCIES TO UNIVERSITIES AND INDUSTRY

As the Committee examines the effectiveness of the transfer of biotechnology from federal laboratories to universities and private companies, it is important to understand the historical and current framework for these transfers.

Over twenty years ago, Congress enacted the landmark Bayh-Dole Act to promote the transfer of government-sponsored research to universities and small businesses. This action was taken in response to concern that the majority of technologies developed with federal funding were not being commercially exploited.

Prior to Bayh-Dole, federal agencies would rarely relinquish ownership of federally funded inventions to the academic and private institutions, even when private sector scientists and engineers actually contributed to the inventions. Valuable technology was left languishing on the shelves of research institutions. For example, in the 1960s, the U.S. government asserted that it owned rights to 5-fluorouracil (an important anti-cancer drug) even though it had provided merely a fraction of the funding that went into discovery. As a result, market entry of this critical product was unnecessarily delayed and industry distanced itself from federally funded university research.

Bayh-Dole authorizes universities, non-profits and small businesses to elect title to inventions made under federal funding agreements. Additionally, Bayh-Dole authorizes federal agencies to grant exclusive licenses in their technologies to private companies. Later, President Reagan extended the policy of Bayh-Dole to large for-profit businesses which today are able to elect title to many inventions they make under federal contracts and grants. The ability to elect title to inventions and to further license valuable technologies gives companies the market exclusivity they need to achieve commercial exploitation.

At the same time, Bayh-Dole reserves to the government a royalty-free license to use the invention for government purposes. Additionally, Bayh-Dole gives the government so-called "march-in rights," which enable it to compel licensing of a federally funded invention if the patent owner has not commercialized the invention in a reasonable time.

Since the enactment of Bayh-Dole, technology partnerships have led to the founding of more than 1,100 companies based on NIH and university research. These technology partnerships and the patents on which they are based are particularly important to small biotechnology companies, which focus their research on breakthrough technologies that arise from basic biomedical research.

At Stanford University alone, over 1,200 "spin-off" companies have been established by current or former students and faculty. Recognized early on by then University President Fred Terman as an important strategy for seed funding of translational research and innovation, the vast majority of these companies were founded with technologies initially developed under government funding. Successful "spin-off" ventures help bring valuable products to market, and also develop the vibrant Silicon Valley surrounding Stanford, which leads in high tech, biotech, and medical device industries. This thriving business ecosystem, in turn enables further R&D initiatives and two-way technology flow between academia and industry. Stanford's Office of Technology Licensing has a robust record of licensing university patents, with royalty income that flows back to the university and the individual inventor. The Cohen-Boyer patent for gene splicing, for example, was supported by NIH grant funding. That patent yielded \$30 million per year in royalty revenue at its peak, for a total value of over one quarter billion dollars to the University, which was spent on further research and education.

THE SMALL BUSINESS INNOVATION RESEARCH PROGRAM IS A VALUABLE SOURCE OF SEED FUNDING FOR THE BIOTECHNOLOGY INDUSTRY, BUT SHOULD BE IMPROVED TO ALLOW GREATER PARTICIPATION BY COMPANIES THAT ARE SUPPORTED BY VENTURE CAPITAL FUNDS

The Small Business Innovation Research (SBIR) program is a competitive, three phase, government funded program that was designed to encourage commercialization of promising technologies. Federal funds are used for the critical startup and early development stages—i.e. those stages that provide proof of concept to attract private equity into further funding rounds. Because the private sector is expected to take over 100% of funding by the third stage, companies are incentivized to expedite commercialization of a particular technology, product, or service.

Since the enactment of the Small Business Innovation Act in 1982, SBIR funding has helped many biotechnology companies compete for federal research and development awards. To qualify for SBIR awards, a small business must be owned by U.S. individuals (as defined by the Small Business Administration's [SBA] guidelines) be

independently operated, for-profit and limited to 500 employees. Ten federal departments and agencies, including the Department of Health and Human Services, are required by SBIR to reserve a portion of their R&D funds for award to small businesses.

Because they help biotechnology companies evaluate new technologies and products at their earliest stage, SBIR awards can be very useful in helping companies to initiate new commercial opportunities. Before—most biotechnology products can become commercially available, however, typically 15 years of work and hundreds of millions of dollars of investment capital are required to complete adequate testing and to secure the necessary approvals.

While SBIRs serve a very useful role, particularly when private equity may be plentiful but directed to late stage private and public companies where the investor's exit strategy is clear and risks are lower, they are by no means a substitute for sustained equity investment. SBA's implementation of the program makes it difficult for companies who also have venture capital (VC) funding to participate in the program.

Under the SBA's current regulations a company applying for SBIR funding must be more than 51% owned by "individuals" who are US citizens or permanent resident aliens and must have less than 500 employees. The SBA has interpreted "individuals" to mean only "natural persons" and not venture capital firms and employee pension funds. Many biotechnology companies have less than 500 employees and obtain the bulk of their funding from venture capital investment. Typical small start-up biotechnology companies that are backed by VC funds are generally more than 51% owned by the VC syndicates. The "individual" shareholders that make up the VC syndicates are often the founders, employees, friends of the company, and angel and family investors. The most promising companies are the ones that attract VC capital. This typical combination of venture funding, industry collaboration and only modest investment directly by individuals boosts "non-individual" ownership above the 51 percent level very early in a company's existence and, in virtually every instance, renders the small business ineligible for SBIR funding. Most if not all start-up biotechnology companies would be ineligible for SBIR funding as interpreted by the SBA.

The SBA has proposed new regulations to clarify the ownership criteria for SBIR awards. However, the proposed regulations do not address the concerns of the industry with respect to VC-backed companies. BIO believes that a provision to remove VCs from determination of size eligibility would allay the concerns of our member companies and fulfill Congressional intent behind the statute. See attached comments filed by BIO. We urge this Committee to express its support for a revised definition of small business that would not penalize those small businesses supported by venture capital funds.

COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENTS ARE AN IMPORTANT VEHICLE FOR PUBLIC-PRIVATE PARTNERSHIPS ON BIOTECHNOLOGY R&D AND SHOULD BE CONTINUED

The Federal Technology Transfer Act (FTTA) allows government and government owned contractor operated laboratories to enter into Cooperative Research and Development Agreements (CRADAs), in order to promote collaboration between the federal government and the private sector. In the medical arena, the goal is to take research "from the bench to the bedside". Under a CRADA, the government shares resources such as personnel, facilities, and equipment with private entities, but does not make cash outlays to the private sector participant. The private sector funds its own activities under the CRADA, thus sharing the total cost of the collaboration.

CRADAs typically allow the private sector participant to retain intellectual property rights to inventions it makes under the CRADA. Also, under recent amendments to the Stevenson-Wydler Act, the private sector participant has a first right of refusal to license any inventions the government makes under the CRADA. Further, technical data that is developed by the government under a CRADA may be protected from disclosure for a period of five years, thus giving the private sector participant a potential competitive advantage in the marketplace.

For biotech companies, CRADAs can be an important opportunity to gain or retain intellectual property rights on biomedical inventions. They can also be helpful by allowing private companies to utilize specialized equipment or tools that are sometimes only available in federal laboratories to test the validity of innovative concepts and new ideas. CRADAs are thus important tools to enable startup biotechnology companies to jump the gap between a useful idea or theory to a successful and profitable product.

NIH has entered into over 400 CRADAs since 1985. One of the most successful CRADAs with NIH was entered into with Aviron (which has since been acquired by MedImmune) in 1995. The CRADA was for a promising influenza vaccine invented at the University of Michigan in the 1960s under US Army sponsorship.— This vaccine had been the subject of NIH-sponsored clinical trials through the 70s and 80s. Despite the lack of a committed industrial sponsor, NIAID had built an impressive base of scientific knowledge around this flu vaccine and its novel form of administration via the nose. Under the CRADA, Aviron and NIAID jointly funded the clinical trials resulting in FDA approval of the vaccine now known as FluMist™.

THE ADVANCED TECHNOLOGY PROGRAM HAS BEEN AN IMPORTANT VEHICLE FOR BIOTECHNOLOGY RESEARCH AND SHOULD BE FULLY FUNDED

The Advanced Technology Program (ATP) was instituted in 1990 under the management of the National Institutes of Standards and Technology. The ATP does not fund product development. Instead, it supports *enabling* technologies that are essential to the development of new products, processes, and services across diverse application areas. This innovative program provides cost-share funding in the critical early stages of R&D, when research risks are too high for other sources of funding. Funding under the program is available to pay up to \$2,000,000 in direct costs over a period not to exceed three years for a single company and up to half of the total project costs for a maximum of five years for a joint venture involving more than one company.

Twenty percent of the Advanced Technology Program funding has gone to biotechnology applications. ATP grants are designed to fill the gap in financing the development of high-risk technologies that biotechnology companies often encounter, and that cannot be financed by venture capital.

ATP grants make a tangible difference to the competitively chosen small companies receiving the assistance, especially during periods when seed investment to fund early, technology-validating R&D is scarce. For example, a grant of \$1.2 million during a biotech investment trough in 1998 accelerated the development of the stem cell culturing device by two years and helped its fledgling developer subsequently attract more than \$70 million in private investment. Another small biotechnology company had just 17 employees when it received a grant in the mid-1990s to develop systems of gene expression analysis. The company leveraged the ATP research into five patents and \$100 million in corporate partnerships, growing rapidly into a billion-dollar company with more than 300 employees and a solid balance sheet that will fund the technology's translation into new medicines.

Since its inception, ATP has fostered development of dozens of biomedical technologies that might otherwise have been delayed for years. Examples of ATP success stories include: an autologous stem cell culturing device that eliminates the need for bone marrow extraction or multiple (up to 140) skin punctures to withdraw blood; an enzyme used in DNA sequencing, including the Human Genome Project, and another enzyme that may replace radioactive substances in diagnostic aids; and a mammography innovation that lowered the cost and widened availability of this life-saving diagnostic procedure. More apropos to today's technology needs is the development of miniaturized, automated DNA-analysis "chips" that are becoming invaluable for rapid, accurate genetic analysis.

The ATP program is of course subject to Congressional appropriations. Notwithstanding the multiple successes of the program, Congress has not consistently funded the program at the necessary levels. BIO believes that continued funding for ATP would reap benefits for health and medical research far in excess of the federal funds invested.

CONCLUSION

BIO supports the continuing efforts of federal agencies to utilize the various vehicles that Congress has authorized for transferring valuable technology from the public to the private sector. As noted, licensing of federally funded inventions and partnering under CRADAs are two critical vehicles for private sector companies to gain access to technology developed with federal support. Additionally, the SBIR and ATP programs provide critical financial assistance to small and emerging biotechnology companies. BIO supports modifications to the SBIR program that would increase the opportunities for companies to participate in the program. Additionally, BIO encourages the Congress to continue fully funding the ATP initiative. The federal government's support helps small companies attract the necessary private sector investment to bring good ideas to the market.

Given the significant technological breakthroughs that have been achieved in the medical and health fields, BIO believes that the federal dollars that are invested in biotechnology research have yielded significant benefits generally for the health of the nation and specifically for the federal treasury.

However, while continued federal support is key to the future of the biotechnology industry, federal funding still represents only about 1.6% of the total funds raised for research and development by the industry. Thus, federal R&D programs must be flexible enough not to stifle the private sector investment that is so critical for bringing products from the bench to the bedside.

Thank you again for your support of biotechnology's efforts to contribute to the advance of health in the United States. I would be pleased to respond to questions from the Committee.

Mr. BILIRAKIS. Thank you very much, Dr. Gardner. And, again, thank you for coming such a long way to be here to help us out. Dr. Neighbour, please proceed.

STATEMENT OF ANDREW NEIGHBOUR

Mr. NEIGHBOUR. Chairman Bilirakis, members of the subcommittee, on behalf of the University of California, I welcome and thank you for this opportunity to testify before this subcommittee.

As Executive Director of Research Administration at UCLA, I am responsible for managing publicly and privately sponsored research on our campus, and for the transfer of its innovative technologies to the marketplace. I hope to demonstrate today that there exists an effective collaboration between American universities, the life sciences industry, and NIH, that yields enormous benefit for our society and for mankind. I will briefly describe some of these benefits as well as several challenges and controversies that have the potential to impede this success. I would ask that you refer to my written testimony for greater detail.

As you have heard already today, university tech transfer began approximately 23 ago with the passage of the Bayh-Dole Act. A prime example of successful technology transfer occurred in 1973, however, well before the Act was contemplated or enacted with the invention, by Cohen and Boyer, of recombinant DNA technology known as gene splicing.

Funded in part by NIH, these two scientists at Stanford at the University of California discovered how to insert genetic material into native DNA. This technique launched a new industry called biotechnology.

At that time, ownership of NIH-funded inventions rested with the government. However, because of a special patent agreement with NIH, the two universities were allowed to own the patent and assume the responsibility for its commercialization. Stanford's Technology Transfer Office licensed the patent to more than 300 emerging companies.

Recognizing that effective license was beyond the government's resources, Congress, in a bold and inspired move, passed the Bayh-Dole Act, and universities took over the responsibility. And since 1980, NIH has played a lead role in implementing the Act, and universities have built effective programs for managing their intellectual property while maintaining their commitment to provide public access to the results of their research.

Major NIH-funded discoveries at the University of California, or UC, have included new technologies for improving radiographic imaging, improved methods to develop and develop therapeutic drugs,

and novel diagnostics for people and animals. In addition, NIH funding has formed a major platform for research that has fostered additional Federal and private funding sporting a plethora of high value products.

Unfortunately, success has led to criticism, which I believe is founded mostly on three misunderstandings. These are: firstly, many think tech transfer is a simple linear process that speeds inventions from the bench to the bedside. In reality, it is a rather complex, slow, and resource-intensive activity, often spanning many years.

UC, for example, spends almost \$20 million per year in managing a portfolio of more than 5,000 inventions and 1,000 active licenses. Almost 1,000 new inventions are disclosed to us each year, and that is with less than 5 percent of those ever being commercialized.

The process is more of a circle with multiple inputs and outputs than something linear. Federal funds encourage support from industry and other sources. Academic research produces early stage scientific knowledge, and that in turn stimulates the development of commercial products. Partnership with industry is invariably essential to convert the results of NIH-funded endeavors to products that can directly aid the public.

The second misunderstanding is that money is often used to measure technology transfer success. This metric ignores the many additional benefits that derive from technology transfer. The education of students that go on to feed the workforce, new companies and jobs that aid regional economies, and the products themselves that save lives and improve the quality of life.

And, finally, many people believe that universities do tech transfer to make money or to get rich. After all expenses are paid, even those universities with gross revenues from licensing in excess of \$20 to \$50 million only retain \$5 to \$10 million of that. And this is reinvested back into the research enterprise. While these funds are of great value to the university, few institutions would view this as an effective way to increase their capital assets.

Imagine a world without knowledge of the human genetic code—recombinant DNA tools to splice and correct genes, ways to map and fingerprint DNA to convict the guilty and free the innocent. All of these technologies, together with vaccines and new drugs, began in universities that were financed in whole or in part by NIH.

It is my fervent belief that this alliance between the NIH, the universities, and the industrial sector, is working well. We must preserve it, but we must also continue to strive to enhance its effectiveness and to ensure that arbitrary impediments are removed for the health of the public and of this Nation. With a greater knowledge and understanding of the tech transfer process and the accomplishments of NIH, and their academic partners, you on this committee I believe will play a key role in protecting these beneficial outcomes.

Thank you very much for the opportunity to testify before you today.

[The prepared statement of Andrew Neighbour follows:]

PREPARED STATEMENT OF ANDREW NEIGHBOUR, ASSOCIATE VICE CHANCELLOR FOR
RESEARCH, THE UNIVERSITY OF CALIFORNIA, LOS ANGELES

Chairman Bilirakis, Ranking Member Brown, Representative Waxman and Members of the Subcommittee: On behalf of the University of California, I welcome this opportunity to testify before this subcommittee on the topic of "NIH: Moving Research from the Bench to the Bedside." As the Executive Director for the Office of Research Administration at UCLA, I am responsible for the management of both publicly and privately sponsored research for the campus, and for the transfer of its innovative technologies to the marketplace. I have enjoyed more than twenty years working in the realm of technology transfer in both academic and corporate sectors. I also serve as a Board Member of the Council on Governmental Relations (COGR), an association of more than 150 leading US research universities, and am the incoming chair of COGR's Committee of Contracts and Intellectual Property.

BACKGROUND

Over the past twenty years or so, the NIH and research universities throughout the United States who receive their funding support from extramural NIH grant programs have developed a collaborative and effective alliance that yields enormous benefit for our society and for mankind. In my remarks today, while I will describe some of these benefits, I will also discuss the challenges and controversies that have the potential to impede this success.

The passage of the Bayh-Dole Act in 1980 was a bold and inspired move that shifted from the government to universities the responsibility for protecting and commercializing inventions made with federal funds. The Act applies to research funded by any federal agency. However, because most life sciences and biomedical research is supported through the NIH, and this segment tends to generate the most intellectual property, it is the NIH that plays perhaps the most visible role in Bayh-Dole implementation. Over the past twenty years or so, the guidance, oversight and coordination provided by NIH has served to build a collaborative alliance between academe and the government leading to more and more effective technology transfer.

In the University of California alone, more than 6,500 individual scientists have reported new inventions since the enactment of Bayh-Dole representing the creation of a vast research enterprise that has brought immeasurable and invaluable benefits to society.

Perhaps the prototypical example of the benefit of federal/university collaboration is the 1973 discovery by Cohen and Boyer of recombinant DNA technology, otherwise known as "gene splicing." In research funded by the American Cancer Society, National Science Foundation and NIH, these two scientists at Stanford and the University of California discovered the means to insert genetic material artificially into native DNA. This technique launched an entire new industry called "biotechnology." As you will note, this invention predated Bayh-Dole. However, because of a special "patent agreement" with NIH, Stanford and the University of California were allowed to elect title to the patent and, in so doing, assumed the responsibility for licensing the invention. During the life of the patent, Stanford's technology transfer office executed and managed more than 300 non-exclusive licenses with this growing biotechnology industry.

With this experience in view, many individuals and organizations believed that the task was well beyond the means and capabilities of the government. Consequently, they encouraged the Congress to consider moving the responsibility for commercializing federally funded inventions from the government agencies to the University receiving the federal grants. Passage of Bayh-Dole conferred not only the right to take title to inventions arising from government-funded research, but also an obligation to commercialize these inventions diligently for the benefit of the public. With this mandate, Universities began the difficult task of developing technology transfer programs equipped to steward their newly acquired intellectual property assets.

TECHNOLOGY TRANSFER AT THE UNIVERSITY OF CALIFORNIA

With the largest academic research enterprise in the US and perhaps the world, the University of California system has built a technology transfer program that many consider to be among the most effective yet developed. Initially, the program was centered in the Office of the President as a central Office of Technology Transfer. As experience grew, the University realized the merits of moving some of the activities to the local campuses, particularly those with large research programs. Presently, the larger campuses (and the federal laboratories managed by the Uni-

versity) perform most of the technology activities at the local campus. The system-wide OTT provides coordination, oversight, policy review, legal support and some licensing support. The individual campuses that have their own technology transfer offices manage the licensing of their portfolios locally. The system as a whole expends approximately \$10-12 million per year in operating expenses and the same amount in "out-of-pocket" patenting costs to manage almost 1,000 new inventions received each year. The University has accumulated a total portfolio of more than 5,000 active inventions in its systemwide portfolio and monitors almost 1,000 patent licenses with industry. In FY02, the University executed 125 new patent licenses and 55 plant licenses. In summary, the process involves the evaluation of inventions, protection of the intellectual property through patent or copyright, marketing to industry, negotiating and executing licenses, and monitoring the licensees' diligence in commercializing inventions.

Since the Cohen-Boyer invention, major discoveries that resulted from NIH-funded research at the University of California have included new technologies for improving radiographic imaging, improved methods to develop and deliver therapeutic drugs, and novel diagnostics for people and animals. In addition, NIH funding has formed a major platform of research that has fostered additional federal and private funding spawning a plethora of high value products. UCLA alone has brought to the public many valuable advances in healthcare including devices to correct brain aneurisms, the nicotine patch to control tobacco addiction, positron emission tomography (PET scanning), and new diagnostics for breast and prostate cancer. All of these examples were either directly or indirectly supported by NIH and the technology transfer process.

Unfortunately, however, these very successes have turned a spotlight onto the process which, in turn, has caused some to ask just how successful are we? Are we getting too rich from tax-payer supported research? Or perhaps we are wasting this resource and not realizing adequate return on investment.

While oversight and monitoring of federally supported programs is clearly appropriate and desirable, some of the criticisms appear to be founded on misunderstandings of the process and the drivers that motivate its participants.

In my view, there are three myths that underlie most of the criticism of the technology transfer process. They can be briefly summarized as:

- (i) Technology transfer is a simple linear activity from "bench to bedside;"
- (ii) Money is a sound measure of performance and value; and
- (iii) Universities commercialize their inventions to create wealth for themselves.

I will now amplify each of these myths.

MYTH #1: TECHNOLOGY TRANSFER IS A LINEAR ACTIVITY

Previous speakers have provided definitions of the term "technology transfer." Many people who are not familiar with technology transfer conjure in their minds a somewhat linear activity, whereby federally funded research in the university results in a new discovery. Then driven by the Bayh-Dole Act, the university technology transfer office: reviews the invention for commercial viability; elects title; files a patent; markets it to industry; negotiates a license; and the product, perhaps a new therapy for a major disease, goes to market. In other words, an academic researcher discovers a new drug and soon afterwards it shows up in the pharmacy.

Like many other things, this process is not as simple as that. In observing that gravity could bend light waves, Einstein showed nearly a century ago that the shortest distance between two points is not a straight line but a curve. Thus, we too should imagine a technology transfer process that is not linear, but rather one whose beginnings and endings merge to form a circle. For example, while public funding supports discovery, the early stage inventions made in the basic science laboratory of a university frequently attract support from the private sector. Collaborations with industry that follow may then lead to the building of new products on the knowledge and platform technologies made by the university scientist. Industry turns these through lengthy development cycles over many years into products. Most product candidates wither along the way; few make it through development and testing to the market. Product sales generate profits and wealth, some of which is returned through taxation to restore the federal coffers. In addition, through sponsored research and philanthropy, industry reinvests some of this wealth into new research. Sometimes new discoveries become the platform for the creation of new companies that bring new jobs to our communities and sustain economic development through taxes. Royalties paid to the university are shared with the inventor and the university portion is used to sustain the technology transfer process, build new research infrastructure, and support new discovery programs.

In fiscal year 2002, 973 new inventions were reported to University of California technology transfer offices adding to a total invention portfolio of more than 5,000 active cases. On receipt of a new invention disclosure, the first task for the technology transfer office (TTO) is to determine what funding sources were used to support the research yielding the new discovery. This is done to establish whether prior rights may be attached to the invention based on commitments to the funding source. If supported with any NIH grants or contracts (or any other federal agency), the invention will fall under the conditions of the Bayh-Dole Act requiring that we report the invention and decide whether or not to elect title and file for intellectual property protection through the US Patent and Trademark Office. To arrive at this decision, the TTO must exercise professional judgment based on a scientific, technical and business assessment to determine the commercial viability of the invention. Is it a profound scientific breakthrough with no commercial utility? Is it perhaps, simply a better mousetrap for which there is no market need? Or perhaps it is so new, that there are no comparable products in the market. The point being that technology transfer is not a straightforward process in which research by NIH always generates inventions with an obvious value in the marketplace. A certain medical school dean once asked me why we didn't only patent "the good ones." Because many University inventions are so unrefined and untested, it is difficult to determine with certainty the future path for the majority of the inventions that faculty researchers disclose. Illustrative of the process is the oft used axiom of the princess kissing frogs in search of a prince.

Once the patent application is filed, the TTO sets about marketing the invention to appropriate industry partners in the hope of finding one willing to develop the invention into a product under a suitable contract or license. Frequently, the inventions themselves are valuable not as an actual saleable product, but as a technology that will assist the corporate partner in developing their own products. A common example arising from NIH-funded research might be the discovery of a new cellular component that is responsible for triggering cancer growth. It may be possible to gain a patent on the discovery of this protein and on its use as a target for drugs that might inhibit its function and stop cancer cells from spreading. The drug, in this example, would be developed exclusively by the company. However, they might need a license to the original invention and access to the knowledge and skill of the university inventor in order to develop their commercial product effectively.

Having found a company interested in licensing the invention, the TTO negotiates a license that establishes the obligations of the licensee to develop the invention diligently at its expense and to pay fees and royalties against future product sales in return for the license to make, use and/or sell the invention.

The "frog-prince analogy" is a good one as there is an enormous winnowing effect with very few discoveries getting through this process and reaching the marketplace. On average, the University of California files new patent applications on 45-50% of the new inventions disclosed each year. Approximately 30% of these will issue as US patents, and less than half of those will ever be licensed. To recap, of the 973 new discoveries received in 2002, only 5% will be licensed. Many of these will fail to reach the market.

To close the loop on this circular process, however, it should be stressed that the discovery is often the beginning of a new process. Exposure to the researcher and his or her invention by the company frequently generates a new interest that results in the company becoming a private sponsor of a new research program in the inventor's laboratory. In addition, under those rare circumstances where a highly commercial invention does yield a successful product in the marketplace, income earned from royalties by the University is reinvested into research, and the companies tax obligations result in sources of revenue to fund future agency research appropriations, thereby completing the circle.

From this discussion, I hope the Subcommittee will appreciate the complexity of technology transfer and the relative difficulty of moving inventions from bench to bedside.

MYTH #2: MONEY IS A SOUND MEASURE OF PERFORMANCE AND VALUE

For the external observer, it is tempting and easy to measure technology transfer by the amount of money it yields. For any given University, this would mean examining the annual gross revenues derived from licensing its inventions. The technology transfer circle is like a catherine wheel, a firework (popular in Great Britain) consisting of a disk with rockets equally spaced around its perimeter. When lit, it spins at high speed and showers energy and light in a broad circumference. Indeed, some licenses generate income, but the research enterprise yields so much more. In reality technology transfer includes the training and graduation of students who

move into the world as trained scientists and professionals. Knowledge is created and shared through publication and presentation. Faculty scientists serve as consultants and advisors to the public and private sectors. While some inventions must be patented to ensure commercial interest and value, not all discoveries benefit society through licensing and commercialization. Counting dollars to quantify technology transfer ignores these other sometimes more valuable benefits that accrue from federally supported research activities in the University.

A letter from Carl Feldbaum, President of the Biotechnology Industry Organization, dated June 11, 2001 to Dr. Maria Friere, then Director of Technology Transfer at NIH, succinctly and thoroughly lists the varied and significant returns on investment that accrue to the public from NIH-sponsored research. These include basic science knowledge and understanding; the development of new therapeutics and diagnostics; scientific training that provides employees for a rapidly growing new biotechnology industry; research tools to advance scientific research; and the licensing of new inventions from both intramural and extramurally-funded research.

Furthermore, a quantitative performance assessment is predicated on the assumption that more money means greater societal value. Is a University that makes many millions of dollars from an improvement in cell phone technology necessarily more successful at technology transfer than one that develops a cure for a rare disease that may yield less than one hundred thousand dollars?

Critics of academic technology transfer who focus on the revenue streams derived from licensing often erroneously contend that universities should not get rich from exploiting tax payer's funds. Simply put, universities do not "get rich" from their technology transfer activities. The University of California, widely held to be one of the most successful university systems in the field of technology transfer averages an annual gross income from licensing of approximately \$80 million. After payment of legal expenses, the cost of providing technology transfer services, and the inventor's share, \$20-25 million is returned to the system to support ongoing research. This amount represents less than one percent of the total research expenditures of the UC system. The annual survey published by the Association of University Technology Managers (AUTM) shows that fewer than ten universities generated more than \$20 million in gross revenues in FY2002. In virtually all cases, this was because each had a single invention that yielded the majority of the income. At the University of California, 25 inventions from its total active portfolio of 5,000 produced 68% of its annual income.

Similarly, few individual inventors receive significant funds from their inventions. Since most inventions yield less than \$10,000 in gross royalties per year, few faculty inventors realize any significant gains from the 35% revenue share that must be split with their co-inventors.

It has also been argued by some that royalty bearing licenses of federally funded discoveries contribute to unreasonable pricing of "blockbuster" drugs. While it has been clearly documented that few if any of these drugs arose directly from federally funded research, it has been unequivocally demonstrated that drug pricing is determined by the high cost of development and testing required before a drug can be sold, and that royalty obligations have negligible effect on market price of these treatments.

Paradoxically, NIH was recently criticized for not charging a high enough royalty for technology it developed that was part of a major drug now marketed by Bristol-Myers Squibb.

Therefore, measuring technology transfer accomplishments by the amount of money an invention generates for the university or the inventors fails to capture the broader benefits to the public that accrue from NIH-funded research and the larger research enterprise.

MYTH #3: UNIVERSITIES COMMERCIALIZE THEIR INVENTIONS TO CREATE WEALTH FOR THEMSELVES

Focusing on the income derived from licensing for one moment, an experienced businessman would conclude that based upon return on investment ratios, University technology transfer is largely unsuccessful. A quick search of the Patent Office database shows that the Regents of the University of California have been awarded 4,313 US patents since 1975. That's more than Pfizer, Inc., (2,774) and less than Merck (6,346). While the University may thus be in the same league as certain Fortune 100 companies, there are fundamental difference in its commercialization strategies. For profit companies focus their research in market segments in which they do business. Typically, they support internal research and development for the purpose of expanding their targeted strategic business interests. Universities not only attempt to broaden their research enterprise across all disciplines, they do not

direct the research objectives of their faculty. Another particularly critical point is that the university relies on their own faculty to decide if it is best to publish their findings or to seek a proprietary position on their discoveries before they are more broadly disseminated. Protecting the right of its faculty to select topics on which they conduct their research and to publish whatever and whenever they see fit are among the basic tenets of academic freedom. Consequently, university inventions that may have great potential value do sometimes find their way in to the public domain for all to use without the exclusionary protection of a patent. If universities were to run technology transfer as a business, we would behave very differently.

The mission of the research university is education, the pursuit of knowledge, and public service. Basic academic studies of bacteria in hot springs in far away places may seem eclectic to some. But imagine how a drug for cancer would have been discovered by a major multinational pharmaceutical company had it not been for laboratory processes that use enzymes isolated from these very bacteria to manipulate genes to produce the drugs that now treat patients.

The primary purpose of technology transfer in a research university is to provide a supportive and sustained environment for the researcher to flourish. Licensing generates corporate collaborations building partnerships with industry. Companies have resources that Universities cannot afford that academic scientists need access to for their research. Some inventions will stall without corporate involvement. Many potential life science-based discoveries need the formulation, manufacturing, testing and marketing skills of corporations to turn them from an academic discovery to one that can be dispensed from the pharmacy. As indicated above, revenues from technology licensing represent less than one percent of our total research budget and a fraction of a percentage point of total operations. Given the cost of technology transfer and the relatively low cash returns, this is an ineffective source of operating capital and the University does not view its purpose to be one of budget supplementation.

Universities measure their success by their contribution to the spinning catherine wheel. Not only how many inventions has it yielded, and how many have made it into the market to provide benefit to the public, but also how many graduates has it prepared for the world. State universities support and contribute to local economic development. Growth of its research enterprise creates jobs in the university itself. Sometimes it generates new ventures that grow into new companies. The leading biotech companies like Amgen and Genentech all grew from academic origins. At the University of California alone, more than 200 new companies have been spun out based on new technologies invented by its faculty in recent years.

CONCLUSION

In supporting the Bayh-Dole Act and our role in technology transfer, universities are faced with a conundrum. On one-hand, some believe that we are getting rich using tax payers' support through federal grants from NIH and other agencies. Conversely, some argue that we should derive a greater financial return on investment and criticize us for being incompetent and wasting federal or public funds.

The reality, however, is revealed when one measures the broader value and benefits that emanate from the university academic enterprise—namely the fundamental advances in knowledge and technology arising directly and indirectly from the creative efforts of hundreds of thousands of expert academic scientists and their students. The enablement of new products that have changed our world, especially in the form of improved understanding of disease, of accurate diagnostics, and effective therapeutics that allow the dying to live and improve the quality of life of so many.

What would the world be like today without our knowledge of the human genetic code; recombinant DNA tools to splice and correct genes; ways to map and fingerprint DNA to convict the guilty and let the innocent free? All of these technologies together with vaccines and new drugs began in universities that were financed in whole or in part with federal funds through the NIH. Imagine a world where our collective expertise that has been built over the past 20 years to bring these and other innovations forward is eroded and impeded by changing the law because a minority feel it's not working—a feeling founded on a lack of knowledge and understanding of the complexity of the task.

The alliance with NIH is working. Guidelines developed and promulgated by the agency encourage the broad dissemination of research tools developed in universities that can facilitate new research discoveries. Giving Universities the opportunity and the right to manage their inventions assures that they will be transferred diligently and effectively in a manner beyond the capabilities and resources of the agency if it were to carry this responsibility alone.

Mr. Chairman, Subcommittee Members, it is my fervent belief that this alliance between the NIH, the universities and the industrial sector is working well. We must preserve it, but we must also continue to strive to enhance its effectiveness, and to ensure that arbitrary impediments are removed for the sake of the public and this Nation. With a greater knowledge and understanding of the technology transfer process and the accomplishments of NIH and their academic partners, you will play a key role in protecting these beneficial outcomes.

Thank you very much for the opportunity to testify before you today.

Mr. BILIRAKIS. Thank you, Doctor. And I will say to you all when we finish up that we would very much welcome suggestions from you in terms of how we can improve the overall process. So please be thinking of that. Help us to help you, so to speak.

Dr. Soderstrom?

STATEMENT OF E. JONATHAN SODERSTROM

Mr. SODERSTROM. Thank you, Mr. Chairman. And I echo the comments of my colleagues here in welcoming the opportunity to address what we think is a very important topic for this government to face.

In my role as Managing Director of the Office of Cooperative Research, I have exactly the same responsibilities that my colleague Andrew Neighbour has. So I won't bother to repeat those.

What I would like to underscore, however, is that in the course of fulfilling our research and educational missions, university scientists often create intellectual assets that have the potential to benefit society and further the university's educational goals. Some of these assets, but by no means all, may result in patentable inventions.

As they initially emerge from the university's laboratories, however, these inventions are not—and I underscore are not—commercial products. Rather, they require substantial investment of time, energy, and financial resources to unlock their potential. That is not the role of the university. That is the role of the private sector. This process is best realized through the significant commercial sector involvement.

Under the protection of the license agreement that we negotiate with companies, they can confidently invest in transforming these intangible assets into tangible products. Prior to the enactment of the Bayh-Dole Act, companies faced significant hurdles in negotiating such agreements with universities. Because the government lacked the resources and links with industry needed to develop and market these inventions, hundreds of value patents and many new chemical entities were sitting unused on the shelves of laboratories throughout the United States.

In addition, U.S. industry was not inclined to brave the government bureaucracy to license these patents. Thus, technology transfer from universities was primarily accomplished from—by publishing the research results, training students for the workforce, and, in some cases, with land grant universities' agricultural extension services.

The ability, however, to retain title and, thus, license the inventions has been a healthy incentive for universities to become much more involved in the technology transfer process, and such incentive was needed. We have ample evidence of that, since participation prior to that was so underutilized.

Since then, we have seen that patent and licensing activities has encouraged faculty and the universities to get involved in a rather time-consuming activity, which has to be done in addition to our primary missions of research and education. University patenting and licensing efforts under Bayh-Dole have fostered the commercialization of many new technological advances that impact the lives of millions of people across this Nation.

Numerous pharmaceutical and medical products, environmentally friendly, or manufacturing technologies, inventions which improve public safety, and information technology services have resulted from the transfer of federally sponsored research results from academic laboratories to the business community and ultimately to consumers.

In many instances, these products and processes would not have reached the public without the incentives that are afforded by this Act. Indeed, the *British News Weekly*—the economists recently concluded that the Bayh-Dole Act was possibly the most inspired piece of legislation ever to be enacted by the American Congress in the past half-century. I agree. If you look at the results, I think you will as well.

Over the last 23 years, nearly 23,000 license agreements have been enacted and are currently active. Last year alone 360 new—I am sorry—in the last 5 years, over 1,500 new products have been introduced in the marketplace. Last year 494 new companies were formed based on licenses from academic institutions. And since 1980, 3,800 new ventures have been created. I think those are astounding results. And if I just look at my own institution—Yale University, which happens to be a substantial recipient of NIH funds—I see the same effect.

The result of the support of NIH funding has been a wealth of new knowledge that has led to discoveries that are transforming our understanding of human disease. Translating this knowledge into new means of diagnosis, prevention, and treatment has yielded new inventions, with the potential for a profound and positive effect upon the welfare and health and safety of humankind.

But if I look, in particular, at one issue that hasn't been mentioned yet today but I want to draw attention to, which is the transformation of the local economy based on this. And based just on Yale's strength in the biomedical sciences, we have been able to help build a biotechnology industry in and around an economically depressed area of New Haven, Connecticut.

The results from the formation—have resulted in the formation of 25 new biotechnology companies in the greater New Haven area. In the last 2 years alone, those companies have attracted \$1.5 billion in private sector investment, all of which is going into further development of NIH-funded research. More importantly, those companies now employ 1,300 people, and they have begun the transformation of more urban areas.

Mr. Chairman, I want to bring to your attention something that I think exemplifies the heart of my testimony. I recently had a conversation with the Vice Chairman of the NASDAQ stock market. In the course of that conversation, he related to me that he believed that based on his estimate 30 percent of the companies that

are currently listed on the NASDAQ exchange owe their value to the results of government-sponsored research and development.

Technologies licensed from academia have been instrumental in spawning entirely new industries, improving the productivity and competitiveness of those companies, and creating new companies and jobs. The Bayh-Dole Act continues to be a national success story, representing the foundation of a successful union among government, universities, and industry, and the success of this three-way partnership cannot be overstated.

Thank you, Mr. Chairman.

[The prepared statement of E. Jonathan Soderstrom follows:]

PREPARED STATEMENT OF E. JONATHAN SODERSTROM, MANAGING DIRECTOR, OFFICE OF COOPERATIVE RESEARCH, YALE UNIVERSITY

Mr. Chairman, thank you for the opportunity to testify before your Subcommittee on the important topic of translating research from the bench to the bedside.

My name is Jon Soderstrom. I am the Managing Director of the Office of Cooperative Research (OCR) at Yale University. The Office of Cooperative Research is the patent management organization for Yale University. I also serve as the Vice President for Public Policy the Association of University Technology Managers known as AUTM. AUTM is a nonprofit organization created to function as a professional and educational society for academic technology transfer professionals involved with the management of intellectual property. AUTM was founded in 1974 as the Society of University Patent Administrators. That group laid the foundation for the association that exists today—more than 3,000 members strong representing over 1,500 institutions and companies across the globe. Neither Yale nor AUTM have received any federal grants, or engaged in any federal contracts or subcontracts that require reporting under House rules.

TRANSLATING UNIVERSITY INVENTIONS INTO COMMERCIAL PRODUCTS

In the course of fulfilling our research and educational missions, university faculty often create intellectual assets that have the potential to benefit society and further the university's educational goals. These assets may include patentable inventions, copyrightable works or ideas that form the basis for commercializable intellectual property. As they initially emerge from the university's laboratories, these inventions are not mature commercial products. Rather, they require significant investment of time, energy and financial resources to unlock their potential. This process is best realized through a strategy of attracting commercial sector involvement. Under the protection of a license agreement, companies can confidently invest in transforming these intangible assets into tangible products. Prior to the enactment of the Bayh-Dole Act (P.L. 96-517), the "Patent and Trademark Act Amendments of 1980" on December 12, 1980, companies faced significant hurdles in negotiating such agreements with universities.

The Bayh-Dole Act created a uniform patent policy among the many federal agencies that fund research. The Act enables small businesses and nonprofit organizations, including universities, to retain ownership of inventions resulting from federally funded research and to manage the licensing of them to industry for commercial product development in the public interest. Prior to the Act, ownership of patents resulting from university discoveries was largely controlled by the federal agencies that sponsored the research. Because the Government lacked the resources and links with industry needed for development and marketing of the inventions, hundreds of valuable patents were sitting unused on the shelf. Government policy at that time was generally to offer non-exclusive licenses under all inventions that it owned—a licensing stance administered under some 24-26 different non-uniform agency policies, which proved to be highly unsuccessful. Under these conditions, U.S. industry was not inclined to brave government bureaucracy to license patents. Thus, technology transfer from universities was accomplished primarily by the publishing of research results, training of students for the workforce and some extension programs established by the land-grant universities. The benefit to U.S. industry of such an unstructured process is undocumented and highly speculative. As the authors of the Act, former Senators Birch Bayh and Robert Dole, recently noted¹:

¹ Birch Bayh and Robert Dole, "Our Law Helps Patients Get New Drugs Sooner," Letter to the Editor, *Washington Post*, April 11, 2002; Page A28

Government alone has never developed the new advances in medicines and technology that become commercial products. For that, our country relies on the private sector. The purpose of our act was to spur the interaction between public and private research so that patients would receive the benefits of innovative science sooner.

The ability to retain title to and license their inventions has been a healthy incentive for universities to become involved in transfer of technology from their laboratories to the marketplace. Such incentive is needed, since participation in patent and licensing activities is time consuming for faculty, and must be done in addition to our primary research and teaching missions. University patenting and licensing efforts under the Bayh-Dole Act have fostered the commercialization of many new technological advances that impact the lives of millions of people across the nation. Numerous pharmaceutical and medical products, environmentally friendlier manufacturing technologies, inventions which improve public safety, and information technology services have resulted from the transfer of federally supported research results from academic laboratories to the business community and, ultimately, consumers. In many instances, these products and processes would not have reached the public without the incentives and procedures afforded to higher education institutions by the Act. As a recent article in *The Economist* noted²:

Possibly the most inspired piece of legislation to be enacted in America over the past half-century was the Bayh-Dole act of 1980. Together with amendments in 1984 and augmentation in 1986, this unlocked all the inventions and discoveries that had been made in laboratories throughout the United States with the help of taxpayers' money. More than anything, this single policy measure helped to reverse America's precipitous slide into industrial irrelevance.

A recent national survey conducted by AUTM³ reports that 70% of the active licenses of responding institutions are in the life sciences—yielding products and processes that diagnose disease, reduce pain and suffering, and save lives (Attachment 1: AUTM Licensing Survey, FY 2001). Most of these inventions involved were the result of federal funding from the National Institutes of Health. While it would be impossible to list all such inventions, a few examples of technologies and products originating from federally funded university discoveries include:

- Artificial lung surfactant for use with newborn infants, University of California
- Cisplatin and carboplatin cancer therapeutics, Michigan State University
- Citracal® calcium supplement, University of Texas Southwestern Medical Center
- Haemophilus B conjugate vaccine, University of Rochester
- Neupogen® used in conjunction with chemotherapy, Memorial Sloan Kettering Cancer Institute
- Process for inserting DNA into eucaryotic cells and for producing proteinaceous materials, Columbia University
- Recombinant DNA technology, central to the biotechnology industry, Stanford University and University of California
- TRUSOPT® (dorzolamide) ophthalmic drop used for glaucoma, University of Florida

These examples of successful new technologies demonstrate that a strong national infrastructure to support technology transfer has been established at academic institutions across the nation since passage of the Bayh-Dole Act. The royalties received from the licensed inventions support such an infrastructure. The Act requires that royalties received by universities from federally-funded inventions be reinvested for research and education purposes, after payment of a share to the inventor and payment of incidental legal expenses associated with patenting and licensing of the invention.

University use of royalty income is complex and diverse. Most frequently royalty income is used for research and educational expense of graduate students, start-up research costs for new or junior faculty, seed money for innovative new projects or initiatives (often provided through an intramural research competition), computer equipment and laboratory facilities renovation. Universities have used royalty income for a variety of innovative programs or initiatives. Examples include summer programs for female undergraduate students interested in science careers, technical assistance programs which provides high technology urban planning and architectural visualization services to inner city communities based on the agricultural ex-

²*The Economist*, "Innovation's golden goose," December 14, 2002

³The Association of University Technology Managers, "AUTM Licensing Survey, FY 2001: A Survey Summary of Technology Licensing (and Related) Performance for U.S. and Canadian Academic and Nonprofit Institutions, and Patent Management Firms." AUTM: Northbrook, IL, 2002.

tension service model, and new laboratory buildings to support the demands of 21st century medical research.

For most universities royalty income does not represent a significant source of revenue when compared with their federal funding or sponsored research expenditures. The Council on Government Relations (COGR) estimates that overall the aggregate university share of royalty revenues is in the range of 3% of total federal funding and of total research expenditures⁴. Some universities do better than others in terms of royalty income received. Most universities, however, do not derive substantial revenue from royalties by almost any standard of comparison. For those universities that derive substantial income from royalties, that success often tends to be associated with one particular invention. There is considerable annual fluctuation in income received, and one-time occurrences (e.g. settlement of a legal dispute over rights to an invention) can result in very large perturbations in income amounts. Thus, relatively few universities derive substantial revenues from royalties, and universities as a whole are not reaping "windfall profits."

Nevertheless, in 1980 there were approximately 25-30 universities actively engaged in the patenting and licensing of inventions. It is estimated that there has been close to a ten-fold increase in institutional involvement since then. The AUTM survey reflects the impact of this growth in activity:

- Over 4,000 new license and option agreements were executed with nearly 23,000 such agreements currently active.
- Nearly 360 new commercial products were brought to the market under license to a commercial partner. Since 1998, more than 1,500 new products have been introduced to the marketplace.
- 494 new companies were formed based on a license from an academic institution. Since 1980, over 3,800 such ventures have been created.
- Approximately \$30 billion of economic activity each year, supporting 250,000 jobs can be attributed to the commercialization of new technologies from academic institutions.

Technologies licensed from academia have been instrumental in spawning entirely new industries, improving the productivity and competitiveness of companies, and creating new companies and jobs. In summary, the Bayh-Dole Act and its subsequent amendments created incentives for the government, universities, and industry to work together in the commercialization of new technologies for the public benefit. The success of this three-way partnership cannot be overstated.

YALE'S EXPERIENCE

Yale's Office of Cooperative Research was created in 1982 in response to the passage of the Bayh-Dole Act that encouraged universities to seek commercial partners to move their discoveries out of the laboratory and into the marketplace. The OCR was charged with extending and expanding Yale University's interaction with the private sector. The duties of the OCR include oversight for patenting and licensing activities, as well as development of university inventions. OCR staff work with Yale researchers to identify inventions that may ultimately become commercial products and services useful to the public.

In FY 2002, approximately \$335 million or 80% of Yale's sponsored research and training was supported federal agencies such as the National Institutes of Health (NIH), National Science Foundation (NSF), Department of Defense (DOD) and Department of Energy (DOE). The largest federal sponsor is the NIH, which provided \$257 million of grants and contracts during 2002. The result of this support has been a wealth of new knowledge that has led to discoveries that are transforming our understanding of human disease. Translating this knowledge into new means of diagnosis, prevention and treatment has yielded new inventions with the potential for a profound and positive effect upon the welfare, health and safety of humankind. Researchers in the Department of Pharmacology of the Yale School of Medicine, for example, together with their research collaborators at other institutions, have played significant roles in developing two key ingredients of the so-called drug cocktail: the reverse transcriptase inhibitor d4T, known commercially as Zerit, and 3TC, known as Epivir. These medicines have fundamentally changed the nature of AIDS therapy during the past decade.

William Prusoff, Ph.D., Professor Emeritus of Pharmacology, has spent a 45-year career at Yale investigating potential antiviral and anticancer compounds, part of the traditional, small-molecule approach. In the late 1950s he synthesized idoxurine, an analog of thymidine, which was the first antiviral compound approved by the

⁴Letter from Katharina Phillips, President, Council on Government Affairs to Dr. Wendy Baldwin, Deputy Director Extramural Research, National Institutes of Health, June 5, 2001.

FDA for therapy in humans. It was used to treat herpes infection of the eye. Dr. Prusoff and his long-time collaborator, the late Tai-Shun Lin, Ph.D., discovered in the 1980s that a thymidine analog, reported in scientific literature by researchers from Wayne State University as a poor anticancer agent, was very effective in slowing the production of HIV. This compound is known as d4T or stavudine. Bristol-Myers Squibb developed the drug under the trade name Zerit and brought it to market in 1994.

Yung-Chi (Tommy) Cheng, Ph.D., the Henry Bronson Professor of Pharmacology, has worked on a parallel course. While Drs. Prusoff and Lin found drugs that work against AIDS, Dr. Cheng has sought ways to reduce their toxicity. Long-term usage of anti-retroviral AIDS drugs leads to a decline in the mitochondrial DNA of certain organs, impairing their ability to function properly. After a month or two of use, these agents can cause problems in nerves, the pancreas, muscles and the liver. Dr. Cheng's laboratory team studies drugs that will be active against the virus but will have no toxicity to the mitochondrial DNA.

One such drug turned out to be 3TC, a compound with positive and negative forms that mirror one another. Originally synthesized by a Canadian researcher and identified as an antiviral agent, samples were sent to Dr. Cheng for study of the drug's toxicity. He found that 3TC's negative form reduced side effects when used in combination with AZT. The combination increases 3TC's efficiency at inhibiting an enzyme HIV uses to reproduce its genetic material. Dr. Cheng identified 3TC as an agent that would be less toxic to mitochondrial DNA than other retroviral drugs.

A new approach to combating AIDS may grow out of work led by John K. Rose, Ph.D., Professor of Pathology and Cell Biology. The agent he developed, based on a common virus found in cattle, has killed HIV-infected cells in culture. He also sees the possibility of developing an AIDS vaccine, using recombinant form of the virus as a vaccine vector. Researchers hope the vaccine will stimulate both parts of the immune system: antibodies to neutralize any free-floating HIV and specialized immune cells to kill any cells that HIV does manage to infect. Early results using a form of the engineered virus showed promise against SIV, the simian form of HIV, for use in animal trials. Dr. Rose is working together with scientists at Wyeth Pharmaceuticals in conducting further animal tests. If it is proven safe and effective in animals, human trials could follow.

These are only a few examples of the life-changing discoveries resulting from Yale's scientific endeavors. Currently, Yale's has licensed eight (8) novel therapeutic drugs being tested in thirteen (13) different clinical trials for such life-threatening diseases as various types of cancer, Hepatitis B and AIDS (see attachment 2: Yale Pharmaceutical Pipeline). The benefit to the public derived from these and other inventions created through the research at Yale and other academic research institutions is incalculable.

THE IMPACT ON LOCAL ECONOMIC DEVELOPMENT

In many communities around the country, the scientific research undertaken by universities has been a powerful engine of local economic development. As President Richard C. Levin recently pointed out⁵, without critical mass in electrical engineering and computer science, Yale—and consequently New Haven—missed out on the technological revolution that spurred the development of Silicon Valley and Boston's Route 128. But Yale has impressive strength in biomedical sciences with unexploited potential to build a biotechnology industry in and around New Haven. With the administration of President Levin, which started in 1993, Yale heightened its involvement in community economic development through specific operations backed by financial investments and increased professional staffing. The results include:

- A commitment to spend over \$500 million to renovate every science laboratory on campus as well as construct 5 new state-of-the-art research and educational buildings.
- A commitment to spend an additional \$500 million to renovate the laboratories at the Medical School including the construction of a recently opened 457,000 square foot building for disease-based research that increased the total lab space by 25%.
- Twenty-five new biotechnology companies have been established in the greater New Haven area, seventeen within the city limits. These firms have attracted over \$1.5 billion in capital and together they now employ 1300 people.

⁵Richard C. Levin, "Universities and Cities: The View from New Haven," Inaugural Colloquium, Case Western Reserve University, January 30, 2003.

- Attracting Winstanley Enterprises of Concord, Massachusetts to purchase the 550,000 square foot former headquarters of the Southern New England Telephone Company one block from the Medical School that it transformed into the George Street Technology Center housing eight biotechnology spin-offs from Yale.
- Working with the State of Connecticut and City of New Haven to attract Lyme Properties (the developers of Kendall Square in Cambridge, Massachusetts) to convert 1 million square feet of former factory space at Science Park into labs, offices and restaurants for additional spin-offs from Yale.

Although these results are just from New Haven, Connecticut, similar scenarios are being replicated at numerous sites across the country. On a nation-wide basis, the results support the conclusion that the Bayh-Dole Act has promoted a substantial increase in technology transfer from universities to industry, and ultimately to the public. There has been a tremendous acceleration in the introduction of new products through university technology transfer activities. These benefits have been significantly enhanced by the adoption of federal policies encouraging technology transfer. Such policies have led to breathtaking advances in the medical, engineering, chemical, computing and software industries, among others. The licensing of new technologies has led to the creation of new companies, thousands of jobs, cutting-edge educational opportunities and the development of entirely new industries. Today, the Vice Chairman of the NASDAQ Stock Market,⁶ estimates that 30% of the companies listed owe their value to the results of government sponsored research and development. Accordingly, the Bayh-Dole Act continues to be a national success story, representing the foundation of a successful union among government, universities, and industry.

Mr. Chairman, thank you again for your time and attention. If there are any questions, I will be pleased to answer them.

[Attachment 1 is available at www.autm.net]

Attachment 2: Yale Pharmaceutical Pipeline

AGENT	LICENSEE	INDICATION	STAGE	PATENT EXPIRATION
Zerit [®]	Bristol-Myers Squibb	HIV/AIDS	Marketed	June 2008
Coviracil [®]	Triangle Pharmaceuticals	Hepatitis B	Phase III	January 2010
Pexelizumab [™]	Alexion Pharmaceuticals	Cardiopulmonary Bypass	Phase III	Pending
Troxatyl [®]	Shire Pharmaceuticals	Acute Myelogenous Leukemia	Phase II	April 2017
Troxatyl [®]	Shire Pharmaceuticals	Solid Tumors (pancreatic cancer)	Phase II	April 2017
Triapine [™]	Vion Pharmaceuticals	Leukemia	Phase II	January 2011
Triapine [™]	Vion Pharmaceuticals	Metastatic Breast Cancer	Phase II	January 2011
Clevudine [™]	Triangle Pharmaceuticals	Hepatitis B	Phase II	December 2013
Elvucitabine [™]	Achillion Pharmaceuticals	Hepatitis B	Phase II	May 2014
Elvucitabine [™]	Achillion Pharmaceuticals	HIV/AIDS	Phase II	May 2014
TAPET [™]	Vion Pharmaceuticals	Anticancer	Phase I	March 2013
TAPET-CD	Vion Pharmaceuticals	Anticancer	Phase I	March 2013
VNP40101M	Vion Pharmaceuticals	Anticancer (Solid Tumors)	Phase I	March 2010
VNP40101M	Vion Pharmaceuticals	Anticancer (Leukemia)	Phase I	March 2010
Ioddu	Achillion Pharmaceuticals	Epstein-Barre Virus	Pre-clinical	Pending
ACH0630	Achillion Pharmaceuticals	Hepatitis B and C	Pre-clinical	Pending
VSV Vaccine	Wyeth Pharmaceuticals	HIV/AIDS	Pre-clinical	Pending

Mr. BILIRAKIS. Thank you, Doctor. You know, we talk about the Bayh-Dole Act and its accomplishments, and think back how much medicine might have progressed if that Act had taken place earlier. And I am told by staff, and I guess some of you all can verify this, that it took about 20 years of discussions before we could get to that particular point. So, my God—

Mr. SODERSTROM. That is absolutely correct, sir.

Mr. BILIRAKIS. Well, Dr. Sigal, please proceed.

⁶Personal communication with .

STATEMENT OF ELLEN V. SIGAL

Ms. SIGAL. Mr. Chairman, members of the committee, I am very happy to be here today. I am here in two capacities—one personally and one as Chairman of the Friends of Cancer Research.

As a personal story, I think you should know that everyone in my family has died of cancer. Everyone. My mother just recently died of pancreatic cancer. My sister died at 40 years old, leaving a 4-year-old child. And my father died of prostate cancer. So I have devoted my life to making a difference in these matters.

Friends is a coalition of all of the major groups in cancer research. It has the professional organizations, the American Cancer Society, ASCO, AECR, it has all of the patient groups, lymphoma, breast cancer, prostate cancer, and many individuals who care and make a difference.

The investment in the NIH and the results and what we have gotten out of it has been staggering to the patient. It has been enormous and well-spent money, and it will—it has made a difference, and in the future it will make an enormous difference.

Patients gain when scientific knowledge and understanding grows, is rapidly disseminated. Patients benefit when they have improved access to meaningful information about their diseases and conditions, and their options for treatment are participation in clinical trials. Patients benefit when the discoveries of the NIH scientists and those researchers supported by the NIH are transferred to the private sector for the complex, risky, and expensive process of development into commercial products.

The United States technology transfer policies are the envy of the world, because the NIH, under the direction of Congress, has made the creation of new products a central goal of the American biomedical research. The most important benefit is it benefits patients and people.

Since Bayh-Dole, Congress has implemented a policy structure that recognizes and builds upon the fact that the marketplace can be a powerful tool in promoting innovation. It is private sector firms that produce the overwhelming percentage of goods and services that underlie the dynamic American economy in the United States.

However, the government, in this case the NIH, plays an important role in expanding the basic understanding of science. It is the knowledge explosion that has been facilitated by dramatic increases in Federal funding for biomedical research. But as Congress after Congress has recognized, the faster, more easily technology can get into the hands of the private sector, the greater the likelihood that a product will be developed and marketed.

As a patient representative and advocate, I want to discuss one concern that arises in discussions of technology transfer. Some well-intended policymakers have urged the government to impose price controls as a pre-condition to private sector licensing or government discoveries. This has been urged in explicit ways and through policies that have a similar net effect.

I can tell you from experience that seeking to guarantee access at a fair price to products using the mechanism is troubling and will not work and will not help the patient, who is the most important part of this equation.

First, reasonable pricing clauses of the NIH have not worked in the past. The number and quality of discoveries that were licensed declined during a 5-year period when such a policy was in effect. Companies who can undertake the risky and expensive process of drug development estimated at over \$800 million per product, do not want vague agreements that have disadvantaged terms when they can invest those resources to pursue a product without strings attached.

Second, companies do not—cannot bear the risk of not knowing what price will be considered reasonable. Government discoveries are licensed so early in the product development that the stage—very little knowledge is known about the potential product. Therefore, it is impossible to define what a reasonable price will be.

Any steps to assure fair prices should be applied uniformly to all products, rather than penalize products created from the NIH. Second, narrowly crafted measures in Medicaid and certain other special Federal programs now are assuring fair prices. Finally, the Congress should recognize that drug price competition is stimulated by policies that advance the development of new products.

It is in the interest of the patients to have more than one therapy on the market. This is critical. This is how we gain knowledge, and this is how we get better products. Recently, yesterday, Friends of Cancer Research announced a public-private partnership with five pharmaceutical companies of the National Cancer Institutes to really work on clinical trials, early stage trials, in the community for underserved patients and geriatric patients.

It is a model of the way a partnership should work between the government and the private sector. Five competing companies came together for this knowledge to help the government, and we, at the National Cancer Institute, work with them for the benefit of patients in the community. That is a positive model of public-private partnerships.

This kind of partnership celebrated yesterday was symbolic of the kinds of relationships that government and the Congress should be fostering. We cannot expect the government to do everything, but neither can we expect the private sector to fund every bit of fundamental research. We need to support and grow partnerships between the government and the private sector, so that patients can be assured that both are pursuing the common good of expanding access to clinical trials by patients, and the developments of new products to treat and cure serious and unmet medical needs.

As the Committee on Energy and Commerce continues its hearings on the National Institutes of Health on behalf of patients and patient advocacy groups, I urge you to keep the following fundamental principles in mind. First, do no harm. The current system of knowledge and management, information, dissemination, and technology transfer at the NIH works remarkably well. Please do not be tempted to undertake actions that would fundamentally jeopardize the record of success and the patient.

Second, as you contemplate the NIH, please keep in mind the necessity of positive partnerships and collaborations between government and the private sector. Patients can ill afford a public process that demonizes either the pharmaceutical companies, biotechnology

companies, and the industry, and the outstanding scientists and researchers at the NIH.

Thank you very much for the opportunity to participate, and I am happy to take questions.

[The prepared statement of Ellen V. Sigal follows:]

PREPARED STATEMENT OF ELLEN V. SIGAL, CHAIRPERSON, FRIENDS OF CANCER RESEARCH

Summary:

Health care progress in the United States over the past 50 years has been remarkable. A key ingredient in many of those improvements has been the evolution and growth of the National Institutes of Health. The success story of the NIH has many sources, especially the vital support given to the NIH by the Congress and this Committee. Another building block relied on by the NIH has been a series of policy decisions that have, in the main, facilitated dissemination of knowledge and appropriate transfer of technology. Patients gain when scientific knowledge and understanding grows and is rapidly disseminated. Patients benefit when they have improved access to meaningful information about their diseases and conditions and their options for treatment or participation in clinical trials. Patients benefit when the discoveries of NIH scientists, and those of researchers supported by the NIH, are transferred to the private sector for the complex, risky and expensive process of development into commercial products. The United States technology transfer policies are the envy of the world because the NIH, under the direction of the Congress, has made the creation of new products a central goal of the American biomedical enterprise.

Background about the Friends of Cancer Research:

Friends of Cancer Research, a Washington, D.C. based not-for-profit focused on public education about the importance of federal investment in cancer research. Friends of Cancer Research has played a leading role, along with our colleagues in the cancer and patient advocacy communities, to advocate on behalf of the NIH and expanded funding for cancer research. The Friends of Cancer Research consists of members of the patient community, government leaders, and firms and institutions in the for profit and non-profit private sector.

Background about Federal Technology Transfer Policy:

In broad historical terms the Congress has—over the past 20 to 25 years—committed itself, in a broad, bi-partisan way to new and improved ways of facilitating technology transfer. For many of the early years in the post-World War II era there was a sense that government research should be owned by the government and that any transfer to the private sector should be avoided. Beginning with work in the Carter Administration and the legislative work of legislative leaders like Senators Dole, Bayh (Birch Bayh), Congressmen Wyder, Kastenmeier, Railsback, Moorhead, and Senator Stevenson the Congress enacted a series of laws to expand the technology transfer of government funded research and development efforts. This testimony is not the time or place to review all these laws, but it is appropriate to comment on the fundamental underlying philosophic premise of these efforts.

Congress has consistently acted over the past several decades to implement a policy structure that is designed to recognize that the marketplace can be a powerful tool in promoting innovation. It is after all private sector firms that produce the overwhelming percentage of goods and services that underlie the dynamic American economy. It is not the government that produces wealth or develops and markets new products. The government—and in this case the NIH—plays an important role in expanding the basic understandings of science. It is that knowledge explosion that has been facilitated by dramatic increases in federal funding for biomedical research. But, Congress after Congress, for decades has recognized the faster and more easily technology can get into the hands of the private sector the greater the likelihood that a product will be developed and marketed.

As a patient representative and advocate let me address one persistent red herring issue that arises in discussions of technology transfer policy. Some well-intended policy makers have urged that the government either engage in explicit government imposed price control measures as a condition to be imposed before any government discoveries be licensed, or policies that have a similar net effect. I can tell you from experience that seeking to guarantee access at a “fair” price to products using this mechanism is misguided and will not work.

First, we have some considerable experience with “reasonable pricing” clauses at the NIH. A policy of that nature was in effect for about 5 years and the number and quality of discoveries that were licensed declined. Companies who can undertake the risky and expensive process of drug development (according to recent independent research by Tufts University the cost, fully loaded, and including the cost of failed research and opportunity costs, exceeds \$ 800 million per product) do not want vague agreements which create disadvantageous terms and conditions compared to other opportunities, including pursuit of internally developed drug and biological candidates.

The second reason that companies did not favor licenses with a “reasonable price” clause was the inherent ambiguity of interpreting what is reasonable. At the time of a technology transfer license is entered into so little is known about a potential new product clarify in defining reasonableness is impossible. The likelihood of a compound making it through the screening process into human clinical trials is daunting (often fewer than 1 out of 5,000 chemicals finish this process). Even those products which enter human clinical trials few (less than 1 out of 100), make it all the way through to marketing. Even the products that make it on to the market are not guaranteed to make money. In fact, according to independent research by Tufts University, only 3 out of 10 marketed products make a positive return and only 1 out of ten generate a substantial return. If, as happened, under the discredited “reasonable price” regime the government waits to determine reasonableness until after the product is developed and marketed there is an inherent bias against successful product development.

If the government wants to obtain a fair price for a product it should act broadly, and fairly, with respect to all drug products and not impose special and onerous rules only on products created from an NIH supported technology transfer process. The Congress has effectuated a series of measures that do, in fact, assure fairness to the government in pharmaceutical purchases. First, the Congress has already underway effective means to securing fair prices to the government through the promotion of a process for the approval of generic drugs. Unlike most other developed nations the United States has a vibrant process of using generic drugs to assure savings to the government and the patient community. The recently adopted amendments to the Medicare bill on generic drugs further the policies embedded in existing federal law and FDA practice.

Second, the Congress has also crafted measures in Medicaid and certain other special federal programs to assure fair prices. Finally, there needs to be broader realization that price competition for drug therapies is stimulated by policies that advance the development of new products. It is after all in the interest of patients to have more than one therapy on the market for a disease or condition. The second, third, fourth or fifth product approved in a particular class of products offer patients the opportunity of improved health outcomes, increased ease of administration, better compliance or often price competition within a particular disease sector. There is no need for the government to either expand the government pricing programs or to create a new, counterproductive scheme within the NIH to review prices for yet undeveloped products.

Comments about Government Private sector partnerships:

On July 9, 2003 the NIH Foundation, in cooperation with the Department of Health and Human Services announced awards for partnerships with the private sector. The companies and partners recognized included Aventis, Bristol-Myers Squibb, Eli Lilly and Company, GlaxoSmithKline, Novartis, as well as the Association of American Cancer Institutes and the National Cancer Institute. This partnership is designed to speed cancer drugs to the market by improving the ways in which early stage cancer trials are designed and conducted. This partnership is geared towards underserved and geriatric patients in the community. Today, only 3-4% of all cancer patients participate in clinical trials and most of those are children. Of children with cancer about 60-70% of them participate in clinical trials. One goal of these partnerships is to dramatically increase access to early stage clinical trials for adults with cancer.

The kind of partnerships celebrated yesterday are symbolic of the kinds of relationships that the government and the Congress should be fostering. We can not expect the government to do everything. We can not expect the private sector to fund every bit of fundamental research. We need to support and grow partnerships between the government and the private sector so that patients can be assured that both are pursuing the common ground of expanding access to clinical trials by patients and the development of new products to treat and cure serious and unmet medical needs.

Conclusions:

As the Committee on Energy and Commerce continues its hearings on the National Institutes of Health, on behalf of patients and patient advocacy groups, I would urge you to keep some fundamental principles in mind. First, do no harm. The current system of knowledge management, information dissemination and technology transfer at the NIH works remarkably well. Please do not be tempted to undertake actions that would fundamentally jeopardize that record of success. Second, as you contemplate the NIH please keep in mind the necessity of positive partnerships and collaborations between the government and the private sector. Patients can ill afford a public process that demonizes either the pharmaceutical and biotechnology industry, or the outstanding scientists, researchers and administrators at the NIH. Finally, the NIH has been successful in recent years because of its outstanding senior management, including the outstanding NIH Directors, Varmus and Zerhouni, and Institute Directors. While it is appealing to some to seek a centralization of control within the Department of Health and Human Services, considerable care should be exercised. There is a risk that by undermining the relative independence and autonomy of the NIH and its institutes morale will deteriorate and the biomedical enterprise will suffer.

Thank you for the opportunity to participate in this hearing. On behalf of the Friends of Cancer Research and the entire patient advocacy community, we wish you well in your important oversight and policy making role. You can, and should be, justifiably proud of your role in creating and nurturing the greatest advances in human health in history.

Mr. BILIRAKIS. Thank you, Dr. Sigal. Thank you for being here, for sharing that with us, and for your courage and your dedication.

Well, I—frankly, virtually every question has been answered already by your testimony. I would ask—in terms of university research partnerships, how do—is there a difference in how, and what is the difference between working with the Federal Government versus the private sector?

Mr. NEIGHBOUR. A complex question, but I think an interesting one. With funding from the Federal Government, we are obviously very concerned about basic knowledge, and we are a lot freer to push the boundaries of knowledge to explore new areas that we think may have 1 day a potential of being a platform for the development of product.

We typically focus on mechanisms, on systems, and understanding diseases, not specifically on creating little white powders that will become drugs to be injected or given to patients. So the nature of the research from the outset is quite different.

The second, probably most fundamental issue that consumes a lot of my time, are the intellectual property issues. As soon as we begin to work with a company, the company has to protect its business. And, consequently, significant concerns about ownership of inventions, access by that company to that intellectual property, become a fundamental part of the negotiation between us and the company.

And we need to maintain certain basic academic tenets which are important to the university, particularly freedom to publish, protection of our institution, and an opportunity to use the results of our research to support other researchers and other activities in the future.

The company tends, of course, to want to establish a monopoly position and take that knowledge forward, invest in it, and develop the product. So there are some fundamental differences, but I think we have learned since the emergence of Bayh-Dole how to manage those differences and create partnerships that serve everyone's needs quite well.

Mr. BILIRAKIS. Thank you, Doctor.

Dr. Soderstrom? Dr. Gardner? Whatever.

Mr. SODERSTROM. I would just like to add one thing to—

Mr. BILIRAKIS. Sure.

Mr. SODERSTROM. [continuing] my colleague, Andrew's comments, because I was actually going to ask—the answer I was going to give you was going to be fairly glib. I was going to say, "Quite well. Thank you." In part because over the last 20 years, as Andrew was pointing out, we have begun to develop norms of behavior and activities, which are mutually supportive.

I want to use one example from Yale that I think illustrates this point, and I actually mention it in my written testimony, so I will refer back to that. But one of the things that the National Cancer Institute has done is funded a number of laboratories around the country that are specializing in certain types of biological assays, which can then be used to test different compounds for activity against a particular disease.

In the case of Yale, the laboratory of Dr. Young Ji Chang is world-famous for screening against things like Hepatitis-B. Also, he was one of the original for setting up—original investigators setting up assays against HIV as well. In the context of that, we receive many compounds from small biotech companies and major pharmaceutical companies, which we then test against these assays, which the NIH funded the development of.

Out of that, we are able to discern things like which ones will have the lower levels of toxicity, less side effects, etcetera, and we are able to give that information back to the companies. That type of partnership I think is particularly effective if we look at just one drug—3TC, which we all recognize as Epovir.

Epovir, the original formulation of 3TC, had many different analogs. But using the techniques that Dr. Chang and his colleagues at Emory University had developed, we were able to identify the specific version of the compound that would have the lowest profile of toxicity, and the most efficacy, particularly when combined with AZT. I think that is an exciting partnership which was afforded by the abilities that we have under Bayh-Dole.

Mr. BILIRAKIS. Dr. Gardner?

Ms. GARDNER. I would just like to add that the vast majority of funding at most research-intensive universities comes from the Federal Government, and that is the kind of funding that fits more with the core values of a university endeavor. The core values of a university endeavor are to pursue fundamental knowledge and disseminate information freely, in the course of that educating the next generation of scientists.

I have worked in both sectors. The core values in industry are product development, and in that context intellectual property and confidentiality are extremely important. So you can see there is a divergence in the core values.

The partnership of the NIH and universities is profoundly successful and very good, because they have similar core values. And my—and this isn't to say that—to knock either set. They are both important, but it does go to the question of, how valuable is the license that comes from NIH or federally funded research through a university or from NIH to a pharmaceutical company?

By nature of the core value of this kind of research, fundamental knowledge, early knowledge dissemination, there are very early stage ideas, nascent ideas. They have not gone through formulation or any of the stages of product development that are so expensive. So it is understanding that that should help to diverge away arguments of high royalty rates or price controls on drugs that have a very early stage or small part from the NIH, important as it is.

Mr. BILIRAKIS. Well, thank you. Dr. Lindberg is still in the room. And I don't know whether any of the other people are here, but I know they are certainly represented here, by request. And I know that they all feel good about what they have heard you say.

I didn't hear any criticisms from you or bureaucratic things that can be cleared up, so hopefully if there are you might furnish them to us in writing later on or possibly even mention them during the further questioning.

The chair now recognizes the gentlelady from California, Ms. Eshoo, for inquiry for 5 minutes.

Ms. ESHOO. Thank you, Mr. Chairman.

I want to thank the panelists and welcome you here today. I think it was President Kennedy that said that—when he made the remarks about the Nobel Prize winners that were gathered in the White House that only one other time had there been such great intellect—I am paraphrasing, of course—that was gathered there, other than the time that Thomas Jefferson dined alone.

So I am reminded of that today, because you are a very distinguished panel, and I think that you have informed the committee very well about your work.

I want to extend a special welcome to Dr. Phyllis Gardner, who, Mr. Chairman, is my constituent and serves with great distinction as the Senior Associate Dean for Education and Student Affairs at Stanford University.

But the background that she just spoke of I think is very important, because there is an enormous linkage and, really, a symbiotic relationship between the universities, both public and private, in our country and then what flows out to the private sector. Dr. Gardner was the President of Research at ALZA Corporation. ALZA, of course, has been acquired now by Johnson & Johnson. But that speaks to a part of it, and so how we fund this research, and how it works through our universities, both public and private, is one of the great stories of America.

This is a unique American story, and I think that if there is anything that—and I said this to some of the panelists before we began—that we somehow have come to a place of such, happily, full appreciation or near full appreciation of this. But I think that we have this pettiness about—that we will always have this, that somehow this is always going to remain.

We have a very full and serious obligation to protect this, to keep the investment in it going, and to do everything that we can relative to the technology transfer that does take place, to Dr. Sigal and her courage. When she said that everyone in her family has died of cancer, that is our challenge. That is our collective challenge. And I think that a society, obviously, is measured by how it takes care of its people, and that is what you are here to talk about today.

Dr. Gardner, what do you think Stanford's technology transfer program has done for the Bay area? Of course, that is a softball to you.

But I think that it is an important story. And how are the technology transfers helping regions, outside of the obvious benefits to health care?

And then, my second question to you is is that a number of my colleagues have asked why the Federal Government doesn't recoup more of its investment in research that leads to products. Why do you think more royalties on products should not be returned to the government? And then, to the full panel, what do you think an appropriate return on investment is for the government?

Now, I have a little different take on this than some of my colleagues on the committee. But I think that it is still—these are still worthwhile questions, so thank you—

Mr. BILIRAKIS. Very worthwhile questions.

Ms. ESHOO. [continuing] all of you.

Mr. BILIRAKIS. I wish you had given the panel 5 minutes in order to answer those questions.

Go ahead, Dr. Gardner.

Ms. GARDNER. First of all, the Bay area is a thriving economy, both in the high tech and the biotech sectors—the high tech sector, starting with Fred Terman and funding Varian, Hewlett-Packard, etcetera, through some government funds, and then proceeding thereon. And then, with the Bayh-Dole Act, also the Cohen-Boyer patent, which brought in a quarter of a billion dollars total to the university at a royalty rate of a tenth of a percent.

That has set—that put forth this thriving economy in the Silicon Valley area. That is the envy of the world that brings people from all over the world to try to imitate it. It is even the envy of many parts of the Nation, and there are other centers that are important. Certainly, San Diego, the research triangle in North Carolina, certainly Ohio State is trying to get there.

I am on the board of a company where they are pushing hard, but we are—we have been at the forefront, and the numbers of jobs created, the affluence created in the local economy, is profound, and that is one of the reasons why I would—not only do we recoup investment from savings—from the better health care that people have, which is a profound savings, and the estimates are in trillions of dollars because of better health of workers.

And not only do we get that, but we also have the stimulus to the economy, to the knowledge-based economy that the rest of the world is trying to imitate. And I just hope that we do not rock that boat, because I believe it comes back to the Federal Government in spades through those two mechanisms.

Mr. NEIGHBOUR. Mr. Chairman, if I could add that one return that has not been mentioned, and is often not measured or talked about by critics of drug pricing, is taxes. It seems to me that at the end of the cycle, the successful drug company that has to cover its manufacturing costs, its development costs, the winners and the losers ends up with a profit that generates taxes that come back into the economy and support NIH appropriations.

They also sustain a health that employs a large number of employees who, like you and I, are taxpayers. And so that measurable

benefit is a very real one and is the basis on which this society is built. So I think return on investment, if one is focusing on dollars, if you do the math, will actually come out ahead.

But I think the more important thing is to not do the math. I think the most important thing is to think about the quality of life and what we would not have if companies and universities and NIH and the other Federal agencies were not sustaining this incredible research enterprise, which, as has been stated, is the envy of the world. There is hardly a day or a week in my office that I am not hosting a visitor from Chile, Korea, Japan, Italy, Germany, the great—Great Britain—Freudian slip there—that wants to know how it is done.

And we know how it is done. We have done it right. And I think anything that would interfere with that process, other than creative improvement, would be a deficit for this Nation.

Mr. BILIRAKIS. I just wish the entire subcommittee were here to—

Ms. ESHOO. I do, too.

Mr. BILIRAKIS. [continuing] listen to these comments. Dr. Soderstrom?

Ms. ESHOO. This is extraordinary.

Mr. SODERSTROM. I am going to add one more to that which—the list, and I alluded to it earlier, which is increased productivity, which we all know that Chairman Greenspan has pointed to as being the engine of the economy right now.

Anyone who read The Wall Street Journal yesterday knows what happens if we don't have healthy workers in our businesses driving our economy. We can only look at Africa, where President Bush is today, and see what happens. We don't face that today. We don't face that because of many of the discoveries that were made with NIH funds that have been translated from academic research into the biotech and biopharmaceutical industry. And I think that is one of the costs—I am not an economist, but I would add—has to be factored in.

Mr. BILIRAKIS. I don't know whether you have anything to add to that, Dr. Sigal, but—

Ms. SIGAL. Just very briefly. I think it is very clear that the mission of the NIH must be innovation, discovery, and knowledge for the public good. Once we start getting involved in returns of investment, we are really going to be in trouble. The return on investment is the public health of the people all over the world.

Mr. BILIRAKIS. Amen to that. Thank you.

Ms. ESHOO. Thank you, Mr. Chairman.

Thank you to the distinguished panelists.

Mr. BILIRAKIS. Mr. Allen, would you like to inquire?

Mr. ALLEN. Thank you, Mr. Chairman.

I very much appreciate the comments of the panel today. And though I have been a frequent critic of pharmaceutical industry drug pricing, there is—I agree with much of what you have to say. But because I am a little concerned that what you say may be taken in a broader context than what you actually said, I want to make a couple of comments.

The passion that drives Dr. Sigal, the cancer in her family, is something we feel in many of our constituents, because there are

two parts to this equation about the availability of prescription drugs. One part is innovation, and I don't believe there is a single person in the Congress who wants to shut down that innovation. And in that sense, you have all of our support.

But the other half of the problem is distribution. And in Maine, I can't tell you—there are thousands and thousands of my constituents who can't possibly afford to take the drugs that their doctors tell them they have to take. And we are next to Canada. Women who are fighting for their lives with breast cancer in Maine have finally learned that Tomoxifen costs one-tenth as much in Canada as it does in the United States, and I assure you the industry is still making a profit up there.

And so what we are—what we try to do is figure out how to deal with this particular problem. And many of you talked about the disadvantages—and I agree with this—of trying to price a product somehow while it is not—while it is still within the NIH framework or in that sort of early research framework. And I don't think we buy that at all.

But we do have a serious problem with Medicare, and it seems to many of us wrong that Medicare beneficiaries should pay the highest prices in the world. They are in the biggest health care plan in the country. If they were organized, that plan would provide them, as Aetna beneficiaries and Cigna beneficiaries and United beneficiaries, with some discount in the price that they pay. But they don't get that, because essentially they have to pay whatever the industry would charge.

And so just a comment to set this in context—that is the issue that I think many of us are struggling with. We don't quarrel with the importance of innovation. We believe in Bayh-Dole. We think that this partnership with the—between the universities and NIH is extraordinarily valuable. But we have to figure out how to make sure the people who need pharmaceutical products can actually get them.

I think it was Dr. Soderstrom mentioned a couple of other comments. I think you mentioned Africa and diseases in Africa. It has always seemed to me that we ought to expect the private sector to do what the private sector, with the assistance of universities, does best. That is, develop innovative new products.

It is not so good at producing products that don't yield a return. Whether it is sleeping sickness or malaria, or whatever, many of the diseases other than AIDS that are afflicting Africa are not getting the attention they deserve.

And, Dr. Sigal, one quick comment. Because in your written testimony you had a reference to the study done at Tufts, I simply can't resist making a couple of comments about that study. The \$800 million that the industry has repeated over and over again is the total cost to bring a new drug to market is based on the study at Tufts.

I view that study as flawed. First of all, half of that \$800 million—half of that \$800 million, according to the study, is opportunity cost. That is what the money could have earned by being invested somewhere else, but there is no more profitable industry in the country than the pharmaceutical industry. So there are reasons

why the investment is so heavy in R&D in the pharmaceutical industry.

The second thing I would say is I think they looked at about 66 different drugs, none of which—none of which—were funded initially by NIH. And so the drugs that they took as—for a sample are—is wildly different from the way most drugs come to the market. That is, most drugs come with some at least initial research that is government-funded through the NIH. And so for those reasons, many of us quarrel with that study a good deal.

But we are with you completely on the need to keep this industry going. We respect, Dr. Gardner, the differences between biotech and pharma, and we simply have to find a way to deal responsibly with the other half of the problem, which is how we get the drugs to people who need them.

I have taken all of my time. I haven't given you time to respond. I apologize.

Mr. BILIRAKIS. Yes, time is up. You know, I have been hoping that this hearing would focus on bench to bedside, which is certainly very, very significant. And for the most part, it has.

I thank you so very much. I know it makes me feel an awful lot better from the standpoint of research, and what it accomplishes, and so many things, the byproducts of research that you all went into, which is just terrific, in addition to the health and the quality of health care, the byproducts economically.

I thank you very much for being here. We will have questions to you in writing. We would appreciate your responses.

And, again, please feel free to let us know—if there are things that you suggest that NIH should do, or FDA or National Institute of Cancer, or whatever, Cancer Institute, or whatever, that you think that maybe we should address or take a look at or ask—raise questions about, or whatever, please let us know.

Dr. Sigal, you are shaking your head, so please feel free to do that. You have got an open invitation.

Thank you so very much for a great hearing. Hearing adjourned. [Whereupon, at 1:10 p.m., the subcommittee was adjourned.] [Additional material submitted for the record follows:]

PREPARED STATEMENT OF SUSAN BRAUN, PRESIDENT AND CEO, THE SUSAN G. KOMEN BREAST CANCER FOUNDATION

Chairman Bilirakis, Rep. Brown, and distinguished Members of the Subcommittee, thank you for the opportunity to submit testimony about the importance of moving research from the bench to the bedside. The Komen Foundation acknowledges and thanks you for your continued leadership and support for improving the quality of care cancer patients receive.

I am privileged to serve as president and chief executive officer of the Susan G. Komen Breast Cancer Foundation. Nancy Brinker established the Komen Foundation in 1982 in honor of her older sister, Suzy Komen, who died of breast cancer at the age of 36. Our mission is to eradicate breast cancer as a life-threatening disease. To this end, we have had to change both the clinical and cultural landscape of breast cancer, and we have.

Today, the Komen Foundation includes more than 75,000 volunteers working through a network of Affiliates and events like the Komen Race for the Cure® to eradicate breast cancer by advancing research, education, screening, and treatment. The Komen Foundation has become the largest private funding source of breast cancer research and community outreach programs in the United States. Since its inception, the Foundation has raised nearly \$600 million in the fight against breast cancer. The Komen Foundation continues to forge many public-private partnerships to produce real clinical results and a better quality of life for thousands of women

and men living with breast cancer. The Foundation has awarded more than 850 grants totaling \$112 million for innovative research. Through funding of programs and resources like the Komen Foundation Award and Research Grant Program, the Komen Affiliate Grant Program, the Komen National Toll-Free Breast Cancer Helpline, the Komen Foundation Website, and other educational materials, the Komen Foundation today is the recognized leader in the fight against breast cancer.

I. BACKGROUND

As the Committee recognizes by holding this hearing, diseases cannot be cured in the lab alone. Eradicating disease requires translating research discoveries into innovative, high-quality patient care. If there is to be any meaningful advancement in eliminating cancer and other diseases, what we learn from biological bench research must be translated to the clinical setting and, ultimately, delivered to patients to advance integrated care and improve quality of life. In addition, these advances must be available expeditiously and in the appropriate manner. Given the Komen Foundation's experience as a supporter of breast cancer research and a champion for early detection and treatment innovations, we believe that our experience can provide the Committee with a "case study" for understanding what is working and what is not in translating research from the bench to the bedside.

Each year in the United States, more than 200,000 women and men are diagnosed with invasive breast cancer. In 2003, approximately 40,600 of breast cancer patients will lose their lives to the disease. Even though breast cancer mortality has declined, the incidence (*i.e.*, the number of individuals diagnosed with the disease each year) remains steady. Research, awareness and education are primarily responsible for lowering the mortality rate because of improvements in screening, diagnosis and treatment.

The Komen Foundation strongly believes that more research will lead to curative interventions in the future. Although research has yet to produce a cure, it has provided important progress in our fight against this deadly disease, and many important innovations hover on the horizon. These advances—once translated to treatment options—will help to lower mortality rates even further and lead to improved and more efficient care and thus a better quality of life for those diagnosed with breast cancer.

In the area of breast cancer, there have been enormous research discoveries that offer a great deal of promise. Yet, breast cancer patients have not been able to realize the full potential of these discoveries because of a widening gap between research and patient care. It is imperative that society eliminates (or at least minimize as much as possible) this gap immediately. To achieve this goal, we must first understand what the gap is; second, consider the impact of access to care issues on the gap; and third, work toward its elimination.

II. UNDERSTANDING THE GAP BETWEEN RESEARCH DISCOVERIES AND TREATMENTS FOR PATIENTS

Barely a day goes by when there is not some exciting new research development announced. Patients hear these announcements and want access to the treatments promised. And yet, bringing that promise to patients is becoming much harder. As the gap between research discoveries and patient care widens, the worst imaginable situation becomes possible: curable innovations are developed but patients cannot get them.

Because of our role in funding innovative research related to breast cancer, the Komen Foundation is particularly concerned about ensuring that bench results translate as quickly as possible into bedside treatment. Although it is true that recent research discoveries have outpaced the ability of scientists and physicians to develop treatments related to them, we believe the widening gap, more importantly, results from two systemic problems within the research and medical fields: (1) challenges created by the existing process by which bench research is translated into clinical treatments, and (2) the decline in the number of physicians who understand how to integrate innovative treatments into their practices or cannot do so because of problems within the insurance reimbursement system.

A. *The Fast Pace of Research Discoveries*

One important reason for the widening of the gap between innovation and patient care is due to a positive development—the explosion of advancements in human genomics. Since James Watson and Francis Crick discovered the structure of DNA, researchers have worked diligently to determine how it functions. We achieved a major milestone when public and private scientists finished mapping the human genome ahead of schedule. Advances in our understanding of human genomics offer

the promise of new ways to attack disease. For example, we can now evaluate diseases in terms of specific, molecular-level changes and propose molecular-level interventions. The genome map opens a new world in terms of defining inherited diseases. Microarray technology will allow for rapid testing of compounds that can target specific proteins or molecular structures in cells, permitting doctors to use new drugs to treat specific kinds of breast cancers/tumors, eliminate painful side effects, and promise longer survival. And, as we learn more about the genetic causes of disease, we will also gain a better understanding of how the environment contributes to diseases and perhaps one day, find a way to prevent certain diseases altogether.

The promises of the advances are extraordinary with researchers working feverishly to apply the new information into treatment contexts. For example, researchers at M.D. Anderson Cancer Center used pharmacogenomics (the study of an individual's genetic expression patterns to tailor treatments for him/her) to analyze tumors' specific genetic make-up to guide treatment decisions. They were able to predict with 75 percent accuracy whether chemotherapy would eradicate tumor cells. Eventually, pharmacogenomics may provide information on the probability of metastasis and the likelihood of a patient developing a recurrence of cancer, as well as predict medical outcomes for the individual.

However, these incredible discoveries are not the problem when it comes to translating research results into treatments. Researchers face some difficult systemic challenges that must be resolved quickly to ensure that patients benefit from these advances.

B. Barriers Created by the Existing Clinical Trial Process

One troubling barrier to eliminating the widening gap between research and treatment are challenges inherent in the existing clinical trial process. As you are aware, obtaining a positive result in a laboratory is only the first step of a long process toward producing a medically acceptable treatment. The Food and Drug Administration (FDA) oversees this process. Once a researcher makes an important laboratory discovery, he/she must determine whether it can be translated into medical practice. Often initial discoveries are found using animal models. However, not all animal model results can be translated into human treatments. After all, as researchers are fond of saying, "mice are not men!"

If a result can be moved from an animal model to a human context, the researcher must shepherd it through the FDA's clinical trial process, in the case of new drugs or devices. This process requires many clinical trials and studies. In addition to the logistical issues involved in developing and conducting an appropriate clinical trial, many researchers are finding it difficult to obtain the appropriate number of research subjects. Participation in clinical trials remains low; less than 5 percent of adult cancer patients currently participate in clinical trials. This may be due to several reasons, including the failure of insurance companies to cover the treatment costs associated with participation in such trials, physicians' lack of time and/or resources to administer such trials, and patient barriers ranging from a fundamental mistrust/misunderstanding of the clinical trial process to access issues (i.e., transportation, child care, etc.). Whatever the reason, low enrollment in trials delays the finding of results and often renders the results obsolete (e.g., if the trial protocol is no longer the current standard of care due to scientific progress). If the results of a clinical study are positive, the FDA will consider a new treatment for approval. The timing for approval varies significantly from treatment to treatment. And, of course, completing this process takes money.

Even if a discovery is not "successful" in terms of translating into a new treatment, reporting a negative result is just as important as reporting a positive one. However, with the idea of "publish-or-perish" dominating most laboratories, many researchers are reluctant to publish negative results. This leads to duplication of efforts and resources and hinders progress toward the ultimate goal of curing diseases.

Another problem is that the current clinical trials system is simply not designed to handle the results of the genomic revolution. For example, the results of mapping the human genome are already being used to shift clinical practice toward individualized medicine. Yet, the existing clinical trial process still requires large numbers of patients to participate in studies that will lead to FDA approval. Although we appreciate the need to ensure statistically significant results, the process must take account of the fact that in the realm of individualized medicine, it will not be possible nor is it appropriate to conduct trials using the same old parameters.

Another important concern arises from the ability to categorize an individual's disease more specifically. For example, patients today who have "breast cancer" may in the future be diagnosed as having a BRCA 1 or 2 cancer, an environmental cancer, or another subspecies of cancer. Cancers will be treated based on their genetic

make-up, rather than their location. As diseases are broken down even further, the financial incentives to conduct these expensive trials will also break down, potentially reducing the willingness of private companies to accept the continuation of the existing system.

Finally, the current clinical trial process takes a long time to complete and is overwhelmed with applications. There is an enormous backlog within the FDA. In 2001, more than 400 cancer drugs were in the development "pipeline" at various stages of the approval process. Although we support and recognize the need to maintain a process that ensures safety and efficacy, the process should not be so time-consuming and onerous so as to inappropriately restrict access to life-saving treatments.

C. Barriers to Adoption of New Treatments by Physicians

Once approved, a new treatment still may not make it to the bedside immediately. Translating bench results into clinical treatments also requires physicians to integrate innovative treatments into their practices. Because of the complex nature of the research, more specialty knowledge is required. However, professionals who treat many diseases become highly specialized. For example, in the oncology specialty, there is a tendency to focus on certain types of cancer in order to keep current and provide the most recent treatment innovations to patients. Gone are the days when a cancer patient walked into several oncologists' offices for treatment. Now, the patient is more likely to receive care from a physician who specializes in a particular kind of cancer. Compounding this problem is the decline in the number of physicians entering the oncology specialties.

Incentives must be available to keep health care providers knowledgeable, trained and willing to provide care to all patients. For example, more funding is needed for provider education programs, such as the Komen Foundation's Interdisciplinary Breast Fellowship Program. This program prepares highly motivated, talented and compassionate physicians for careers devoted to serving the multi-specialty needs of breast cancer patients. The Program awards individuals grants of up to \$30,000 over a two-year period for dissertation research. Three-year grants of \$45,000 per year for postdoctoral fellowships are also available. The Program also enhances physicians' understanding of patients and seeks to develop a better treatment environment for future patients. Through this program, physicians develop the skills they need to integrate new treatments into their clinical practices. However, more programs like this are needed.

In addition to doctors and patients learning about new treatments and their willingness to adopt them, reimbursement issues must also be resolved. Before a treatment is used widely, Medicare and other third-party insurers must accept the treatment and provide adequate reimbursement for it. Generally speaking, there is a lag between the availability of a treatment and its approval for reimbursement. Even if an insurer agrees to pay for an innovative treatment, it will often establish complex reimbursement requirements that physicians find burdensome, decreasing the likelihood that the treatment will be used. This issue is not trivial. A recent Lewin Group survey found that increased reimbursement documentation is of more concern to oncologists than is the stress of dealing with the issues of death and dying. Without adequate and straightforward reimbursement policies in place, physicians are likely to avoid integrating innovative treatments into their practices.

We are concerned about recent trends toward cutting reimbursement rates for necessary, life-saving cancer treatments. For example, both the House and Senate versions of the Medicare prescription drug benefit would cut cancer care reimbursement by 30 percent! Without adequate reimbursement rates, patients who cannot afford to pay out of pocket for their treatments will not be able to receive innovative therapies and the dollars poured into research will have been for naught.

IV. THE IMPACT OF ACCESS TO CARE ON THE GAP

Even if we overcome these systemic challenges, additional barriers continue to block research discoveries from reaching a patient's bedside. Of most concern to the Komen Foundation is the issue of access to quality care. While the Komen Foundation greatly appreciates the Federal government's commitment to funding cancer research, we are concerned that the War on Cancer appears to be morphing into the War on Cancer Care as funding for programs directed toward improving access to care are left to wither with little to no funding increases or experience cuts. To ensure the translation of research innovations into treatment advancements, it is essential to ensure that every American has access to these improved clinical practices.

The access problem does not lie with patients. They are eager to apply the new medical advances. Rather than focusing on their doctor's advice alone, patients now

come to visits armed with data and expecting high quality care. The news of scientific achievements is fast breaking, and the Internet helps disseminate information about new innovations faster than ever before. Eight years ago, there were 124 cancer drugs in the pipeline of biotechnology and pharmaceutical companies. Today, there are 402. Patients are demanding that these innovations be made available rapidly.

Until a cure is available or until cancer can be prevented, patients are demanding quality cancer care today, and they won't settle for anything less. For Americans with breast cancer, quality cancer care means a great many things. It means hope. It means a chance at survival. It means receiving guidance to make the best decisions about comprehensive and integrative treatment. Concurrently, patients use complementary methods of care and advanced spirituality to improve outcomes, to manage side effects, to sustain their "wholeness" and to advance their healing. Numerous surveys indicate that breast cancer patients are among the most frequent users of complementary and alternative therapies during the course of their cancer care. Cancer care is not quality care if it does not include the proven range of essential conventional, complementary and integrative services that help breast cancer patients battle their disease.

Yet, their excitement and enthusiasm for these new treatments is quashed when they learn that they will not be able to access these innovative treatments. As already described, before patients have access to new treatments, physicians must be willing to provide them, and reimbursement for them must be adequate. If not resolved, these problems will only lead to an even wider gap.

In addition, outreach programs must be adequately funded to ensure that all Americans have access to these therapies. The under- and uninsured are truly disadvantaged by the current system. For the breast cancer community, the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) works to remedy this gap. But, for it to succeed, it must be funded at adequate levels. The Komen Foundation is a strong supporter of NBCCEDP, but also a realistic one. While the program has helped hundreds of women, even more have been turned away because of a lack of funding. Other outreach programs are suffering from similar funding concerns.

The Komen Foundation recognizes, however, that outreach and education are not jobs for the Federal government alone. We also provide funding and support for outreach and educational efforts at both the National and Affiliate levels. Patients must learn about what standard of care they should receive and what questions they should ask of their providers. The Komen Foundation helps to address this void through its Helpline, Website, and educational materials and programs for both patients and providers. Komen Affiliates nationwide address this void through their support of unique local outreach programs that meet the specific needs of their communities.

V. ELIMINATING THE WIDENING GAP

The promises of treatment innovations should not be overshadowed by the concerns raised today. We must continue to work to bring the promises of research to cancer patients. A quick fix will not eliminate this widening gap. Therefore, we suggest that the Subcommittee focus on (1) understanding the problems that have led to the gap through formal studies and evaluations; (2) examining the current clinical trial process with an eye toward revising it to take account of new biomedical advances; (3) providing adequate reimbursement rates for cancer care; and (4) calling for adequate Federal funding for physician training programs and patient outreach and educational programs.

As the Subcommittee considers how to minimize the gap between research developments and clinical treatments, it is important to understand the problems that have led to the gap. First, we must learn more about how bench research translates into bedside practice. At a minimum, it is essential to ask:

- What is the strategic direction for the research? Who sets it?
- How is collaboration fostered and duplication avoided?
- How does the research process help or hinder elimination of the gap?
- How is a research idea translated to a research project, then to clinical trials, and then to approval by the FDA?
- How does a clinically proven treatment become a standard of care?
- Where does this process break down?

Second, it will be necessary to review and assess in a comprehensive manner the existing clinical trial process and the FDA's role in approving new treatments. This means:

- Evaluating the existing clinical trial process to determine what changes must be made to make it more responsive;
- Increasing participation in clinical trials;
- Educating patients and physicians about clinical trials;
- Reviewing reimbursement policies related to care provided to clinical trial participants;
- Ensuring that the clinical trial process is appropriately structured to address issues related to individualized medicine; and
- Assessing the FDA's structure and funding to determine how to eliminate the existing backlog of "pipeline" drugs.

Third, it is necessary to evaluate reimbursement amounts in both the private and public insurance markets. Medicare reimbursement amounts often set the standard for private insurance rates. Therefore, it is critical that these amounts provide physicians with adequate reimbursement for their services. We encourage the Committee to examine reimbursement policy to ensure adequate coverage for innovative treatments, especially in cancer.

Also important is reducing the paperwork burden and the "audit fear factor" in reimbursement procedures and streamlining the processes for providing reimbursement codes for new technology. There should also be incentives to ensure that the newer, targeted biological innovations are available quickly to patients for whom other treatment options have been exhausted.

Fourth, for research to continue to produce the innovations at the speed that modern knowledge will allow, sustained support of the Federal research budget is mandatory. In addition, funding for physician training programs should focus on expanding specialist education opportunities, both within medical training programs and continued medical education. Funding for patient outreach and educational programs must be increased to eliminate access to care barriers that block research advances from reaching the bedside.

As a first step, the Komen Foundation urges you to call for a study by the Institutes of Medicine (IOM) to measure the disincentives that block rapid dissemination of proven innovations, using breast cancer as a "pilot area" from which further research can be designed. A Federally sponsored demonstration project focusing on integrated care and its effect on quality care, quality of life, efficiency and cost effectiveness would also provide important information about how the research and treatment gap can be diminished. The Komen Foundation would welcome the opportunity to work with you on developing such a demonstration project.

This process will be difficult and time consuming, but valuable. We applaud the Subcommittee's willingness to undertake this review, as well as its desire to work with the scientific, medical and patient communities to eliminate this troubling gap.

Please be assured that the Komen Foundation will continue its commitment to not only fund ground-breaking research to help put an end to breast cancer for future generations, but also to support those currently fighting breast cancer who must use the technology of today in their efforts. We appreciate the opportunity to submit this testimony, and thank you very much.

