

**MANAGING BIOMEDICAL RESEARCH TO PREVENT
AND CURE DISEASE IN THE 21ST CENTURY:
MATCHING NIH POLICY WITH SCIENCE**

JOINT HEARING
BEFORE THE
**COMMITTEE ON ENERGY AND
COMMERCE**
HOUSE OF REPRESENTATIVES
AND THE
**COMMITTEE ON HEALTH, EDUCATION,
LABOR, AND PENSIONS**
U.S. SENATE
ONE HUNDRED EIGHTH CONGRESS
FIRST SESSION

OCTOBER 2, 2003

Serial No. 108-56

Printed for the use of the Committee on Energy and Commerce and the
Committee on Health, Education, Labor, and Pensions



Available via the World Wide Web: <http://www.access.gpo.gov/congress/house>

U.S. GOVERNMENT PRINTING OFFICE

89-964PDF

WASHINGTON : 2004

For sale by the Superintendent of Documents, U.S. Government Printing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512-1800; DC area (202) 512-1800
Fax: (202) 512-2250 Mail: Stop SSOP, Washington, DC 20402-0001

COMMITTEE ON ENERGY AND COMMERCE

W.J. "BILLY" TAUZIN, Louisiana, *Chairman*

MICHAEL BILIRAKIS, Florida	JOHN D. DINGELL, Michigan
JOE BARTON, Texas	<i>Ranking Member</i>
FRED UPTON, Michigan	HENRY A. WAXMAN, California
CLIFF STEARNS, Florida	EDWARD J. MARKEY, Massachusetts
PAUL E. GILLMOR, Ohio	RALPH M. HALL, Texas
JAMES C. GREENWOOD, Pennsylvania	RICK BOUCHER, Virginia
CHRISTOPHER COX, California	EDOLPHUS TOWNS, New York
NATHAN DEAL, Georgia	FRANK PALLONE, Jr., New Jersey
RICHARD BURR, North Carolina	SHERROD BROWN, Ohio
<i>Vice Chairman</i>	BART GORDON, Tennessee
ED WHITFIELD, Kentucky	PETER DEUTSCH, Florida
CHARLIE NORWOOD, Georgia	BOBBY L. RUSH, Illinois
BARBARA CUBIN, Wyoming	ANNA G. ESHOO, California
JOHN SHIMKUS, Illinois	BART STUPAK, Michigan
HEATHER WILSON, New Mexico	ELIOT L. ENGEL, New York
JOHN B. SHADEGG, Arizona	ALBERT R. WYNN, Maryland
CHARLES W. "CHIP" PICKERING, Mississippi	GENE GREEN, Texas
VITO FOSSELLA, New York	KAREN MCCARTHY, Missouri
ROY BLUNT, Missouri	TED STRICKLAND, Ohio
STEVE BUYER, Indiana	DIANA DEGETTE, Colorado
GEORGE RADANOVICH, California	LOIS CAPPS, California
CHARLES F. BASS, New Hampshire	MICHAEL F. DOYLE, Pennsylvania
JOSEPH R. PITTS, Pennsylvania	CHRISTOPHER JOHN, Louisiana
MARY BONO, California	TOM ALLEN, Maine
GREG WALDEN, Oregon	JIM DAVIS, Florida
LEE TERRY, Nebraska	JAN SCHAKOWSKY, Illinois
ERNIE FLETCHER, Kentucky	HILDA L. SOLIS, California
MIKE FERGUSON, New Jersey	
MIKE ROGERS, Michigan	
DARRELL E. ISSA, California	
C.L. "BUTCH" OTTER, Idaho	

DAN R. BROUILLETTE, *Staff Director*

JAMES D. BARNETTE, *General Counsel*

REID P.F. STUNTZ, *Minority Staff Director and Chief Counsel*

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS

JUDD GREGG, New Hampshire, *Chairman*

BILL FRIST, Tennessee	EDWARD M. KENNEDY, Massachusetts
MICHAEL B. ENZI, Wyoming	CHRISTOPHER J. DODD, Connecticut
LAMAR ALEXANDER, Tennessee	TOM HARKIN, Iowa
CHRISTOPHER S. BOND, Missouri	BARBARA A. MIKULSKI, Maryland
MIKE DEWINE, Ohio	JAMES M. JEFFORDS (I), Vermont
PAT ROBERTS, Kansas	JEFF BINGAMAN, New Mexico
JEFF SESSIONS, Alabama	PATTY MURRAY, Washington
JOHN ENSIGN, Nevada	JACK REED, Rhode Island
LINDSEY O. GRAHAM, South Carolina	JOHN EDWARDS, North Carolina
JOHN W. WARNER, Virginia	HILLARY RODHAM CLINTON, New York

SHARON R. SODERSTROM, *Staff Director*

J. MICHAEL MYERS, *Minority Staff Director and Chief Counsel*

(II)

CONTENTS

	Page
Testimony of:	
Shapiro, Harold, Chair, Committee on the Organizational Structure of the National Institutes of Health, President Emeritus and Professor of Economics and Public Affairs, Department of Economics and Woodrow Wilson School of Public and International Affairs, Princeton University	29
Varmus, Harold, President, Memorial Sloan-Kettering Cancer Center, and former Director, National Institutes of Health	16
Zerhouni, Elias A., Director, National Institutes of Health, United States Department of Health and Human Services	9
Material submitted for the record by:	
American Cancer Society, prepared statement of	200
Martin, Jeffrey C., Chairman of the Board, Parkinson's Action Network, prepared statement of	199
National Academy of Sciences, prepared statement of	203
Toomey, Hon. Patrick J., a Representative in Congress from the State of Pennsylvania, prepared statement of	198
Varmus, Harold, President, Memorial Sloan-Kettering Cancer Center, and former Director, National Institutes of Health, response for the record	207

MANAGING BIOMEDICAL RESEARCH TO PREVENT AND CURE DISEASE IN THE 21ST CENTURY: MATCHING NIH POLICY WITH SCIENCE

THURSDAY, OCTOBER 2, 2003

JOINT HEARING OF THE U.S. SENATE, COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS, AND THE U.S. HOUSE OF REPRESENTATIVES, COMMITTEE ON ENERGY AND COMMERCE,

Washington, DC.

The committees met jointly, pursuant to notice, at 10:07 a.m., in room SD-106, Dirksen Senate Office Building, Hon. Judd Gregg, Chairman, Senate Committee of Health, Education, Labor, and Pensions, presiding.

Members present Committee on Health, Education, Labor, and Pensions: Senators Gregg, Kennedy, Mikulski, Harkin, Murray, and Clinton

Members present Committee on Energy and Commerce: Representatives Bilirakis, Greenwood, Shimkus, Pitts, Ferguson, Rogers, Dingell, Waxman, Brown, Wynn, Green, DeGette, Capps, and Allen.

Also present: Representative Stephanie Tubbs Jones.

Mr. GREGG. If we could bring the hearing to order. First, it is a pleasure to have a chance to chair this hearing which is going to look into the issues of how we are proceeding in our health research community, especially of course, the NIH community. It is a great pleasure to be joined by our House colleagues in this joint hearing. I do not think I have participated in a joint hearing on the Health, Education, and Labor Committee before. I think it is a nice precedent and very constructive to the process, first because it gets us some camaraderie and collegiality, but also because it, I suspect, saves Dr. Zerhouni from having to testify two times, and be put through the process twice.

We are going to limit opening statements, if there is no objection, to the chairmen and ranking members of the two committees, and then we will go right to Dr. Zerhouni.

The purpose of this hearing is to get a background as to how NIH is handling the huge increase in funding which has come to it as a result of the commitment of this Congress and the American people to health research. We recognize that NIH is an extraordinary resource for our Nation that is doing exceptional work, and we increased the funding of NIH 100 percent in the last 5 years in order to give it the resources to accomplish its goals. The ques-

tion is: are those dollars being effectively used, and how can we assist NIH in attaining its goal, which is to improve the health care in the United States?

I am not going to go into a more in-depth statement. I am looking forward to hearing from Dr. Zerhouni, and I will yield to the chairman of the House committee, Mr. Bilirakis.

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

Good morning to all of you. I first want to commend Chairmen Tauzin and Gregg for working together to organize this joint hearing. I will keep my remarks brief, but I did want to say that Chairman Tauzin is at the White House, called on suddenly by the President. I think it is on the energy issue.

And additionally extend my sympathy to Senator Gregg, who recently lost his father. I think it is above and beyond the call of duty, the fact that he has taken time to be here today for this hearing.

Mr. GREGG. Thank you.

Mr. BILIRAKIS. I am pleased to welcome our distinguished guests here today, and I would like to extend a special thank you to Dr. Elias Zerhouni, who is the Director of NIH, for his leadership and innovation, and of course, thank and welcome Dr. Harold Varmus, former Director of NIH, and Dr. Harold Shapiro, Chairman of the National Research Council's Committee on the Organizational Structure of NIH. I am sure all three of you will improve the committee's understanding of the organizational structure of NIH and the changes that could help NIH to adjust to meet the challenges of the 21st century.

We recently completed our efforts to double the budget at NIH. However, with a dramatically increasing budget it is also important to ensure that the American people get the most out of this massive investment of resources. It is essential that NIH utilize their resources in ways that most effectively reflect the needs today.

On Wednesday, Dr. Zerhouni announced a \$2.1 billion 5-year plan to lay the groundwork for future medical advancements, which he referred to as the roadmap. It is designed to help researchers, physicians and drug companies turn scientific findings into new therapies, and I know we all look forward to hearing more about his roadmap.

NIH over the years has grown not only in cost but also in the number of institutes and centers. In 2001 Congress directed NIH to have the National Academy of Sciences study the current structure and organization of NIH and determine if it was optimally configured. Their report, published in July, contains many interesting suggestions, many of which we will hear here today, for restructuring the NIH. Dr. Shapiro, of course, is here to discuss the findings of the report, and we all look forward to hearing his thoughts.

I thank all three of you gentlemen for your willingness to testify, and again extend my thanks to Chairman Tauzin and Chairman Gregg, and their staffs, all of our staffs, for all their hard work they put into this hearing.

Thank you, Mr. Chairman.

Mr. GREGG. Congressman Dingell?

Mr. DINGELL. Mr. Chairman, thank you for scheduling this hearing on the National Institutes of Health and the future of that great institution. I hope this hearing will be the first of many, and I hope they will be friendly.

The NIH is the crown jewel of biomedical research in this country and in the world. It is a magnificent collection of resources, of talent, devotion and energy. It is the envy of the world. Its contribution to health, science, and research has been incalculable. More importantly, it is the source of hope for millions of people who suffer and die unnecessarily because techniques to prevent, treat, or cure their ailments are not currently available. Major changes in the structure and operation of NIH should be undertaken with extraordinary care.

We have a distinguished panel before us today. First I welcome Dr. Harold Shapiro. Under his leadership the Institute of Medicine recently published a report, *Enhancing the Vitality of the National Institutes of Health, Organizational Change to Meet New Challenges*. This is a thoughtful and extensive analysis of key challenges facing NIH in the 21st century.

I also welcome back our old friend, Dr. Harold Varmus, who has made a tremendous contribution to the success of NIH.

I am of course pleased that Dr. Zerhouni is here to share with us his plans, or roadmap, for the future of NIH.

I have grave concerns about part of that roadmap, the program now under way for outsourcing many of the jobs currently held by NIH employees. I am unaware of any reason that this outsourcing needs to take place. I am also unaware of any benefits to be achieved. I am aware of the fact that damage done to NIH will not be easily repaired, and I think we should embark on a course of this kind with extraordinary care and with extraordinary diffidence, not just to NIH, but to what this can do to the future of medicine and medical research and science in this country.

The outsourcing program has caused great concern among NIH employees and many of its key stakeholders such as academic health centers that actually conduct much of the research supported by NIH dollars, as well as the patients whose hopes and fears are directly tied to the success or failure of NIH.

I would note that much of NIH's work is done outside the walls of the institution by different private and public institutions with whom NIH has research contracts and different arrangements for doing this kind of research.

Why then is outsourcing necessary? Is it that we are serving science, or are we just serving some kind of curious right-wing privatization ideology? People like that oft times have ideas. They do not know why, and they cannot justify it, but they proceed to carry them forward anyhow despite the consequences. What jobs will be outsourced and which ones will not be outsourced? What is the timeframe for completing this process, and what criteria are being applied? Outsourcing is an instrument which creates disorganization, fear, concern, and difficulty. Successful organizations do not embark upon tasks which contain these kinds of risks.

This is also a very blunt instrument and can cause much collateral damage to NIH, to the scientists there, to science and to the general overall undertakings of this Nation with regard to scientific

research. It poses enormous risk to do great harm to NIH and to the scientific research now going on there. We need to have a candid assessment of the damage that it has done, and we need to see what it is going to do to the human, scientific, and cultural fabric at NIH.

Another subject that I hope our witnesses will address today is the persistence of major health disparities. There are numerous articles and studies that document the fact that such disparities exist between sexes, races and between people. There are two important books published by the Institution of Medicine on this. Why do the disparities continue? What should the Congress be doing about them? Perhaps this should be the focus of the hearing today.

In any event, I thank you for having this hearing, Mr. Chairman. I look forward to participating actively. I hope we will have a number of them, and I hope we will have the proponents of this weird idea for outsourcing before us so that we might discuss their rather strange views in greater and more thoughtful detail. Thank you, Mr. Chairman.

Mr. GREGG. Thank you, Congressman.

As I mentioned at the opening of the hearing, it is not our tradition, at least on the Senate side—I guess it might be different on the House side—to have a lot of opening statements because we like to get right to the witnesses. But we did want to give all the chairmen and the ranking members the opportunity to do opening statements. If other members want to do an opening statement, obviously we will do that, but it would be nice if we could get on with the statements. But certainly, Congressman Brown, as ranking member, if he wants to make a statement, it is very appropriate.

Mr. BROWN. Thank you very much, Mr. Chairman. I appreciate your good work and also the good work of Chairman Bilirakis and Ranking Member Dingell.

Thank you, Dr. Zerhouni, for being here this morning. I am confident of your leadership and impressed with your vision for the National Institutes of Health. Thank you.

I want to take a moment to thank you for speaking of support of the Christopher Reeve Paralysis Bill introduced by my colleagues Chairman Bilirakis and Senator Harkin earlier this year, and welcome Harold Varmus and Harold Shapiro. I look forward to hearing their testimony also.

Congress allocated significant budget increases over the last 5 years, as we know, to support basic research and biomedical sciences at NIH. The research accomplishments achieved throughout the country in large part through NIH investments have been nothing short of remarkable. It will be unrealistic, we know, to expect future funding increases comparable to the investments we have made over the last half decade, but as we contemplate approving the smallest budget increase NIH has received in decades we must not ignore the potential we unleashed when we doubled the NIH budget.

I keep coming back to whether the priorities of this administration and this Congress are in any ways related to the priorities of the Nation. We passed \$3 trillion worth of tax cuts overwhelmingly benefiting the wealthiest Americans in this country, and then we allocate the lowest budget increase to NIH in a decade? Did we not

just map the Human Genome Project? Have we not seen one remarkable accomplishment after another remarkable accomplishment from NIH? The fiscal year 2004 Appropriation Bill falls short of what is needed to merely keep up with inflation and research costs, and of the increase in the number of research project grants for fiscal year 2004, 344 total new research grants, 323 are designated for biodefense research, only 21 are designated for nonbiodefense research. Research aimed at saving lives and promoting health should not take second place to biodefense. Both types of research are and should be national priorities. Dr. Zerhouni, I am concerned the administration is making you choose between and among research priorities that should never compete for Federal funding.

Earlier this summer the National Institute of Allergy and Infectious Disease was dealt a major blow when the administration siphoned millions of dollars from the Institute to pay for the development of an anthrax vaccine. Despite the administration's explicit commitment to battle AIDS, to battle TB and to battle malaria worldwide, the dollars drained from NIAID reduced research on these three infectious diseases that together every year kill 6 million human beings. Reemerging diseases like TB and malaria, and newer threats like anthrax and smallpox and SARS, all weaken our national security. Funding for research in these areas should better reflect that.

Scientists are just beginning to tap into the tremendous potential inherent in human genomics. Cancer treatment is rapidly evolving. Research on spinal cord injury is helping people with paralysis breathe on their own for the first time. We cannot afford to drop the ball now. Too many lives are at risk.

I thank the Chairman.

[Additional statements submitted for the record follow:]

PREPARED STATEMENT OF HON. BARBARA A. MIKULSKI, A U.S. SENATOR FROM THE
STATE OF MARYLAND

Chairman Gregg, thank you for holding this joint oversight hearing on NIH. I am pleased that Dr. Zerhouni, Dr. Varmus and Dr. Shapiro are here today to discuss the best ways to move NIH into the new millennium. NIH is saving lives and improving our nation's health.

I am the Senator from Maryland and for Maryland, and I am proud that NIH is in my home state. Employing nearly 18,000 people, my constituents are both employees and neighbors of NIH. NIH is a jewel in the nation's crown, but it also faces challenges to stay on the cutting edge of science, while making the highest and best use of its resources.

Many of the advances in medicine in the 20th century are the results of American discovery and innovation. Over the years, the American people have invested in NIH, and it is paying off in improved prevention, diagnosis and treatments for diseases. I strongly supported the bipartisan doubling of the NIH budget over five years and am pleased that this goal has been met. But, with resources comes accountability. We must stay the course to make sure that investments are made wisely. NIH must continue to make a return on the public's investment, whether it is by recruiting the best and the brightest employees or providing patients with access to the fruits of NIH discoveries.

Dr. Zerhouni has asked the right questions. NIH must push the frontiers of science and be prepared to respond to new threats of bioterrorism and infectious diseases, as well as issues such as chronic diseases that impact the health of our nation's aging population. Congress and NIH must take swift steps to make sure they will have access to new discoveries, and cures and live healthier lives.

I am optimistic that NIH will continue to bring discoveries to patients, from basic science to the bedside, and meet the challenges of the new century. I look forward

to the testimony of our witnesses, as well as an open discussion about the findings of the recently released Institute of Medicine (IoM) report on the structure of NIH and the proposed NIH Road Map.

PREPARED STATEMENT OF HON. MICHAEL B. ENZI, A U.S. SENATOR FROM THE STATE OF WYOMING

Congress has just reached an important bipartisan goal: doubling the federal health research budget of the National Institutes of Health (NIH). Achieving that goal, however, comes with the responsibility to make sure that we are spending the taxpayers' money wisely, so I welcome this opportunity to join with our colleagues from the House of Representatives to hold this hearing.

If we spend the new money well, our doubling of the NIH budget over the past five years will accelerate our race to help us better understand the mechanisms of diseases and find the tools with which to prevent and cure them. I know many researchers and advocates would like to see us double the NIH budget every five years, but this is an unrealistic expectation.

Nevertheless, I am confident that the NIH will still receive healthy financial support for the foreseeable future. When you realize that the base funding level at the outset of this fiscal year is twice what it was five years ago, you don't have to be an accountant to understand that a small increase from that base in percentage terms actually turns out to be a significant amount of money.

The focus of today's hearing, however, is not how much money we should spend through the NIH. It's whether our money is being spent wisely on our national health research priorities.

Scientists, researchers, and other health and medical experts should be the ones who decide which specific projects are the most promising and deserve funding. Congress should not decide which grant applications to fund.

However, Congress needs to ensure that NIH spending reflects national priorities, and that spending on any particular disease bears some relationship to the burden that disease places upon society.— If Congress needs to be clearer in our direction to the NIH, then we need to hear that from the NIH.

The Institute of Medicine (IOM) of the National Academies just released a report called "Enhancing the Vitality of the National Institutes of Health: Organizational Change to Meet New Challenges." Congress called for this report to assess whether the current structure and organization of the NIH are appropriate to respond to the scientific needs of today and the future. I'm pleased that Dr. Harold Shapiro, who chaired the IOM's Committee on the Organizational Structure of the NIH, is here to discuss the report. I'm also pleased that Dr. Elias Zerhouni, our NIH director, is here to respond to the report and to talk about the "NIH Roadmap for Medical Research," the agency's plan for addressing the major opportunities and gaps in biomedical research that no single institute at NIH can tackle alone.

I'm also glad that Dr. Varmus, our former NIH director, is here to share his thoughts on what's working at the NIH and what could work better. He has written and spoken on the issue of NIH organization, and he has suggested that a significant re-organization of the NIH is in order. I am intrigued by Dr. Varmus's argument that the NIH would be more manageable and more effective scientifically if the NIH had far fewer institutes covering broader areas of science.

The number of organizational units within the NIH has grown over the years, in response to the pleas of disease advocacy groups and scientific associations and the direction of Congress. Dr. Varmus has argued that fewer and bigger institutes would be more effective because they would have more adequate resources to support complete programs in promising areas of research, and more flexibility to respond to emergent public health needs.

Interestingly, the "NIH Roadmap" implicitly acknowledges that the proliferation of units within the NIH umbrella can be a roadblock to research progress. I hope Dr. Varmus will elaborate on his thoughts in light of the recent release of the "NIH Roadmap."

I also hope all three of our panelists will give some thought to the future of health research from a "human resources" perspective. In other words, are we providing enough opportunities for young scientists to build their careers "particularly those young scientists who conduct their research at institutions that have not traditionally been among the leaders in the receipt of NIH support?"

Today, more than ever, fewer of America's best and brightest are electing to pursue careers as scientists. There are many reasons for this, but I believe one of these reasons is that young scientists lack independent funding opportunities during their

postdoctoral years that would enable them to build early foundations for their careers.

Young scientists are the key to our making the most of the dramatic increase in NIH funding. Our top students need to see attractive career paths in science, or they will apply their brilliance in other careers, to the detriment of the American biomedical research enterprise. I would welcome the thoughts of our witnesses on what we need to do to make careers in the biosciences more attractive to young scientists, and what role the NIH could or should play.

I thank our witnesses for their time, and I thank Chairman Gregg and Chairman Tauzin for working together to organize this important hearing.

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

Thank you, Chairman Gregg. I will be very brief, and I urge my House colleagues to be brief or to waive their opening statements so that we can get to the important testimony of our witnesses today.

I welcome the opportunity to join my Senate colleagues today to hear testimony about how to strengthen the National Institutes of Health. I am pleased that we have testifying before us the current NIH Director, Dr. Elias Zerhouni, as well as former NIH Director, Dr. Harold Varmus. Together, these two men represent a decade of leadership at the NIH. Notably, the last time Congress made sweeping legislative changes to the NIH occurred ten years ago. It is high time that both House and Senate authorizing Committees take a serious look at NIH to help solidify the fundamental role medical research plays in improving public health for years to come.

Without a doubt, the National Institutes of Health is the world leader in biomedical research. We have invested significant taxpayer resources to speed the discovery of new methods to treat disease and improve public health. We recognize that taxpayer dollars invested in medical research will yield untold benefits to all Americans. At the same time, we must ensure that the investments we have put in place at the National Institutes of Health are fully maximized.

With 27 institutes and centers that independently establish priorities and set research agendas in addition to the Office of the Director, it's not hard to figure out why patient advocacy groups—and even Congress—have a tough time tracking medical research conducted at NIH. That's why we need to explore a variety of legislative proposals to revitalize the NIH, including organizational structure changes. In doing so, we may want to consider establishing a system of greater transparency of NIH research activities to guarantee that NIH is held accountable for taxpayer investments.

This will be the third hearing the House Committee on Energy and Commerce has held this session to evaluate programs at the NIH. I am hopeful that the information learned from this forum will help us in our efforts to reauthorize this incredible Agency.

PREPARED STATEMENT OF HON. CLIFF STEARNS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF FLORIDA

Mr. Chairman, thank you for holding this hearing today on the organizational structure of the National Institutes of Health. I am intrigued to explore Dr. Zerhouni's "NIH Roadmap for Medical Research," and appreciate Dr. Varmus and Mr. Shapiro's contributions.

In May we observed the sequencing of the human genome and the 50th anniversary of the description of the double helix, which makes up the DNA. As past chairman of the Task Force on Health Care and Genetic Privacy, I commended the folks at NIH for their outpouring of work. Now, we are taking the opportunity to look at the outpouring of work, and ask, what might we do even better? How do we prioritize? Should we consolidate? Be more open to other Departments and Agencies? Americans invest significant tax dollars to fund NIH research, and patients. As the authorizing Committees, it is our responsibility to ensure that NIH is held accountable on behalf of the taxpayers and patients. It is our responsibility to remove barriers that unnecessarily delay the incredible progress we are making in improving human health. And it is our responsibility to ensure good prioritizing and value dictate where resources go. During the FY2004 Labor-HHS Appropriations (HR 2660) this Summer Rep. Toomey (PA) had an amendment which would have prevented the NIH from further funding four specific grants that they are currently funding. The amendment did not cut any funding to NIH, it simply prevented the

agency from funding these four projects. The amendment failed; I did vote for it. In the debate, some Members of both parties stated that Congress should not micro-manage the NIH, that these were peer-reviewed studies. Yes, we should not micro-manage, but we should ask that the NIH conduct itself wisely as the taxpayers ask. I think some discussion of Dr. Zerhouni's vision for strengthening and improving might lend even more constructive accountability, across institutes and divisions and fields of science. I look forward to the testimony.

PREPARED STATEMENT OF HON. HENRY A. WAXMAN, A REPRESENTATIVE IN CONGRESS
FROM THE STATE OF CALIFORNIA

Thank you for the opportunity to make a brief opening statement.

The National Institutes of Health is the most important and successful medical research organization in the world. It funds more research than any other public agency. It has produced more cures, more breakthrough treatments, and more hope for millions of patients around the world than any other group of scientists. I look forward to hearing from Dr. Zerhouni about his plan to build upon this record of success.

I am concerned, however, that ideology and politics are interfering with NIH's scientific mission and compromising the agency's effectiveness.

Much of this interference is coming from the Bush Administration. Nominees to NIH's prestigious scientific advisory committees are being screened for their political beliefs, including whom they voted for in the last Presidential election. This undermines science and is unacceptable. HIV and AIDS researchers have been warned to expect extra scrutiny if their grant applications contain particular words that might upset social conservatives. This too undermines science and is unacceptable.

According to scientists inside and outside of NIH, the Office of Management and Budget's aggressive push for privatization is undermining morale and sapping productivity. Meanwhile, there is serious concern that Secretary Tommy Thompson's proposal to transform the Commissioned Corps of the Public Health Service could push world-class investigators out of NIH altogether.

These actions make as much sense as the President's misguided stem cell policy, which leading scientists have said undermines our ability to find cures for diseases that afflict millions of Americans.

I hope we can explore some of these issues today. I also would ask my colleagues not to compound the problem of political interference at NIH by second-guessing the agency's peer review process. Topics such as risk-taking, sexual dysfunction, and loss of biodiversity are legitimate areas of scientific exploration. It sets a terrible precedent for Congress to strip funds from scientifically valid projects simply because they do not comport with an ideological agenda.

I look forward to the testimony of the witnesses.

PREPARED STATEMENT OF HON. LOIS CAPPS, A REPRESENTATIVE IN CONGRESS FROM
THE STATE OF CALIFORNIA

Mr. Chairman, like many of the members here today I am a proud supporter of the NIH.

The United States has the best medical research in the world, and some of the most advanced health care.

These achievements are directly the result of the amazing job that the National Institutes of Health has done and the resources we have provided them.

This rare joint hearing we are holding today is an excellent use of our time. It has been several years since we reauthorized NIH. We should correct that.

And it is clearly our role to oversee the NIH and make sure they are operating effectively.

From time to time it is important for us to review the NIH, consider reports on its effectiveness, and hear testimony from experts.

But I do want to caution my colleagues against becoming to eager to find fault in these institutions.

They have been an amazing success story.

And while there may be some ways we can improve their operation, we should not make changes that might jeopardize the impressive record of the NIH.

For example, the IOM recently suggested that Congress should review the special status of the National Cancer Institute.

This is something to consider.

But lets remember that cancer care in this country is the best in the world.

And the very same IOM report holds the NCI up as a model for other institutes to follow.

The research done by the NCI since its special status was granted has led to great advancements in cancer care.

Before we jump to any conclusions about eliminating NCI's special status we should remember the doctor's credo "do no harm."

We should not rush to embrace any measures until we are certain they won't undermine the very institutions we want to enhance.

The Energy and Commerce committee has already moved to precipitously in another way that threatens to wreck cancer care in this country.

The Medicare prescription drug bill includes a provision that cuts cancer care funding by \$16 billion over 10 years.

This was designed to address an overpayment for cancer medications, but it fails to take into account an underpayment for physician services.

The massive cuts this creates will lead to the closing of cancer centers across the country, especially in rural areas.

Our approach should not have been one sided. We should have fixed both problems. But we didn't.

We should not make the same mistake with the NIH.

We should consider all recommendations carefully and implement the changes that make sense.

But we should be sure not to rush through changes that will impair the NIH.

Mr. GREGG. I would like to proceed to Dr. Zerhouni at this time unless there are other people who feel they need to make an opening statement.

Dr. Zerhouni?

STATEMENT OF ELIAS A. ZERHOUNI, DIRECTOR, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. ZERHOUNI. Thank you very much. Chairman and members, I am honored to appear before this joint hearing of two of the most distinguished committees of the U.S. Congress. I will make a slide presentation. I have submitted my written testimony.

What I would like to cover for you today is first and foremost what Congressman Dingell referred to, and that is that NIH spends its dollars primarily outside of NIH. Eighty-five percent of the \$27.2 billion of the NIH budget in 2003 goes to support over 220,000 scientists around the country in 2,800 institutions. About 11.8 percent of the budget is spent at NIH for NIH research and 3.2 percent of the budget is dedicated to management.

What I would like to focus on is to tell you how powerful your support has been in advancing health in our country. Your bipartisan support over the years has made a huge difference in the way disease is now treated and managed. I will give you a few examples. When you look at coronary heart disease and you look at the 1970's, if you projected what the mortality of this disease would be in 2000 if we had not done any research, the number would be 1.3 million deaths. The actual number is 514,000. There has been a 50 to 60 percent reduction in mortality in coronary heart disease, saving just in 2000, 850,000 lives. This progress was due to the many advances that, as you mention, NIH supported in many ways.

Another example of progress due to your support is the history of AIDS. As we discovered the cause of AIDS we were able to develop behavioral strategies, understand how to have a safe blood supply. As you looked at this, you saw in 1993 a decrease in the incidence of AIDS, even though we had no cure, and then by 1995 a marked decrease in the death rate from AIDS because of the de-

velopment of modern drugs. Clearly, the doubling is something that we have used to accelerate our research in fighting this disease. We have more than 80 new innovative drugs in development, and more importantly, because of the doubling of the budget, we have nearly three times the number of vaccines in Phase I trials that we had in 2001.

One more recent example of the benefits of your support is illustrated by the SARS outbreak. Let me be very categorical about this. The doubling of the budget allowed us to invest in human genome research and led to better DNA sequencing technology to finish the human genome faster. Most importantly, it allowed very powerful new ways to identify microbes and viruses through their genomes. It is because of that that we were able to identify the cause of SARS in record time and protect the country in conjunction with our sister agency, the CDC. There is no doubt that the investments you have made have paid off in many ways.

But the challenges are not stopping. Let me describe for you what we see at NIH as the rising challenges that public health has to face in this country. No. 1, as we have been successful in reducing the impact of acute short-term diseases, the diseases that we face today are more chronic, more long term, and 75 percent of our health expenditures are related to chronic diseases. Because we have been successful, life expectancy has increased in our country and we are dealing with a more aging population. Health disparities remain a challenge and we intend to do everything we can to reduce health disparities. But in addition to that there are new challenges. We are dealing with emerging and reemerging diseases. You have heard about SARS, West Nile virus, but there are others that are emerging: obesity, diabetes, which we need to tackle, and that is not to say that biodefense, the newest mission of the NIH, is not a large challenge as well.

What are we to do and what is NIH doing to address these challenges? I would like to show you how we have addressed this since I have become Director of the NIH. Clearly, as you see the challenges and the increasing cost of health care, it is absolutely clear that we have a major challenge in front of us that will require us to understand life sciences better and accelerate the pace of discoveries and translate these discoveries even faster from laboratories to patients and use novel approaches that have to be orders of magnitude more effective. If you really look at the way we treat and prevent disease today, and we continue to do this, we just would not have enough resources to pay for that 50 years from now. So the discoveries we have to make have to be 10, 30, 40 times more effective than what we have today.

How do you do this? It was clear to us that we needed, with the leadership of NIH, to get together and define new strategies, and this is what is referred to as the NIH Roadmap for medical research. How did we get there? First and foremost we asked ourselves what are the areas of science that we need to stimulate and how do we stimulate these areas of sciences and how do we translate that more effectively than we have?

Perhaps the key thing is to realize that we are dealing with an unprecedented time of opportunity. The discoveries we have made, the number of opportunities for treating particular biological tar-

gets is much greater than we have ever dreamed of before. We understand the genome and its structure, but we have challenges ahead of us that can be characterized in three core priorities. One is new pathways to discovery. We need to explore those. Two, we believe that research teams of the future will be different than the ones we have today, and three, we think the Nation needs a better clinical research system.

Let me be more explicit about that. I am showing you here an image from Dr. Subramaniam at NIH here in Bethesda, one of the first images of the complex enzyme called pyruvate dehydrogenase. This enzyme is made of multiple proteins that have been encoded by genes. We have 33,000 genes, but we have hundreds of thousands of proteins, and they come together in very complex molecular machines. This structure here is able to process thousands and thousands of small molecules that you see at the top here called pyruvate, remove hydrogen from pyruvate, at an efficiency rate that is unmatched in the known engineered world. This molecule is only but one of millions of molecules that are interacting in our cells. So the challenge for science is to understand the complexity of these biological networks of molecules, and every day in the scientific literature we identify new actors, new parts of the network, new molecules.

What we do not know is how all of these molecules work together. We believe that is the next frontier in life sciences and we need to accelerate discovery in that frontier, but that will also require new kinds of science teams. We think that the scale and complexity of 21st century research requires new organizational models. The silos that we have experienced in the past need to be broken. We need to create larger multi-disciplinary teams that are going to be more coordinated, whether it be for clinical research or basic research. They have to combine physical, biological and information sciences, and more importantly, we have to stop being conservative in our research, and we need to explore pioneering areas.

I see research as an adventure where you need pioneers that open new land like the Lewis and Clark expedition, and you need settlers that go behind the pioneers. That balance, when you are facing the challenges that I am describing, needs to be thought about all the time, and this is what we want to do through the NIH Roadmap.

Last but not least, we need to translate our discoveries into practice, and this will require us to rethink the entire system of research, how our patients relate to their community doctors and to academic doctors. Research used to be done in academic centers. It is now done at the community level. I mean the treatments are at the community level because we are dealing with chronic long-term diseases, and that needs to be taken into account. But we cannot do it unless there are better information systems. We have 7 different information dictionaries for medical research, 7 different ones that are used in computer systems throughout the country. It is like running a country with 7 different languages. We need to tackle this, and create new partnerships of research between patients, community physicians and academic physicians, that will accelerate research. So the vision is the country needs a reshaped, recast national global research system, where patients have come

together in certain diseases we have seen progress, whether it be in pediatric leukemia or in cystic fibrosis. 30,000 patients are organized in 198 sites with 14 academic centers, and the life expectancy, without a cure, from cystic fibrosis has gone from 10 years to 40 years.

When you look at the roadmap implementation, to come back to the organizational challenge that I think you are trying to also look at today, you have to ask yourself a question. How do you manage and how do you stimulate cross-cutting investments across fields of science when NIH is organized in silos and has different appropriations? When there is a compelling case, as in the roadmap, because we consulted 300 plus leaders around the country. Our directors concluded that these three core priorities needed a common pool of investment. So all the directors came together to fund this initiative with \$128 million in 2004, about 2.1 cumulative by 2009. But it illustrates one of the challenges we have. It is a complex organization and we have managed this organization on a system of excellent peer review. It is the envy of the world. Everybody who comes to me from overseas, the first question is: how do you organize your peer review? It is very complex, very rigorous, and has integrity to it because it involves scientific review as well as national advisory councils that include public members and receive public advice. Despite all the funding, because of the increased scope of missions that we have, the success rate is still 30 percent, one of the most competitive in the world. We turn down 70 percent of all applications.

There are other challenges for you to consider, and this is where I would like to finish my testimony. There are revolutionary changes in science. Not only that, but science is converging, as we understand the molecules and how to translate that into complex networks to affect disease and to prevent disease. We know that doing research in cancer can affect discoveries in AIDS. That happens. Doing research on cardiac disease can affect treatments in cancer. That has already happened with the drug Gleevec. The breadth of mission of NIH has increased because the old causes of disease are still there. We still have health disparities. But as we are successful, we are creating new challenges. The organization is complex. The key word here is that we have a greater need for scientific and administrative coordination, and to balance the three. We need to balance science and its opportunities, the public health priorities and society, in what I think is the core challenge for NIH, to find better ways and effective ways of managing its total portfolio, defining its priorities and allocating resources in a way that is much more nimble than what we are doing today.

Is the structural approach of the past where we created a structure every time we needed something the right one? I do not think so, because from my standpoint as Director, the complexity that you reach with that is unmanageable unless you have better ways of functionally managing the portfolio.

That is my message for you, members of the committees, and Chairman, and I am looking forward to your questions. Thank you very much.

[The prepared statement of Elias A. Zerhouni follows:]

PREPARED STATEMENT OF ELIAS A. ZERHOUNI, DIRECTOR, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Chairmen and Members, I am honored to appear before this joint hearing of two of the most distinguished Committees of the United States Congress. This hearing is especially timely. The five-year doubling of the NIH budget is completed. As the 21st century begins, the pace of discoveries in the life sciences is accelerating at an unprecedented rate. One of the most extraordinary scientific achievements of all time, the sequencing of the human genome, was accomplished ahead of schedule and under budget. The doubling of the NIH budget is fueling many scientific advances, but the extraordinary complexity of these new biological discoveries is creating daunting scientific and management challenges.

I have now been the Director of NIH for more than a year. I can tell you that the Agency deserves its reputation as the crown jewel of government. NIH is home to many brilliant and dedicated employees, who are united by the noble mission of finding cures and better treatments for disease and disability. NIH, together with our research partners—patients, scientists, and research institutions—is leading the way in medical innovations that prolong life, reduce suffering, and improve the quality of life.

For example, the mortality of acute heart disease and stroke has been reduced by more than 50 percent. New cancer therapies have prolonged life to the point that over 9 million people are now cancer survivors in our country. Many of the important cancer treatment breakthroughs, including discovery of the molecular and genetic underpinnings of cancer, more effective drug treatments and cures for childhood leukemia, resulted from NIH-sponsored research.

The safety of the blood supply is vastly improved because of tests for Hepatitis B and C and HIV, developed through NIH-funded research. A pertussis vaccine was developed as the result of NIH research. Amazing breakthroughs in the treatment of heart disease arose from NIH research, including valve replacement surgery, the discovery of the role of high blood cholesterol as a major risk factor for heart disease, new drug treatments, and the knowledge about how to reduce risk factors. NIH research led to the identification of the virus that causes AIDS, the technique for detection of the virus, and most of the effective treatments for HIV/AIDS. The ability to quickly create candidate vaccines for emerging infectious diseases, such as the West Nile Virus, comes from NIH work.

These discoveries changed the landscape of disease as compared to the past, when acute and lethal conditions were the norm. Now we are seeing the influx of more chronic and manageable illnesses. People are living longer. Witness the aging of our population and the rise of chronic diseases.

NIH will play a major role in the next generation of medical breakthroughs. They include mining the sequence of the human genome for new strategies of preventing and treating disease. The more we learn about human biology, in health and disease at the smallest levels of our cellular structure, the faster we will find much needed cures and treatments.

Our past successes also force us to greatly expand our efforts, as we now face a larger spectrum of challenges. We still face persistent health disparities. We are hard at work developing comprehensive scientific-based responses to the new threats of bioterrorism and infectious diseases. It should be noted that were it not for the advances in genomics and other fields prompted by the doubling of the NIH budget, it is doubtful that we would have had the tools to identify the cause of SARS and help contain the disease as quickly as we did. As SARS demonstrated, in a world growing ever smaller, the dangers of existing and emerging infectious diseases loom large.

The number of research grants awarded by NIH has grown from 27,000 to 43,500 during the period of the doubling. We managed to increase this number while containing administrative and research support costs.

Also, we believe that the investment in NIH has had a leveraging effect in the private sector. For example, R&D spending by PhRMA members exceeded the NIH budget for the first time in 1991. The private sector now spends more for research than the public sector. And the investment by medical schools in research facilities and faculty has grown from \$3.2 billion from 1990 to 1997, to \$5.4 billion from 1998 through 2002, and is expected to rise to \$9.5 billion during the next five years.

Obviously, after a period of rapid growth, the challenges for a knowledge-driven organization as complex as the NIH can be daunting. As a scientist in charge of the largest publicly-funded medical research agency in the world, I have my own questions about the future direction of NIH. I believe that no outstanding organization can remain great without regularly reviewing its operating principles and plans and subjecting itself to critical reexamination.

I challenged the NIH leadership with the following questions:

- Are we creatively pushing the frontiers of science?
- Are we efficiently transforming that science into medical applications?
- Are we organized to insure a maximum return on the public investment?
- Are we allocating resources to all of the most critical priorities?
- Are we responding to emerging or exceptional opportunities?

This past year, I worked closely with the Institute and Center Directors in an intensive re-examination of NIH management processes. We agreed on significant changes that, I believe, will make us more responsive: to the changing landscape of science; to the demands of public accountability; and most importantly, to the patients who want and need to receive the results from research more quickly.

For example, we transformed the NIH governance structure by creating a smaller steering committee of 10 directors with rotating, 3-year memberships. I chair the new committee's twice-monthly meetings, which are convened to expedite consideration of issues of Agency-wide importance. This is one of the governance structure changes we are implementing in order to greatly streamline corporate decision making at NIH. Our intent is to create more open and transparent processes that will lead to greater administrative effectiveness and usher in a new culture of shared governance and collaborations across all Institutes and Centers at NIH.

Another example of how we will make NIH more responsive is the "NIH Roadmap," a blueprint we began implementing this month. Planning of the Roadmap started soon after I became NIH Director in May 2002. I convened a series of meetings to explore whether there were obstacles to scientific progress or gaps in our system of research that could not be addressed by one Institute alone, but is the responsibility of NIH as a whole.

Developed with input from more than 300 nationally recognized leaders in academia, industry, government and the public, the NIH Roadmap provides a framework for what we see as the strategies necessary to optimize the entire NIH research portfolio and accelerate the translation of discoveries into cures and treatments.

After an intense process of discussion and scientific review, the directors of NIH's 27 Institutes and Centers have agreed on an approach that we have announced in the past few days. The NIH Roadmap identifies the most compelling opportunities in three main areas:

New pathways to scientific discovery;

Research teams of the future;

Re-engineering the national clinical research enterprise.

These NIH Roadmap initiatives will be funded through a common pool of resources comprised of voluntary contributions from Institutes and Centers beginning, along with the Director's discretionary fund, with a modest budget for these initiatives of about 130 million dollars in Fiscal Year 2004. In the future, we expect to continue this effort from available funds appropriated to the NIH.

Our new governance systems and the NIH Roadmap are coincidentally responsive to many of the concerns recently raised by the National Research Council/Institute of Medicine (NRC/IOM) report: *Enhancing the Vitality of the National Institutes of Health: Organizational Change to Meet New Challenges*. The NRC/IOM concluded that NIH continues to do an outstanding job of managing and leading the biomedical research enterprise in the United States. But this is not the time to rest on our laurels. We need to create new strategies to manage the Federal investment in biomedical research.

The historical method of managing the research portfolio at NIH has been to set priorities by the creation of new Offices, Centers and Institutes. This is what I would call the "structural" approach to the portfolio management of NIH. It is often done without full consideration of how structural changes impact the research portfolio.

We must now ask ourselves: Under the current state of science, is this approach sustainable? We lack a formal trans-NIH portfolio review and management process. The need to manage the total NIH portfolio in the context of 27 separate structures and several special purpose offices, each with their separate budgets, is much more challenging than when the agency was smaller.

Currently, the overall NIH system of research ensures that Federal dollars are used to support the best science, follow the greatest research opportunities, and respond to public health needs. As a matter of internal policy, the NIH intramural program comprising Federal laboratories and investigators is small, representing about 10 percent of our resources. More than 80 percent of our budget goes to the extramural community of researchers, private sector scientists and institutions. And most of those funds are given to unsolicited, investigator-initiated research ideas.

Grant applications are vetted by the premiere peer review process in the world. Applications are reviewed by NIH staff as well as scientific experts from across the research community. The review process has multiple steps, including examination by independent advisory councils consisting of non-government experts, including the lay public. Research involving human subjects is reviewed by Institutional Review Boards.

Yes, NIH has served the cause of public health very well. We cannot, however, maintain the status quo. We must adapt. We must be innovative.

Consider the use of investment strategies in the financial community. In the financial arena, one wants to see a proper balance between ongoing performance, diversity of the company's investment portfolio, and the ability to pursue new opportunities that will maintain growth. Admittedly, scientific investment strategies are more difficult to predict because we do not know how or when progress and breakthroughs will come, but this kind of portfolio review and management, the kind of discipline used by the best financial strategists, has some value at NIH. Our challenge is to maintain a well-balanced research portfolio.

The current structure of NIH, with its separately-funded Institutes and Centers, does not facilitate trans-NIH initiatives. This particularly true when a much needed investment is viewed as unrelated to the specific mission of an institute and as such, is not supported by the Institute's constituencies. For example, the Human Genome Project, was first launched not by the NIH, but at the Department of Energy. Initially, this project was resisted by various NIH constituencies because it was seen as a high-risk project with little direct relevance to the missions of existing Institutes and Centers. There were great fears that it would take away from the RO1 grant mechanism, the mainstay of NIH research. It required the strong and persistent leadership of a few visionary scientists, including Nobel laureates James Watson and Harold Varmus and James Wyngaarden, to create the Center and, eventually, the Institute, which successfully completed this enormously complex project.

Science is converging as the result of the discovery of unifying concepts, methods, and biological mechanisms that link apparently disparate diseases. The closer we are to the roots of biology, the more our definitions of what diseases are and how they affect us are changing. How will we adapt the structure of NIH to this new taxonomy of disease? In the past, because of the incomplete state of our knowledge, NIH institutes are currently organized around diseases, organ systems or stage of life. In the future, this will likely need to change and we should implement a regular process of review and propose, at appropriate intervals, modifications to the NIH structure.

The NRC/IOM report, although not proposing drastic changes in the structure of NIH, strongly recommends the establishment of a permanent NIH-led process by which any addition, elimination or consolidation of mission-specific structures is studied. I fully support this recommendation.

As we look into the future, I would urge the Congress not to alter the peer review system, which is the cornerstone of NIH's success. Peer-reviewed research earned our country over half of all Nobel prizes in the sciences, with 5 laureates at the NIH itself, and dozens more directly trained or supported by NIH. These discoveries have led to the development of a vibrant economy around the life sciences placing our country at a huge competitive advantage. We should all work to preserve and protect the peer review system from undue influence.

NIH continues to be successful, in part, because of the diversity of approaches to the conduct and support of research taken by the decentralized Institutes and Centers. This characteristic should be preserved, but better coordinated and constantly reviewed and adjusted based on the emerging complexities of science. Often research done in one Institute eventually finds its greatest application in the mission of another, illustrating both the convergence of science and its unpredictability. As an example, the recently discovered cancer drug Gleevec was first developed as a potential drug for cardiac disease. Another successful cancer drug, Tamoxifen, was originally developed as an anti-hormonal drug. It failed, but then proved to be effective in the treatment of breast cancers that were responsive to hormones.

In looking at the independence of the Institutes and Centers, I agree with the position elucidated by the NRC/IOM, that we need to also address the appropriate authority of the NIH Director. In addressing this issue, we need to consider the serious responsibilities given to the NIH Director—coordinating, planning, and managing the entire portfolio.

I also support the NRC/IOM recommendation that NIH standardize data management. This effort will require new administrative investments in information infrastructure—more modern tools for portfolio analysis, reporting, and management. I understand that our advocates and Congress want appropriated funds to go to re-

search. In large part, I agree with this, but good stewardship also requires modern information systems.

I look forward to working with both Committees and the entire Congress in implementing improvements in NIH that will make research more efficient, and as a consequence, speed the pace of discovery—medical advances that will ease suffering and change the way we live.

I will be pleased to answer any questions that you have. Again, thank you for the opportunity to share my vision with you today.

Mr. GREGG. Thank you very much, doctor. I think that was a good overview, which will lead to a lot of questions. In the Senate we are not used to so many people showing up for a hearing, and I am looking at the time that we allot for questions. I recognize that our next two folks, who have very substantive commentary on NIH, probably would not get heard from until 12 o'clock. So I was wondering if you would mind, doctor, if I ask Dr. Varmus and Dr. Shapiro to join you at the table here and give their opening statements, and then we could do questions of all three of the members of the panel. Do you have time?

Mr. ZERHOUNI. I enjoy all the help I can get.

Mr. GREGG. Dr. Varmus, Dr. Shapiro, we certainly appreciate your taking the time to come and give us your thoughts, and of course Dr. Varmus left a wonderful legacy at NIH, something that he can take great pride in and the American people can take great pride in, and Dr. Zerhouni has done an extraordinary job of building on. I have said this before at hearings that we have had where we have had senior officials from our Federal health community, whether it is CDC or NIH or other scientific communities, we are so extraordinarily lucky as a Nation to have people of your ability willing to do public service. So we thank all three of you for your commitment to the national interest, but we especially thank Dr. Zerhouni for doing it today and Dr. Varmus for doing it in the past.

Why do we not hear from Dr. Varmus?

STATEMENT OF HAROLD VARMUS, PRESIDENT, MEMORIAL SLOAN-KETTERING CANCER CENTER, AND FORMER DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Mr. VARMUS. Thank you, Senator. Members of the committees, thank you very much for holding this important hearing. As you probably know, my own career is closely intertwined with the life of the NIH. I was trained there. My research was supported there. I was charged to lead it for several years, and now I am the Director of an NIH supported comprehensive cancer center in New York.

You have heard from Dr. Zerhouni about why NIH is universally revered, because of its discoveries, its diverse programs, its rigorous peer review in support of a variety of disciplines, and indeed NIH has been richly rewarded by bipartisan support from the Congress, budgetary increases, its ability to attract important leaders to bring young people into biomedical sciences, and the increases that have been accorded to the NIH have attracted more funding, more investment by industries and academic institutions to create a biomedical research enterprise in this country that is unparalleled in the world.

At the moment we are poised for even greater discoveries than you have heard about in the past as a result of many of the things that Dr. Zerhouni outlined for you, and this is needed because we

have an aging population. We are concerned about infectious diseases and bioterrorism. There is concern about health disparities and we have rising health costs in this country.

I am going to focus my remarks on a number of things that I believe can make a strong NIH even stronger, perhaps not perfect but stronger. I am going to group my brief remarks under three rubrics, three things that I am concerned about. First, a need to counter the deleterious effects of a continuous proliferation of institutes and centers of the units that make up the NIH. Second, my concern about the need to augment the authorities of the NIH Director, especially if we are going to achieve the kinds of ambitious programs that Dr. Zerhouni has outlined with his NIH Roadmap. Finally, I would like to say a few words briefly about the need to insulate, in a continuing way, NIH from partisan politics.

As I was leaving NIH I began to reflect about the effects of the continually increasing number of institutes at the NIH and my ability or the ability of my successors to effectively plan. The existence of many autonomous units at the NIH has had many advantages. It creates advocacy for the Institutes. It inspires independence and creative thinking, but it also makes planning at the NIH difficult. There are many independent leaders. It is difficult to go into a room and try to do strategic planning of the kind Dr. Zerhouni has managed to achieve, and as you have heard, trans-Institute efforts are essential in the new scientific environment where we have new kinds of research teams where we are bringing different disciplines together and trying to attack a deep understanding of how biological systems work.

If we were to make NIH again I believe we would make it differently, but I also acknowledge that what exists is very difficult to undo and we need to work within the system that we have. It has been successful, and one approaches any radical change with timidity appropriately.

I believe it would be useful to consider, as this joint committee contemplates the possibility of reform or reauthorization of the NIH, to contemplate ways to make the continued planning for the NIH a simpler and more effective process. For example, rather than try to confuse institutes to make a smaller number, to consider ways to make institutes that have similar objectives to work more effectively together in planning. For example, to use the institutes that address problems of the brain, of which there are now several, to work together in a cluster to plan new initiatives that would serve the interests of all of the people who are invested in the future of those institutes. There need to be ways to incentivize individuals who run those institutes to work together. The clusters can be used to promote administrative efficiencies, for example, to put intermural research programs together as has been achieved already in the neurosciences, and to allow administrative functions like personnel recruitment and purchasing to go on in a more efficient manner without a need to delegate those functions to a more centralized place.

I would also urge that the committee consider ways to create additional legislative barriers to the creation of new institutes and centers. New institutes and centers may on rare occasion be justi-

fied, but only after a more rigorous process of review than currently exists.

Creating a more effective planning mechanism by clustering institutes needs to be augmented by increasing the authority of the NIH Director. That means the NIH Director has to have more discretionary authority over appropriated budgets to carry out the kinds of plans you have heard about under the roadmap. The office of the Director is fairly slim with respect to scientist administrators, and the Director needs to have the authority to bring in more scientists, to work in a programmatic role in developing plans for the next steps in the roadmap. I believe it would be useful to authorize the formation of an executive committee of institute directors. Dr. Zerhouni has formed such a committee recently. I believe that could be done by choosing the heads of the clusters I proposed, and finally, in order to make his role as a planner more effective, I would suggest trying to normalize the status of the institutes and their directors, including reversing the traditional special privileges for institutes like the National Cancer Institute, and establishing terms of service that are clearly delineated with careful review before reappointment.

Finally, a few words about insulating NIH from partisan politics. I have long believed, and I think this committee agrees, that the selection of leaders and advisers for the NIH should be based on a knowledge of science and medicine and not on other factors that may reflect devotion of potential leaders and advisers to political activities and other favoritism. I would argue, and I have argued for many years, that the NIH Director should be appointed for a 6-year term with one option, to uncouple the appointment of the NIH Director from the electoral process, and I believe that the selection of all Institute Directors should be in accord with those general principles.

Mr. Chairmen and members of the committee, I appreciate the attention you are giving to the NIH. I have tried to keep my remarks brief so we can have time for discussion of these issues. Thank you very much.

[The prepared statement of Harold Varmus follows:]

PREPARED STATEMENT OF HAROLD VARMUS, PRESIDENT, MEMORIAL SLOAN-KETTERING CANCER CENTER, FORMER DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Mr. Chairmen and Members of the Committees: I appear here today as a former Director of the National Institutes of Health, a position I held from November, 1993, until the end of 1999. For the record, I am currently the President and CEO of the Memorial Sloan-Kettering Cancer Center in New York City; I received the Nobel Prize in Physiology or Medicine with Dr. J. Michael Bishop in 1989 for studies of cancer genes conducted over several years at the University of California, San Francisco; and I serve as Chairman of the Joint Steering Committee for Public Policy, a group representing several scientific societies.

I would like to begin with a few general observations about the NIH. I was trained as a scientist in the NIH intramural program, my research as a faculty member was supported by NIH grants, and I was given the privilege of leading the agency for over six years. Throughout my career and especially during my tenure as Director, I have unwaveringly admired the NIH as an effective force for good in the world, one created and fostered by our government, and thus a source of pride for all Americans. Of course, I am not alone in this opinion. The nearly universal reverence in which the NIH is held can be attributed to several things: its long history of discovery and progress against disease; its diverse programs in research, training, and communication of new knowledge; its essential contributions to the vitality of some of our greatest institutional resources, including our universities,

medical schools, and health-oriented industries; the multitude of disciplinary approaches with which it pursues better health through science; and the rigorous, competitive review processes it uses to evaluate and insure the high quality of all of its scientific activities.

For these reasons, our country's leaders have traditionally provided non-partisan and enthusiastic support for the budget and the programs of the NIH. This support has allowed the agency to retain the spirit and excellence of an intellectual community in the setting of government; to recruit many of the nation's best physicians and scientists to serve as Directors of Institutes and Centers (ICs), research administrators, and intramural laboratory personnel; and to perform in a fashion that justifies the hopes of the public and Congress and incites envy in many other countries around the world.

This enthusiasm for the NIH has helped to double its budget over the past five years and to create an environment in which expectations of future progress exceed its remarkable past achievements. The human genome and the genomes of many other organisms have been read at unanticipated speed; new and powerful tools for analysis of genes, cells, and intact organisms have been developed; many brilliant people have been trained in biology and related sciences; and academic institutions and major health-related industries have invested in new programs and buildings to exploit new knowledge and advance health. These opportunities are matched by obvious needs—those created by our aging population and the prospects of prolonged disability; by new concerns about emerging infectious diseases and bio-terrorism; by persistent, unacceptable levels of disease both in developing countries and among the less affluent citizens of our own; and by the rising costs of health care. For these reasons and others, we need a strong NIH, now more than ever, if we are to confront these issues and seize the recently created opportunities.

Although the NIH is a strong agency, it is not perfect. Because it is strong, we should undertake changes only with caution. But because we should also strive for perfection, it is appropriate that we consider what should be done to make the NIH even better than it is. To that end, I would like to describe three concrete proposals that I would recommend for your consideration in any legislative effort to reform or reauthorize the agency.

1) COUNTER THE DELETERIOUS EFFECTS OF IC PROLIFERATION.

The continued growth of the number of Institutes and Centers at the NIH has complicated management of the agency, especially at a time when scientific opportunities call for more coordination among IC's to develop large, expensive, multi-disciplinary programs.

During my final year as Director of the NIH, I began to discuss publicly my concerns about the detrimental effects of the growing numbers of ICs on the planning, management, and funding of NIH's scientific programs. I argued then and would argue now that the continued proliferation of NIH ICs—presently 27, with a recent birth rate of about five per decade—threatens the capacity of the agency to seize important opportunities and undermines the ability of the NIH Director to lead. While acknowledging that enthusiastic advocacy for many individual ICs has budgetary advantages for the NIH and that a significant reduction in their number would be politically difficult and even perilous, I proposed a path to a more manageable and efficient agency by fusing the existing institutes into five large units, led by Institute Directors, and a sixth unit, NIH Central, led by the NIH Director. (These ideas are explained more fully in an article in *Science* magazine, volume 291, pages 1903-1905, March 9, 2001; see <http://www.sciencemag.org/cgi/content/full/291/5510/1903>).

By the time the *Science* article appeared, Congress had directed the NIH to fund a National Research Council (NRC) study of the organization of the agency. (Dr. Harold Shapiro, who led that study, will review its findings and recommendations with you shortly; I would be pleased to comment on the study in response to questions.)

While I accept the NRC panel's conclusion that widespread fusion of IC's is impractical and perhaps inappropriate at this time, I continue to believe that steps must be taken to overcome the effects of Balkanization at the NIH on the planning and support of its scientific programs. There are several reasons for this. It is very difficult if not impossible to conduct strategic planning routinely with twenty seven IC Directors and several Deputy Directors of the NIH. Existing ICs vary greatly in the size of budget and staff, so that many cannot afford to carry out important programs entailing the clinical, multi-disciplinary, or technologically sophisticated research required by modern biomedical science. All ICs are understandably protective of existing resources and programs, making collective efforts difficult to initiate and

maintain, especially when budgetary increases are small, as seems likely to occur in the immediate years ahead.

What steps, short of IC fusions, can be taken? The current NIH Director, Elias Zerhouni, has recently completed a Herculean planning process to produce the just-announced NIH Road Map, a highly commendable blueprint for coordinated efforts designed to advance research broadly—through technology development, interdisciplinary training, and clinical research—and to which all ICs have pledged to contribute.

This remarkable process and outcome, however, will be difficult to achieve on a regular basis, especially if it requires participation by all ICs and if the ICs are not receiving budgetary increases that stimulate new initiatives.

I suggest a few steps to simplify inter-IC program planning and more efficient use of resources in the future. (a) Authorize the formation of “clusters” of ICs to propose and fund large, mutually beneficial initiatives. Although the composition of “clusters” should be subject to further discussion, one possible arrangement would conform to the five fusions I proposed earlier. (b) Provide financial incentives to ICs that develop and support coordinated efforts. (c) Use the “clusters” to achieve administrative efficiencies (e.g. in personnel management and procurement functions) and consolidate intramural research programs, in the fashion illustrated by the Neuroscience Initiative now underway on the NIH campus in Bethesda. (d) Establish legislative barriers to the creation of new ICs by requiring an extensive review process that guarantees a well-documented need for any newly authorized unit.

2) AUGMENT THE AUTHORITY OF THE NIH DIRECTOR.

As discussed in the preceding section, the NIH is organizationally complex and difficult to lead. Regardless of the methods that are used to control the number of ICs or to encourage collaboration among the ICs, it is time to consider measures that would provide the NIH Director with a stronger role in research planning. This would improve the management of the agency and make the Director’s job more attractive to prospective candidates.

I envision several ways to do this. (a) The NIH Director should be given greater discretionary authority over the appropriated budgets of the ICs, so that he or she can encourage the kinds of inter-IC or trans-IC programs mentioned above. (This could be achieved with a larger Discretionary Fund, an enhanced Transfer Authority, or a larger direct allocation to the Office of the Director, with the option of later transferring those funds to ICs for project management and continued support.) (b) The Office of the Director (OD) should be enlarged to include a cohort of scientist-administrators who could take a more active role in the planning of research programs in concert with the ICs. These individuals, who might be short-term government employees on leave from academic or industrial positions, would be responsible for proposing and initiating innovative research programs that would ultimately be transferred to one or more ICs. (c) The NIH Director would be authorized to assemble a small group of IC Directors to serve as an Executive Committee to plan new initiatives. The members of this group would ideally represent the thematic “clusters” of ICs described earlier and serve limited terms on the committee. (d) To optimize the planning process and avoid uncertainties in status, all ICs and their Directors would have the same authorities. To achieve this, the special privileges conferred upon the National Cancer Institute would need to be reversed by Congress, as also recommended by Dr. Shapiro’s panel. I also support the panel’s suggestion that IC Directors serve fixed terms, with the option of renewal.

3) INSULATE THE NIH FROM PARTISAN POLITICS.

NIH is a creation of government and is appropriately subject to oversight by the Executive and Congressional branches. But it works best when the selection of its leadership and advisors, the review of its operations, and the allocation of its fiscal support are based on performance, scientific needs, and public health objectives that can be endorsed by both parties.

Several means can be considered to re-enforce the traditional bipartisan approach to the NIH. I have long supported the idea that the NIH Director should be appointed for a fixed term of about six years, with the option of an additional term, to separate the selection of a Director from electoral politics. Second, the selection of the Director of the NCI should be conducted in the same manner as the selection of other IC Directors, in accord with my earlier recommendation that the NCI be treated like the other ICs. Third, Congress should endorse the concept that all the leaders of the NIH and the members of Advisory Councils and other review panels should be selected on the basis of their knowledge of the medical and scientific

issues faced by the NIH and its components, not as rewards for political views or favors.

In closing, I would like to thank the members of this Joint Committee for undertaking a careful review of the NIH and for conducting this hearing. As I have emphasized, the NIH is a remarkable agency, and it offers an unusual opportunity for constructive oversight. Any beneficial actions will be applauded widely by a public eager for the government's support of advances against disease.

I would be pleased to try to answer any questions you might have.

H22

Copyright 1999 Information Access Company,

a Thomson Corporation Company;

ASAP

Copyright 1999 American Association for the Advancement of
Science
Science

September 10, 1999

SECTION: No. 5434, Vol. 285; Pg. 1654 ; ISSN: 0036-8075

IAC-ACC-NO: 55882139

LENGTH: 3052 words

HEADLINE: View From the Top of a Biomedical Empire; the National Institutes of Health; Interview

BYLINE: MARSHALL, ELIOT

BODY:

As politicians square off for another fight over social spending, Harold Varmus discusses how NIH has achieved exceptional growth recently, and how its organization could be improved in the future

Six years ago, Harold Varmus arrived in Bethesda, Maryland, a very green new director of the National Institutes of Health (NIH). Although he had achieved distinction as a basic scientist--sharing a Nobel Prize in 1989 for research on genes that cause cancer--his administrative skills were largely untested. He had never run an organization bigger than his 20-person lab at the University of California, San Francisco. The challenges would be immense even for a seasoned administrator. Bureaucratic and fraught with internecine rivalries, NIH is the world's largest basic research center. In 1993, when Varmus took over, it employed more than 17,000 people and boasted a budget of \$11 billion--and it was clearly in distress.

The NIH research hospital, the Clinical Center, was falling apart. The building had long been slated for replacement, but Congress was wary of releasing the hundreds of millions of dollars the new construction would cost. Hampered by a tight budget, NIH was pinching its funds to support extramural grants. At the same time, many of NIH's best and brightest intramural scientists were fleeing the Bethesda campus for jobs in academe and industry. Varmus himself and two colleagues wrote in 1993 that they were concerned about "outmoded procedures" at NIH and threats to the "long-term viability" of U.S. biomedical research (Science, 22 January 1993, p. 444). Given the many problems, observers wondered whether it made sense to tap Varmus, a devotee of "pure research" and a novice in politics, to lead NIH in this difficult period.

Today, the record suggests that such worries were exaggerated. NIH's reconstructed Clinical Center is on course for completion in 2002. NIH is enjoying in 1999 not only the largest federal appropriation ever, but also the largest 1-year increase--a boost of \$2 billion, for a current budget of \$15.6 billion. The overall "success rate" for extramural grants--the percentage of approved investigator-initiated applications that get funded--is as high as it has ever been, heading toward 33% this year, up from 23.6% in 1993. Many small but destructive "brush fires," as Varmus called them in an interview with Science in 1993--controversies over employment discrimination, sexual harassment, scientific misconduct--seem to have fizzled out. New leaders have taken over key posts, like the long-vacant directorship of the National Institute of Mental Health, now filled by former Harvard professor Steven Hyman. Whether all this makes Varmus the Clinton Administration's "most effective backstairs politician," as a New Yorker article called him in June, or the lucky heir to favorable politics is debatable. But the record suggests that at least part of the credit is his.

Science September 10, 1999

At a meeting last month, Science invited Varmus to reflect on what he sees as his major accomplishments at NIH, his disappointments, and some ideas about NIH's future. A condensed version of his conversation with Science's news and editorial staff, edited for clarity and concision, follows.

Reviewing NIH's budget, Varmus argues that his decision to seek modest growth in the mid-1990s established the agency's credibility. This, he says, paid off handsomely in larger appropriations when the U.S. budget deficit began to fade in 1999. He's also proud of his record in recruiting new scientists to NIH, including 12 institute directors. His concerns include the fragmentation of NIH's administrative structure, now divided into 25 major institutes and offices. He also regrets that the NIH director does not have adequate authority to launch major scientific initiatives on his own. And he wishes his efforts to rationalize the scientific jurisdictions of the review panels that rank grant applications for NIH had moved along more rapidly.

The only subject Varmus placed off limits was his own future. He declined to talk about the rumor that he is being considered for the presidency of the Memorial Sloan-Kettering Cancer Center in New York City. When asked about his plans, Varmus would only say, as he has many times before, that his tenure is determined by the president. However, he also said in the past that he considered a term of "about 6 years" about right for NIH director.

Q: NIH got a 2% increase in the president's 2000 budget. Are you expecting more?

A: I think it's not unreasonable to envision an increase of approximately 10%. But at this point, it is very dangerous to make that kind of prediction.... It's obvious that the Committees that are responsible for paying us are short of cash.... We don't want to see social programs and educational programs that are supported by those committees suffer just to pay us.... I think the mood of the country is to support science, and when push comes to shove, there will be some kind of omnibus, emergency appropriation that allows NIH to be reasonably supported, and, hopefully, other science as well.

Q: Is there an upper limit on NIH's budget in your mind?

A: If we turn our attention to neglected areas [undersupported grants, infrastructure, instrumentation] and exploit new opportunities ... we would accommodate very well a doubling over a period of about 5 years.... What concerns me more is the structure of NIH. NIH has prospered in part because of the strong advocacy we've enjoyed from members of Congress and the public.... On the other hand, this has been responsible for making an institution that has become much more complex over the years.... It makes me think that at some point there will have to be a moment [when everyone says]: Whoa, let's have a look at how NIH is organized. Let's try to simplify that organization, make it more rational, more manageable.

Q: What would the ideal NIH look like?

A: The proposal I threw out for the sake of argument [at Jackson Laboratory in Bar Harbor, Maine] was one in which there were roughly six institutes, of roughly comparable size [embracing internal medicine, cancer, environment and infectious diseases, human development and aging, brain and behavior, and an NIH central]. The central component would be the home of the NIH director and would include the clinical center and the review groups. It would also undertake special initiatives that do not become part of the commitment base but are expected to come and go. And it would provide also a little more scientific authority for the director. One of the things we have to be concerned about in the future is what kind of authority and leadership the NIH director can command. So much goes on in categorical institutes that there is a danger of having ... very little for the NIH director to do but maintain conformance with broad policy issues....

Q: How would that structure improve things?

A: It would allow more flexibility in budget formulation. Priority setting wouldn't be quite as focused on what percentage increase each institute gets each year. Movement between fields would occur more effectively.

Q: Is the NIH director's authority more limited than you expected?

A: It's mixed.... There is inevitably a kind of tension, because the institutes have independent authorities and independent budgets. I certainly have had the sense that it is difficult to follow through on scientific initiatives that I try

Science September 10, 1999

to get under way myself. A good example might be malaria, where I've tried to push funding and develop international consortia.... It is a slightly frustrating experience. Without a laboratory of my own I think I would feel pretty starved for scientific conversation.

Q: What accomplishments have given you the most satisfaction?

A: One is surviving a period in which the budget prospects looked very bleak. There was much amusement about my early speeches in which I emphasized living within a "steady state." But I do think that was a useful position to take. It was realistic. I think it gave NIH credibility. We were willing to say: Look, the budget situation is tough; if you can give us some reassurance of stability, that we're not going to get cut, we will try to live within reasonable means. I think that was a smart approach. With that reasonably high level of credibility within Congress and the Administration, we prospered when the economic status of the country improved.

Second, I would point to recruitments. I think I've been incredibly successful, and lucky, in not just attracting some good talent, but imbuing the scientific community with a sense that public service is something that people should look forward to in their career. A good scientist should say at some point, there is an opportunity here to pay back the federal government. And you can have a tenure in public office that is enjoyable, not inconsistent with thinking about science, and not even inconsistent with practicing some science.... All those things have affected my ability to recruit institute directors, scientific directors, lab chiefs.... We have had some colossal successes.... The spirit in Bethesda is quite different.

We've also had success in trying to cope with the erosion of support for clinical research. One of the biggest issues that faced me when I came to NIH was the dilapidated condition of the clinical center, a sense that clinical research had had its day. ... Well, as you can see, we are building a wonderful new building. Clinical research has been given important lifts from new training that affects the extramural community and from a number of programs we've started intramurally.

Q: Is it healthy for a person to be director of an institute for 20 years?

A: Not necessarily. [But] it may not be wrong. One of the things that I've done that may not have gotten as much attention as it should is that I've instituted 5-year reviews. I have a group of five or six people who go out and solicit opinions from a very broad swath of people who are affected by the institute and then I and the chair of the committee get back to the institute director the opinions that have been collected. Those opinions have made a difference.... My personal feeling is that institute directorships should not be considered lifetime entitlements. The most healthy situation would be for people to come and do those jobs for 5 or 10 or 12 years. Less than 5 years is probably too short a time to have an imprint. As in any way of life, change is usually a good thing.

Q: How substantial are the changes' you've made in peer review?

A: We have made some big improvements. Looking back on what I thought was important 5 or 6 years ago, there's no doubt that we've streamlined peer review in at least two important ways. First, by doing triage. On the whole, in 98% of the cases, it's been a very successful enterprise. Second, by implementing a modular grant formula so that you don't have to be so precise about your budget. You can submit your budget in \$25,000 increments. That's clearly the wave of the future. It's essentially going to be implemented across the board. We've had some improvement in setting criteria for review, especially in putting innovation--novelty--into the review process.... We've made a limited effort to incorporate the public into the review process. I started with a degree of skepticism. But in certain areas--for example, clinical trials--it's quite appropriate to have people who represent health care consumers....

Q: What about unfinished work?

A: There are a couple of areas where I think things have happened more slowly. Reorganizing the peer review study sections. That's now coming along. [National Academy of Sciences president] Bruce Alberts and his colleagues are doing the "boundaries report" [remapping the scientific jurisdiction of panels] and have published a policy forum in Science (Science, 30 July, p. 666). I think we're on the right track.... The other thing that's been disappointing to me is electronic review of grant applications. I thought we could get electronic submission and review into practice much more quickly than we have.

Q: The Administration's computing initiative has fallen flat with Republicans on the Hill. Are you concerned that the NIH computing initiative could have similar problems?

A: No ... I think we are prepared to make the case, and would be listened to by our appropriators, that computer science is undersupported, and that the flood of new genomic data and from imaging and other new fields of biological science demand personnel and software and hardware that we don't have. The competition from industry for talent and the undervaluing of computer scientists by our grantee institutions are problems that we need to rectify. ... This requires at least bidisciplinary training in computer science and biology.... I'm reluctant to say, here is a request for \$100 million. What we are saying is that [the computing initiative] is a consortium of many institutes--at least 10, maybe 15 new centers--to train and support computer scientists who know biology. It's a little bit here, a little bit there. There isn't going to be one package that can be cut.

Q: The Defense Advanced Research Projects Agency (DARPA) gives program chiefs great latitude to create new initiatives. People suggest that NIH and the National Science Foundation should adopt a DARPA-like philosophy. What do you think?

A: I've been advocating that myself the last few years.... The initiatives we're thinking about are much more expensive than the traditional grant and would be undertaken by teams. One novel effort is being made by the National Institute of General Medical Sciences where [director] Marvin Cassman has come up with "glue grants" in which investigators who work on a single problem--in one case G proteins--form a complex network and ask for money to support the whole endeavor. This group then identifies common needs and asks for money to help support building databases, getting certain structures done.

Q: NIH plans to distribute scientific articles through PubMed Central. Suppose publishers went to Congress and complained that NIH is trampling on private enterprise: How would you explain the policy?

A: We support the research; we want the research findings to be available to our communities in the easiest, most searchable way. If technology has given us the tools to promote the dissemination of the information, I think we should use them. ... We have an opportunity here to put anybody who has a desktop computer in contact any time day or night with the current scientific literature. That seems to me a very important public service.

Q: Early this year, NIH enunciated a controversial policy of supporting the research use but not the derivation of human embryonic stem cells. If you could do it over, would you handle that policy any differently?

A: No ... I solicited a legal opinion [from the Department of Health and Human Services] on what we could do legally. It is not my view necessarily of what should happen. ... I think we should be supporting research with embryonic stem cells. I also think we should be supporting research on the derivation of stem cells from spare embryos. It may not be politically appropriate to do that at this point. But that is my view, and it is a consistent view.... I think any ethical evaluation has to take into account the consequences of not doing research that would benefit living people who have serious diseases now or in the future. I take that responsibility very seriously.

Q: How useful is the Council of Public Representatives (COPR, a consumer advisory group created this year at Congress urging)?

A: That's hard to evaluate, because it has only met once.... When we advertised the positions on the council, we got hundreds of applications from interesting and energetic people. Rather than say you're in, you're out, I said you're all in. Just 20 of you are the council and the rest of you are COPR associates. And I would like to build on that cadre.... They are our advocates out there in the community, and sometimes our critics. That's all right. I would like to expand the COPR associates to thousands, hundreds of thousands. Why not? It's a way of building an advocacy community that's really paying attention to the details.

Q: On AIDS research.' The field seems to have plateaued. Is it being funded well enough?

A: I would say it's not a static situation. We are increasing our investment in vaccine development tremendously. And that also involves a very serious investment in immunology. I think we have here a novel problem in immune

response, but one that will be applicable to vaccines against tuberculosis, malaria, hepatitis C, other organisms that coexist with a host even though there is a partial immune response. Secondly, we are making a greater effort in behavioral research in AIDS. Right now the emphasis has got to be on prevention.... At the same time we are recognizing that there are serious deficiencies in even the quite good drugs that have been developed. There is much more interest in drug design than there was a few years ago, in understanding the nature of viral resistance to drugs and how drug combinations work together. It is a changing field; it's not static at all ... although the AIDS budget is no longer rising faster than the overall NIH budget.

Q: How long will you stay in this job?

A: I'm a presidential appointee....

Q: Any regrets about what you were not able to do because you were in Washington?

A: My [scientific] productivity probably could have been greater. Actually I've had a very good lab experience.... I would rather have a little more time to read scientific literature.

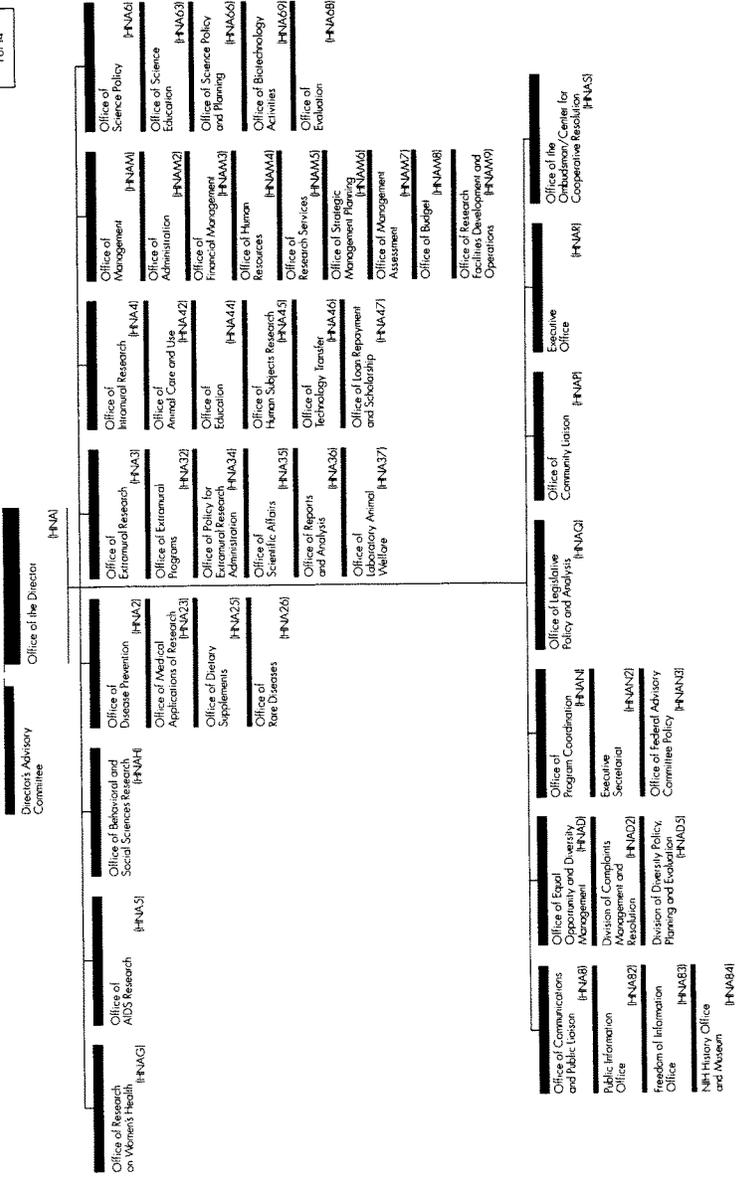
Q: Has it affected your physical training?

A: Washington has been great for my physical training, because I live 12 miles from NIH. I ride [my bike] to work almost every day. I've also taken up sculling. The ideal day begins for me with a ride to the boathouse, about 4 miles, then I row for 45 minutes, then I ride my bike out to [NIH], then ride home after work through Rock Creek Park. That's a beautiful day.

IAC-CREATE-DATE: September 11, 2000

LOAD-DATE: September 12, 2000

Office of the Director, NIH



Mr. GREGG. Thank you, doctor. I think those are very helpful thoughts, especially the three major points you are making.

It is a great pleasure to be joined by Dr. Shapiro, who is kind enough to chair the IOM committee on NIH organization, looking at it from the outside, as a professor emeritus of significant reputation from a small struggling school somewhere in New Jersey, which those of us from New Hampshire hardly admit exists. We look forward to Dr. Shapiro's thoughts.

STATEMENT OF HAROLD SHAPIRO, CHAIR, COMMITTEE ON THE ORGANIZATIONAL STRUCTURE OF THE NATIONAL INSTITUTES OF HEALTH, PRESIDENT EMERITUS AND PROFESSOR OF ECONOMICS AND PUBLIC AFFAIRS, DEPARTMENT OF ECONOMICS AND WOODROW WILSON SCHOOL OF PUBLIC AND INTERNATIONAL AFFAIRS, PRINCETON UNIVERSITY

Mr. SHAPIRO. Thank you, Mr. Chairman.

Mr. Chairman and distinguished members of the committee, I am pleased and honored to be here to participate in these important hearings. As the Chairman just indicated, I am President Emeritus both of the University of Michigan and Princeton University and currently serving as Professor of Economics and Public Affairs at Princeton. I mention this since I feel slightly embarrassed with the word "doctor" here in view of dealing with NIH where I have real doctors sitting on my right. I hope no one will get sick while I am here. If you do, I am not the kind of doctor you want to put your trust in.

I am pleased to be here, and I guess more importantly than my previous positions as President of Michigan and Princeton, is that, as the Chairman indicated, serve as Chair of the committee appointed by the National Research Council, which issued the report entitled "Enhancing the Vitality of the National Institutes of Health, Organizational Change to Meet New Challenges." I have already submitted my full testimony to the committee and its staff along with a copy of the committee's report. I hope, Mr. Chairman, you will think it appropriate to include these latter documents in the committee's record, since in the brief time I want to take this morning I can only give a brief summary of the committee's key observations and recommendations.

Let me begin by making two preliminary observations. First I want to pay tribute to all of those who have made NIH a success over the many decades of its existence. This includes Members of Congress, the administration, health advocacy groups, and of course a virtual army of dedicated biomedical scientists. I want to pay special tribute to the many contributions Dr. Varmus has made, not only to biomedical sciences but to NIH, and similarly to Dr. Zerhouni, whose current plans for NIH at least strike me as extraordinarily innovative, helpful, and as I will say in a few moments, in many ways very consistent with the kinds of ideas that our committee has recommended.

The second preliminary comment I want to make, it is important I think that we all understand and reflect, as has already I guess been referred to in Dr. Varmus' and Dr. Zerhouni's remarks, that NIH is currently structured as a loosely organized federation of

units, particular institutes and centers, that has by design emphasized a very decentralized mode of operation. It has been structured in this manner on the grounds of the most creative ideas that bubble up from individual investigators who are closer to their science and to the nature of our evolving health concerns.

The question before our committee, however, was that whether given the changes occurring in the scientific frontier and our evolving health concerns as articulated by Dr. Zerhouni just a few moments ago, whether or not in these circumstances there were compelling reasons to change this loosely federated structure and/or other standard modes of operation at NIH.

It is important to say that NIH, as we all recognize, is an extraordinary dynamic organization, but we still have to ask the question whether its basic underlying structure has now become, at least in part, an impediment to future progress. I think that was one of the implications of Dr. Zerhouni's remarks as well as what Dr. Varmus has said. It is certainly a conclusion of our committee that some change was necessary. Some kind of important evolution, development of mixed strategies to achieve the objectives that NIH has before us would vastly improve its capacity to meet the challenges that are ahead of us.

Perhaps the two most important conclusions we reached were that it was our judgment, first it was our judgment, that while the core strategies that have served NIH so well for the last decades should remain the bedrock of NIH operations, despite the fact that that should remain the bedrock, new and complementary strategies are needed if we are to enjoy the greatest benefits from our growing investments in biomedical research and training. Second, that the widespread consolidation of existing institutes and centers, while certainly a very coherent and attractive idea to think about, it was in our judgment not the best strategy to deploy at this time. In short, while we believe that some important changes are necessary, we believe also that there are better alternatives to the widespread consolidation of existing units. We identified a number of new but what we believe are essential organizational characteristics that should be incorporated into NIH's organizational structure as quickly as possible. Our report provides detailed recommendations in this respect.

In summary, NIH now needs, at least in the judgment of our committee, a number of enhanced capacities to meet the challenges that are before us. First it needs an enhanced capacity for NIH as a whole to both demonstrate strategic intent and respond quickly and effectively to new challenges through the adoption of what we term trans-NIH initiatives.

Second, it needs an enhanced capacity to take greater and more coherent leadership and responsibility in the arena of clinical research, as Dr. Zerhouni himself mentioned just a few moments ago.

Third, we need an enhanced capacity to insist on the adoption of best practices throughout the organization. There has been an extraordinary number of very creative leaders of the various institutes over time, who have developed really very innovative ways to deal with the challenges before the Institute. It is our judgment, however, that these best practices often did not survive their leadership and certainly did not spread to other institutes. NIH needs

an enhanced capacity to manage the research portfolio of NIH as a whole, as Dr. Zerhouni mentioned just at the conclusion of his remarks, and in particular, to make their research portfolio somewhat less risk adverse than it is. They need an enhanced capacity to provide for accountability to NIH's various constituencies and to ensure appropriate levels of turnover and leadership at all levels.

Finally, an enhanced capacity to demonstrate that its current organizational structure is not frozen in place, and the availability of a thoughtful public process to consider any proposals for the addition, subtraction and merger of institutes and centers. I take this latter recommendation as consistent with what Dr. Varmus noted just a few moments ago, to have some type of open public process and thoughtful consideration before institutes and/or centers are created, closed or merged or any other change of that nature.

In order to achieve these objectives—and this will be my final remark because I want to leave as much time as possible for questions—in order to achieve these objectives, it was our conclusion, again, quite similar to what Dr. Varmus mentioned a few moments ago and I believe what Dr. Zerhouni was referring to, that Congress would have to take action to increase significantly the authority, responsibility and accountability of the Director of NIH in a manner which we have detailed in our report. I will be glad to respond to particular questions about that. Indeed, important institutional change is necessary either to achieve the new objectives our committee has set out and Dr. Varmus and Dr. Zerhouni have also articulated, but indeed even to sustain the important initiatives that Dr. Zerhouni described so carefully just a few moments ago, the capacity to sustain those over time, in my view, and I believe in our committee's view, is just not attainable without major change in the authority, responsibility and accountability of the NIH Director.

So, Chairman, thank you very much. I hope these brief remarks were helpful, and I will be glad to answer any questions you may have.

[The prepared statement of Harold Shapiro follows:]

PREPARED STATEMENT OF HAROLD SHAPIRO, CHAIRMAN, COMMITTEE ON THE ORGANIZATIONAL STRUCTURE OF NIH, NATIONAL RESEARCH COUNCIL/NATIONAL ACADEMY OF SCIENCES AND PROFESSOR OF ECONOMICS AND PUBLIC AFFAIRS, PRINCETON UNIVERSITY

Good morning, Mr. Chairman and members of the House and Senate Committees. My name is Harold Shapiro and I am currently Professor of Economics and Public Affairs in the Department of Economics and the Woodrow Wilson School of Public and International Affairs of Princeton University. I serve as Chair of the National Research Council's Committee on the Organizational Structure of NIH, and I would like to thank the Congressional Committees for this opportunity to discuss the recommendations in our report. The Research Council is the operating arm of the National Academy of Sciences, National Academy of Engineering, and Institute of Medicine.

The Committee on the Organizational Structure of NIH was assembled by the Academies in response to a Congressional request for a study to examine whether, given the many changes in both our health concerns and the nature of the scientific frontier the organization and structure of NIH are optimally configured to most effectively pursue its mission in research and training given the realities of the Twenty-first Century. The Congressional request was a wise acknowledgement that the world we live in is changing rapidly, with science, evolving health concerns and the structure of the institutional mechanisms supporting science and advanced research training being among the most fast-paced areas of change. All enterprises, be they

large or small, need to be able to adapt to change and must continually consider new ways to meet the challenges of the future if they are to remain effective. The greatest risk to successful organizations is the danger of becoming entrenched in the very things that have made them successful at the expense of needed adaptability.

The composition of the Committee on the Organizational Structure of the National Institutes of Health was designed to ensure that the views of the basic science, clinical medicine, and health advocacy communities were all adequately represented. In addition, the Committee has members who are experienced in the management of large and complex organizations, including a former NIH director, two former NIH institute directors, two persons with backgrounds in senior management of major industrial entities, and a specialist in organizational issues. Several Committee members also had considerable experience in government operations.

The Committee held six two-day meetings over the ten months between July 2002 and April 2003. At its initial meetings, past and present representatives of NIH, Congress, voluntary health groups, scientific and professional societies, and industry were invited to provide perspectives on the issues before the Committee. The Committee met publicly with the current NIH director as well as several former directors, and also heard presentations from or interviewed staff in the NIH Director's Office and the directors of 18 institutes or centers. Prior reports and relevant literature were reviewed. Finally, several Committee members conducted town meetings at their home institutions and elsewhere, inviting scientists, administrators, and students to tell us their views. Thus, the Committee was able to hear, consider, and discuss a diverse range of facts and opinions about the organizational structure of NIH. The Committee completed and released its final report, "Enhancing the Vitality of the National Institutes of Health: Organizational Change to Meet New Challenges", in late July, and I would be happy to submit a copy of the report for the record along with my testimony.

The strong system of federal support for US science and technology has produced five decades of discovery and innovation that have literally changed the way we live and yielded great social dividends for the citizens of our country and beyond. In many ways, NIH is unsurpassed among the array of federal agencies that support scientific research, providing 80% of the federal government's contribution to biomedical research. From a humble beginning in the late 19th century as a one room laboratory with a \$300 government allocation, NIH has grown into a \$27 billion per year organization that justifiably enjoys enormous public and Congressional support. NIH's success in its mission of science in pursuit of fundamental knowledge and the application of that knowledge to extending healthy life and reducing the burdens of illness and disability has been enormous. NIH's investment in biomedical research has helped produce remarkable results in terms of declining rates of disease, longer life expectancy, reduced infant mortality, and improved quality of life. All those who have played a role in making NIH such a success over the years, including many of you on the House and Senate Committees that have organized this hearing, have earned the gratitude of current and future generations.

Although not explicitly articulated in the charge to our committee, it has been suggested that one key underlying motivation for Congress's request for our study is the concern that the large number of institutes and centers at NIH, which now total 27, has fragmented the agency and made it too unwieldy to address effectively the research and training challenges now emerging on the biomedical frontier. While extremely mindful of this concern we approached our task in a considerably more general fashion by asking ourselves what organizational changes, including the widespread consolidation of existing units, would be most likely to enhance the vitality of NIH and increase its flexibility and responsiveness. Our deliberations were also influenced by the fact that there is much more to assessing an organization's effectiveness than reflecting on the number of units on its organization chart, and we assessed, therefore not only the organizational configuration of NIH, but also the key processes, internal cultures and authorities that all play key roles in determining the quality, creativity and imagination that might characterize NIH-wide decision making.

Although the Committee spent a significant amount of time at every one of its six meetings debating the merits of various proposals to drastically consolidate NIH's institutes into a far smaller number of entities, in the end we came to the consensus view that the widespread consolidation of institutes and centers is not the next best organizational step for NIH to undertake, as the expected benefits of such a strategy would in our judgment be less than the expected costs involved. What does the Committee mean by "costs"? Any thoughtful major reorganization would necessitate a lengthy and complex information gathering and decision making process that would include numerous hearings involving members of Congress and their staff and a wide variety of interests in the various health advocacy and scientific

communities. Our discussions, correspondence and meetings made it quite clear that there would be very little agreement among these communities on what the right way to reorganize NIH is, and there would probably be dozens of conflicting ideas in play and few clear avenues for narrowing these down. Moreover we believe that these discussions and negotiations would be long and contentious and with a quite uncertain outcome. More importantly, the Committee is firmly convinced that many of the goals that might be achieved through large-scale consolidation of institutes, such as giving NIH a greater capacity to respond to new challenges, enabling NIH to respond as a whole to critical strategic initiatives, making NIH's research portfolio less risk averse, and launching a major reorganization of its clinical research activities could be achieved more rapidly and effectively through other changes dealing with authorities, culture and processes.

NIH has developed as a loose federation of units that operate largely independently of both each other and the Director. Moreover the individual institutes and centers have operated in a very decentralized manner reflecting the view that the best ideas flow up from the laboratories of individual scientists. This policy has demonstrated its power and we believe that this approach should remain the bedrock of NIH's program. However, given the changing environment in the biomedical sciences and the nature of our evolving health concerns we believe that this basic strategy needs to be supplemented by a series of new approaches. One reason that NIH has the complex federated structure it has today is that in the past, the response to new problems or opportunities has often been to create new organizational entities, such as the Office of AIDS Research or the National Human Genome Research Institute, to deal with them. If, however, there were other ways for the NIH leadership to redirect or reconfigure resources, this would obviate the need to create new entities as the only institutional response. *Our Committee came to believe strongly that the creation of new organizational entities at NIH is not the best or most effective means of ensuring that a problem receives adequate attention in the biomedical research portfolio, and that NIH needs a better mechanism for responding.* Instead, the Committee recommends that NIH begin to use a process for identifying major crosscutting, or "trans-NIH" (for research that cuts across the purview of several, if not all, the institutes and centers), research initiatives via periodic" perhaps every two years "strategic planning that engages all of NIH and is open to input from the public as well as the scientific community. Such research is especially important given the increasingly interdisciplinary nature of science today. Although individual institutes do mount new initiatives on their own, these are usually directed primarily at the interests of their own constituencies and rarely closely coordinated with the work of other institutes. An example of the kind of area that would make a good focus for such a trans-NIH initiative is proteomics, for which the institutes could benefit from the development of common tools and approaches if they worked closely together. Another is the study of obesity, which is rapidly becoming a major national health problem. Because obesity is associated with a variety of health problems that cut across the concerns of many institutes, such as heart disease, diabetes, and arthritis, the responsibility for dealing with it does not fall clearly into the portfolio of any one institute. As a result, it is difficult for NIH to demonstrate that there is any systematic and coordinated approach to addressing the causes and consequences of obesity. The same would be true in many other areas. In the absence of such a demonstration, a variety of health interest groups are calling for the creation of a National Institute on Obesity. *But the Committee believes that a trans-NIH strategic initiative to address such problems often would be a far better solution than the creation of a new institute or center.*

For this to become workable, however, Congress must give the NIH Director more authority. The Director currently has very little ability to insist that "best practices" spread quickly across all units, or to reconfigure NIH's resources or mobilize funding for new initiatives except at a very small scale. We believe that Congress should amend NIH's authorizing legislation to formally charge the NIH Director to conduct such trans-NIH strategic planning, and that the Director should be able to require the institutes and centers to commit a certain percentage of their budgets for their participation in the trans-NIH research identified through the strategic planning process. The individual Institutes, however, would retain the authority to decide just which of the trans-NIH initiatives they wish to participate in. We suggest that five percent of each institute's and center's budget should be invested the first year of the program, but that number could grow to 10 percent or higher within four to five years. While this may initially sound like a proposal to cut institute budgets by diverting funds elsewhere, our thinking is that an open and inclusive strategic planning process in which all institutes participate would generate enough excellent ideas for trans-NIH initiatives that each institute would readily be able to identify one or more of these ideas that would be of relevance to their own interests and

portfolios. Thus, we believe that participation in one or more trans-NIH initiatives would enhance the research portfolio of all the institutes. To underline these points we are not suggesting that any funds be moved among institutes or to the Director's Office for the trans-NIH initiatives. Rather the percentage of funding to be invested in any given year, for example, five percent, of an institute's budget would be held in "escrow" until the Director certifies the acceptability of that institute's plans for participation in the chosen strategic initiatives.

I would like to comment also on the committee's recommendations that affect the Director's Office. First, the Committee recommends that a special projects program be established in the NIH director's office to fund risky, cutting-edge research that offers high potential payoffs in terms of scientific breakthroughs, and new treatments. We imagine this program being patterned after the Defense Advanced Research Projects Agency, or DARPA, in the Department of Defense. The NIH director's special projects office could help overcome some of the hindrances to the pursuit of highly innovative, or "risky," research that exist now. High-risk proposals, which may have the potential to produce quantum leaps in discovery, do not fare well in the review system and are rarely funded by NIH because they are often not backed up with extensive preliminary data. This is because the review system is driven toward conservatism by a desire to maximize results in the face of limited funding, large numbers of competing investigators, and considerations of accountability and equity. Another unintended effect of this conservatism is a bias against young investigators. The peer review system at NIH has served this country very well and should continue to do so over the next decades. However, it is our view that NIH also needs a complementary strategy that would help overcome the inherently conservative bias of the existing peer review framework. The committee believes that the new program would succeed best if it were located in the NIH director's office and were funded with new money. We recommend that Congress provide 100 million dollars for the director's special projects program in the first year, with the budget eventually growing to as much as one billion dollars a year.

Second, the Committee does not believe that the Operations budget for the Office of the Director (OD) is adequate. Although the overall OD budget may look substantial, most of it is earmarked for the various program offices that have been created to address particular topics, such as the Office of Research on Women's Health and the Office of AIDS Research. When a problem that affects NIH as a whole arises, the Director frequently has to go "hat in hand" to beg for contributions of funds from the institutes to respond, which, to say the least, is highly inefficient and not guaranteed to produce satisfactory results.

Turning back now to the number of institutes and centers, the Committee made one other very important recommendation. Although the committee did not believe that a wholesale consolidation is called for at this time, we do not believe that NIH's organizational structure should remain frozen. As the pace and nature of scientific discovery continues to quickly advance, and as our health concerns evolve, some institutes and centers will become more relevant than others. Therefore, we recommend that a formal public process be established for reviewing whether institutes and centers should be added, eliminated, or combined with others. This process should involve Congress, the scientific community, patient advocacy groups, and the NIH Council of Public Representatives and other NIH advisory committees. Although Congress would still need to vote on whether or not to change the number of institutes, this formal review process could be initiated by the NIH director. We would also hope that Congress would not take action on proposals to create, combine, or eliminate institutes or centers until there has been an opportunity for this process to play out and for the NIH Director to thoroughly consider its results and make his or her recommendation to Congress.

The Committee suggests that this public process should be used first to review two mergers favored by the committee. First, we believe that the National Institute on Drug Abuse should be combined with the National Institute on Alcohol Abuse and Alcoholism. These two groups share a similar mission and the causes of, as well as the treatment for, drug- and alcohol-abuse are likewise similar. Second, we think that the National Institute of General Medical Sciences should merge with the National Human Genome Research Institute. Now that the genome institute has successfully completed its namesake mission, it makes sense for it to rejoin the general medical sciences institute, from which it originated and which has a lead role in funding basic biomedical research. Moreover, the cultures of these two units might very well invigorate each other. Again, I would stress that although the Committee saw merit in these proposed consolidations, it is our recommendation that no action be taken until the public process we propose has been conducted.

On the other hand, because of unusually persuasive arguments and exceptional needs, the Committee did recommend that one reorganization be acted upon imme-

diately. We strongly believe that several intramural and extramural clinical research programs should be combined into a new entity that replaces the National Center for Research Resources and transforms it into a National Center for Clinical Research and Research Resources. The importance of clinical research in translating the knowledge produced by basic science into improved health cannot be overstated, but this translation is today hampered by high costs, regulatory uncertainties, incompatible databases, and a shortage of qualified investigators and willing patient participants. We believe that putting clinical research under this new umbrella will trigger new collaboration and data sharing among researchers from different fields. The recommended consolidation of clinical research under one roof builds upon the recommendations made by other prestigious groups and leaders in recent years that NIH needs to do more to facilitate the translation of basic research into cures and treatments.

As I said earlier, we identified several other organizational and administrative changes and mechanisms that could, as the title of our report suggests, enhance the vitality of NIH. Let me touch on a few of them.

To begin with, we looked at the length of terms served by the director and the heads of the institutes and centers. We decided that the NIH director should serve a six-year term unless removed sooner by the president. Having a term of six years may—like that for the director of the National Science Foundation—allow the director to transcend changes in administration. Re-appointment to a second and final six-year term should be contingent on a performance review by outside experts and the recommendation of the Secretary of Health and Human Services.

Directors of the institutes and centers should be appointed to five-year terms with the option for a second, and final, five-year term. And authority to hire and fire these directors should be transferred from the HHS secretary to the NIH director. We believe that the service terms we've recommended will provide stability as well as fresh ideas to NIH.

We also took a second look at the special status of the National Cancer Institute. The NCI director is appointed by the president and NCI's budget—about 17 percent of the overall NIH budget—bypasses the desk of the NIH director and is completely outside the director's influence. The Committee suggests that Congress reexamine the appropriateness of the special status given to NCI.

With regard to the effort by HHS to centralize or outsource administrative functions, known as the "One HHS" initiative, the committee felt strongly that, while eliminating government inefficiency is always a worthwhile goal, the "One HHS" initiative may fail to appreciate the strong link between administrative functions at NIH, such as personnel recruitment and aspects of grants management, and the larger scientific enterprise. Any move to centralize or outsource these functions should be carefully reviewed first to determine how it may affect NIH's special mission of scientific and medical discovery.

We also noted that the Research Management and Support budgets, which pay for administrative and facilities management costs at the institutes and centers, have barely grown in the past decade despite the huge increases in the overall NIH budget. As a consequence, NIH is left with inadequate funds to cover overhead costs. Congress should increase Research Management and Support budgets.

We also addressed concerns that many of NIH's advisory committees are restricted to pro forma roles, populated by too many individuals with conflicts of interest, and are sometimes perceived as being politicized. We concluded that participation in these committees should be solely based on a person's scientific or clinical expertise or on his or her substantial involvement in a health or research issue. NIH should also reform their advisory council system to ensure that these bodies are sufficiently independent, are routinely involved in priority setting and planning and are engaged in discussions with institute and center leadership to provide it with honest feedback and enhance its accountability.

Finally, our committee understood that it is the quality of leadership at all levels, as opposed to organizational structure, that is central to NIH's vitality. In the long run, the recruitment of outstanding leadership, the commitment to individual scientists as the main sources of new discoveries, and reliance on the competitive review system for determining grants will remain the essential keys to NIH's continuing success.

Thank you again for the opportunity to discuss the recommendations of our report. I would be happy to answer any questions you may have.

Mr. GREGG. Thank you, Dr. Shapiro. That is an excellent statement, and I happen to agree with much of what you said and appreciate that background and that support of that view.

Since the Senate is hosting this, I think the courteous thing to do is to allow our House Members to go first in questioning, and so I will yield to the chairman of the committee, and we will go from the chairman to the ranking member on the House side, then we will go from the chairman and ranking member on the Senate side. Then we will go back to House Republican, House Democrat, and then we will go back to Senate Republican, Senate Democrat. It will be 5 minutes in the first round here.

Mr. BILIRAKIS. Thank you very much, Mr. Chairman. First I would ask unanimous consent that all members of the committee who have an opening statement, that they be made a part of the record.

Mr. GREGG. Of course.

Mr. BILIRAKIS. I have a couple of foundational questions, but I think I will just start right off with Dr. Shapiro. Current law, as I understand it, and the staff understand it, already permits many of the recommendations outlined in an NAS report, including the Trans-NIH Initiative recommendation. In your opinion, why are the institutes and centers so reluctant to work with one another? I think that is pretty darn foundational.

Mr. SHAPIRO. I cannot really give you a fully satisfactory answer as to why the heads of the various institutes and centers have not worked in a more cooperative fashion in the past, but I think that, as has been mentioned by others here, Dr. Zerhouni referred to the silos, these were created by Congress as separate institutes, funded separately, and in that kind of structure you have very little incentive to work together, not a sufficient incentive to work together. So I think it is true that under current law a great deal more cooperation could take place. I think your assessment is correct, and indeed Dr. Zerhouni has demonstrated that, that even under the current situation, more can and I am sure will be done, but I think it would be helpful, at least in my judgment and the judgment of our committee, if some changes were made to make it clear that it was Congress's intent and desire that NIH as a whole be able to exhibit strategic intent and take on the most important strategic challenges in cooperation, sort of requiring that all the institutes participate in these kinds of trans-NIH initiatives.

Mr. BILIRAKIS. When we finish up here and just before you are excused, if I can use that term, we would say to you that we will be offering you many written questions—Dr. Varmus is familiar with this—and ask for your response. I guess I would say right at the outset, in 5 minutes questioning and maybe an additional 5 minutes, if we have the time and whatnot, we are not going to be able to get all of the answers. I guess I would strongly suggest to you on behalf of NAS that you would maybe suggest to us in writing some ideas of how this could be done. I realize that we cannot legislate what is inside the mind of a person and the heart of a person as far as cooperation and whatnot goes, but at the same time there must be some things that we can do, so please, please, feel free to do that.

Mr. SHAPIRO. Very glad to do that.

Mr. BILIRAKIS. Dr. Zerhouni, I would ask you—Dr. Varmus and you both were I guess in the same position regarding some of the structural changes that need to be made. Now, of course, Dr. Sha-

piro has also mentioned something to that degree. Do you have the authority to make these changes, the changes that you would like to make? Do you have the authority to conduct the roadmap the way you would like to, these structural changes?

Mr. ZERHOUNI. You can conduct a planning exercise. What you cannot do is have funding for these exercises because funding is separated. The only authority of the Director is a 1 percent transfer authority which has been rarely used because it is really designated for emergent use, and you cannot plan this over many years. So every significant initiative relies fundamentally on the acceptance by the Directors for funding the common initiative. This is the unique thing about the roadmap, that there was enough consensus to create a common pool, but tomorrow that consensus could disappear, Number 1.

Number 2, there is always a tension between an institute and the Director of NIH. Why? The Institute receives direct appropriations, has its own advisory councils, its own constituencies. The directors of the institutes I have found very willing to collaborate and work with the NIH Director. The problem is that they are accountable to their constituencies, so that when they have to make a decision as to whether they fund an extra center for a particular disease for which they are under pressure, versus contributing to a common pool, you can imagine where the tension is. This is a structural tension that is part of the system that I think we need to pay attention to and control better, because as you know, culture does not change unless fund flows change, and that is my message.

Mr. BILIRAKIS. Yes, sir, Dr. Varmus?

Mr. VARMUS. I would like to endorse the comments that Dr. Zerhouni just made. In my experience the NIH institute directors are extremely interested in trying to promote collaborative activity, but they do feel these pressures. You have to remember that even with the considerable expansion in the NIH budget, only one in three or one in four, in some cases one in five grant applications are funded, and they are under tremendous pressure from their constituencies to try to fund more grants out of their own institute, rather than donate money to a common pool. When I was at the NIH we did do a number of coordinated efforts that required contributions from all the institutes, to support research on Zebrafish and to build a map of the rat genome and do a number of other things that were important, but the continued enthusiasm on the part of institute directors for these NIH Director organized collaborative studies began to diminish with time. We need some way to create more incentives, more flexibility.

Elias did an extraordinary job in building the roadmap effort, but that needs to be an ongoing effort that is supported by scientific staff within the office of the Director and built in with incentives that encourage institute directors to contribute, even require them to contribute to some central pool.

Mr. BILIRAKIS. Well, just do not leave it up to us. We are in an ivory tower here and we do know something—

Mr. VARMUS. I thought we were the ivory tower.

Mr. BILIRAKIS. Give us some suggestions.

I would recognize the ranking member of the full Energy and Commerce Committee, Mr. Dingell, to inquire.

Mr. DINGELL. Mr. Chairman, I thank you.

Dr. Zerhouni, welcome, and Dr. Shapiro and Dr. Varmus, welcome. It is a privilege to see you both.

Is this plan to privatize, is this written anywhere? Is it written down?

Mr. ZERHOUNI. You are referring to the A76 Outsourcing Plan, sir?

Mr. DINGELL. The idea of transferring jobs out of NIH.

Mr. ZERHOUNI. This plan came, as you know, from OMB. It is a directive from the Office of Management and Budget.

Mr. DINGELL. This is an OMB plan?

Mr. ZERHOUNI. Right. It is not an NIH plan, sir.

Mr. DINGELL. Good. I am comforted to hear that because I was beginning to wonder if we ought not start by privatizing your job.

Mr. ZERHOUNI. As you know, we have 85 percent, as you mentioned, 85 percent of our activity is outside of the Federal Agency. But the plan is from OMB. The plan is obviously something that the Agency has to respond to. We have tried to do as much as we can to respond as effectively as we can. We have just won the first competition.

My instinct about this was that our people are really the best people—

Mr. DINGELL. Doctor, I happen to agree with you. Let me try and find out. Is this plan in writing?

Mr. ZERHOUNI. From OMB?

Mr. DINGELL. From OMB or is it in writing at your agency?

Mr. ZERHOUNI. Yes, both. The plan from OMB is written. The directors that come to us are explicit, and we have basically followed those, and I certainly can share them with you.

Mr. DINGELL. Would you submit those both, please, to us?

Do we need a governmental core to NIH? Do we not need a governmental core in addition to all of the outsourcing which is done now, 85 percent?

Mr. ZERHOUNI. I think it is very important to have an intramural program of Government scientists dedicated to public health priorities that no outside institution either has the capabilities or the interest to sustain.

Mr. DINGELL. Thank you, doctor.

Dr. Varmus, what do you think about that?

Mr. VARMUS. An intramural program is extremely important.

Mr. DINGELL. Dr. Shapiro?

Mr. SHAPIRO. I also think it is extremely important to have an intramural program. I think, as our report indicates, that some—as Dr. Zerhouni himself has carried out—some changes are necessary to ensure that continuous revitalization of the intramural program, but having it I think is extremely important.

Mr. DINGELL. Gentlemen, would you each—and I apologize, but I am very limited on time and I have to respect my colleagues and the chair. Will you please each briefly tell us about the negative aspects of this outsourcing program so we can see its virtues and its curses, starting with Dr. Varmus.

Mr. VARMUS. I am concerned that the outsourcing proposal is being somewhat misapplied in the context of what NIH does. NIH has already sought out among the most talented scientists and ad-

ministrators in the country, the effort to outsource. NIH does some contract work already, and as Dr. Zerhouni has pointed out, most of the funds at the NIH are used in the extramural research community, but for the maintenance of the administrative functions of the NIH and the research done in the intramural program, I believe that for the most part the NIH, virtually all categories, has already done a very good job in recruiting highly talented people who have been subjected to rigorous review through outside bodies, and that this is sending a wave of unnecessary anxiety and bureaucratic duplication to the Agency.

Mr. DINGELL. Thank you.

Dr. Shapiro?

Mr. SHAPIRO. Yes. Our committee and myself was also very concerned with this initiative, and we think it is on the whole not well thought out and in some sense ill advised. Sometimes centralization serves everybody's interest by increasing efficiency. Sometimes it serves no one's interest by undermining the capacity and freedom to manage at NIH. My own view of the current initiatives coming out of OMB then through HHS to NIH is that they are threatening and threaten to undermine some of the vitality of the organization, and I think they have to be, as you indicated earlier, more carefully thought through.

Mr. DINGELL. Nowhere is it to be found in the National Research Council Institute of Medicine's study, is that correct?

Mr. SHAPIRO. Recommendation Number 1 deals with the centralization of management functions which is the response to that. That is the first recommendation. It is on page 40 in the report.

Mr. DINGELL. I ask unanimous consent, Mr. Chairman, that that be put in the record, the entire summary of recommendations here so we can have a look at it.

Mr. GREGG. That is fine.

[The material follows:]

**Enhancing the Vitality of the
National Institutes of Health:
Organizational Change to Meet New Challenges**

**Committee on the Organizational Structure of the National
Institutes of Health**

**Board on Life Sciences
National Research Council**

**Health Sciences Policy Board
Institute of Medicine**

**NATIONAL RESEARCH COUNCIL
INSTITUTE OF MEDICINE
*OF THE NATIONAL ACADEMIES***

THE NATIONAL ACADEMIES PRESS 500 Fifth Street, N.W. Washington, DC 20001

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This study was supported by Contract/Grant No. XXX between the National Academy of Sciences and XXX. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect the views of the organizations or agencies that provided support for the project.

Library of Congress Cataloging-in-Publication Data

or

International Standard Book Number 0-309-0XXXX-X
Library of Congress Catalog Card Number 97-XXXXX

[Availability from program office as desired.]

Additional copies of this report are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055; (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet, <http://www.nap.edu>

Copyright XXXX by the National Academy of Sciences. All rights reserved.

Printed in the United States of America

THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Bruce M. Alberts is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. Wm. A. Wulf is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Harvey V. Fineberg is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Bruce M. Alberts and Dr. Wm. A. Wulf are chair and vice chair, respectively, of the National Research Council.

www.national-academies.org

**COMMITTEE ON THE ORGANIZATIONAL STRUCTURE OF THE NATIONAL
INSTITUTES OF HEALTH**

HAROLD T. SHAPIRO, *Chair*, Princeton University, Princeton, New Jersey
NORMAN R. AUGUSTINE, Lockheed Martin Corporation, Bethesda, Maryland
J. MICHAEL BISHOP, University of California, San Francisco, California
JAMES R. GAVIN III, Morehouse School of Medicine, Atlanta, Georgia
ALFRED G. GILMAN, University of Texas Southwestern Medical Center, Dallas, Texas
MARTHA N. HILL, Johns Hopkins University School of Nursing, Baltimore, Maryland
DEBRA R. LAPPIN, Princeton Partners Ltd., Denver, Colorado
ALAN I. LESHNER, American Association for the Advancement of Science, Washington, DC
GILBERT S. OMENN, University of Michigan, Ann Arbor, Michigan
FRANKLYN G. PRENDERGAST, Mayo Clinic Cancer Center, Rochester, Minnesota
STEPHEN J. RYAN, University of Southern California, Los Angeles, California
SAMUEL C. SILVERSTEIN, Columbia University College of Physicians and Surgeons, New York, New York
HAROLD C. SLAVKIN, University of Southern California, Los Angeles, California
JUDITH L. SWAIN, Stanford University School of Medicine, Stanford, California
LYDIA VILLA-KOMAROFF, Whitehead Institute, Cambridge, Massachusetts
ROBERT H. WATERMAN, Waterman Group, Inc, Hillsborough, California
MYRL WEINBERG, National Health Council, Washington, DC
KENNETH B. WELLS, University of California, Los Angeles, California
MARY WOOLLEY, Research!America, Alexandria, Virginia
JAMES B. WYNGAARDEN, Duke University, Durham, North Carolina
TADATAKA YAMADA, GlaxoSmithKline, King of Prussia, Pennsylvania

STAFF

FRANCES E. SHARPLES, Study Director, Board on Life Sciences, Division on Earth and Life Studies (DELS)
FREDERICK J. MANNING, Senior Program Officer, Board on Health Sciences Policy, Institute of Medicine
ROBIN A. SCHOEN, Senior Program Officer, Board on Life Sciences, DELS
BRIDGET K.B. AVILA, Senior Project Assistant, Board on Life Sciences, DELS
LYNN CARLETON, Research Intern, Board on Life Sciences, DELS
KATHI E. HANNA, Writer
NORMAN GROSSBLATT, Senior Editor, DELS

BOARD ON LIFE SCIENCES

COREY S. GOODMAN, (Chair), Renovis, Inc., South San Francisco, California
R. ALTA CHARO, University of Wisconsin, Madison, Wisconsin
JOANNE CHORY, The Salk Institute for Biological Studies, La Jolla, California
JEFFREY L. DANGL, University of North Carolina, Chapel Hill, North Carolina
PAUL R. EHRLICH, Stanford University, Stanford, California
DAVID J. GALAS, Keck Graduate Institute of Applied Life Science, Claremont, California
BARBARA GASTEL, Texas A&M University, College Station, Texas
JAMES M. GENTILE, Hope College, Holland, Michigan
LINDA GREER, Natural Resources Defense Council, Washington, DC
ED HARLOW, Harvard Medical School, Cambridge, Massachusetts
KENNETH F. KELLER, University of Minnesota, Minneapolis, Minnesota
GREGORY A. PETSKO, Brandeis University, Waltham, Massachusetts
STUART L. PIMM, Duke University, Durham, North Carolina
JOAN B. ROSE, Michigan State University, East Lansing, Michigan
GERALD M. RUBIN, Howard Hughes Biomedical Research, Chevy Chase, Maryland
BARBARA A. SCHAAL, Washington University, St. Louis, Missouri
RAYMOND L. WHITE, University of California, San Francisco, California

STAFF

FRANCES E. SHARPLES, Director
ROBIN A. SCHOEN, Senior Program Officer
ROBERT T. YUAN, Senior Program Officer
KERRY A. BRENNER, Program Officer
MARILEE K. SHELTON-DAVENPORT, Program Officer
EVONNE P. Y. TANG, Program Officer
BRIDGET K. B. AVILA, Senior Project Assistant
DENISE GROSSHANS, Senior Project Assistant
LYNN CARLETON, Project Assistant/Research Intern
BHAVIT SHETH, Project Assistant
SETH STRONGIN, Project Assistant

PREFACE

The strong system of federal support for US science and technology has produced five decades of discovery and innovation that have not only literally changed the way we live, but deepened our understanding of the human condition, of our position in the universe, and of our relationship to other forms of life. This use of public resources is widely agreed to have yielded great social dividends for the citizens of our country and beyond. In many ways, the National Institutes of Health (NIH) is unsurpassed among the array of federal agencies that support scientific research, providing 80% of the federal government's contribution to biomedical research. From a humble beginning in the late 19th century as a one room laboratory with a \$300 government allocation, NIH has grown into a \$27 billion per year organization that justifiably enjoys enormous public and congressional support. NIH's success in its mission of science in pursuit of fundamental knowledge and the application of that knowledge to extending healthy life and reducing the burdens of illness and disability has been enormous. NIH's investment in biomedical research has helped produce remarkable results in terms of declining rates of disease, longer life expectancy, reduced infant mortality, and improved quality of life. All those who have played a role in making NIH such a success over the years have earned the gratitude of current and future generations.

This report was undertaken in response to a congressional request that wisely acknowledged the fact that the world we live in is changing rapidly. In such a world, all enterprises, be they large or small, need to be able to adapt to change if they are to continue to be effective. Indeed in a rapidly changing environment, the greatest risk to successful organizations is the danger of becoming entrenched in the very things that have made them successful at the expense of some needed adaptability. Science and the understanding of health and disease that emerges from science together with an evolving set of health concerns are among the most fast paced areas of change. An organization such as NIH that is dedicated to research and training related to the nation's health concerns must continually consider new ways to meet the challenges of the future. What Congress wants to know is whether NIH's "organizational structure" is right for the times.

As NIH's budget and the number of its organizational units have grown, the complexity of its operations and the ability of its director to manage the overall enterprise have become extremely challenging, especially in light of the loosely federated structure that Congress has established for the NIH. Moreover all would agree that there surely are some limits to the number and variety of units that any organization's structure, even a loosely federated one, can accommodate. The highly decentralized structure that NIH has evolved over its long history is, in fact, one that most of NIH's constituencies prefer, celebrating the benefits and tolerating the costs of this form of organization. Moreover, these constituencies have often pointed to NIH's obvious success, as if that settled the issue. While NIH's success is to be celebrated, success alone does not answer fully the question of whether there is a better way to proceed, particularly as one faces a future where the world of biomedical science is being rapidly transformed in virtually all its dimensions.

In carrying out its task, our Committee discovered that defining an optimal degree of centralization or decentralization for NIH is not a simple matter. Indeed the right balance

between centralization and decentralization is likely to shift over time as circumstances change. The current level of decentralization, together with the institutional relationships among the institutes and centers on the one hand and the study sections and advisory committees on the other, has the great strength of mobilizing a vast array of talent to participate in key decisions. In addition, this mode of operation has the added benefit of helping to secure the support of a large number of constituencies that can point to one or more facets of the organization that reflects their most important concerns. On the other hand, this complex and decentralized organizational structure makes it more difficult for the NIH director to mobilize significant resources to focus on new programs of strategic importance that should engage all the institutes and centers, to support broad based interdisciplinary efforts, and to cooperate in other ways across existing organizational and bureaucratic boundaries.

What became clear to us was that there is no compelling set of management principles that would help either in defining an optimal organizational structure or in identifying the optimal balance between centralization and decentralization for a research organization like NIH, which must not only productively interact with an unusually complex network of constituencies, but also must deal with the inevitable uncertainties and tensions involved in setting a research agenda. In fact, we recognized that the vitality of NIH is only modestly dependent on its formal administrative and organizational structure, but is very dependent on other aspects of the organization's culture and reward system, particularly its capacity to attract and obtain high quality leadership at all levels. In light of such considerations, it was not possible, or useful, to constrain our efforts narrowly to matters that relate purely to NIH's organization chart. While we tried to take a modest approach to our task, the strong and inevitable symbiosis among mission, priorities and organization meant that we had to consider aspects of all these matters.

In the end, our Committee decided that while the current organizational structure of NIH represents a fundamentally useful response to the legitimate demands made by its varied constituencies, some changes are needed to help NIH meet effectively the new demands of the next decades. While there may be no particular number of institutes and centers that can be shown to be optimal, we came to believe that NIH would be well advised to forge a new set of strategies that could be available to re-deploy some of the efforts of the existing institutes and centers or focus new resources on a revolving set of strategic trans-NIH initiatives that seem compelling. This report presents a variety of ideas identified by the Committee as opportunities for organizational change to improve the agency's responsiveness and flexibility and assist it to continue to accomplish its mission successfully.

Readers of this report should not interpret its recommendations as in any way seeking to undermine the primacy of investigator-initiated science or of the excellent peer review system in place at NIH. The Committee believes that the tens of thousands of NIH-supported scientists working at a couple of thousand institutions must remain the bedrock of NIH's programs. Though not perfect, NIH's peer review system is the best guarantee we have overall that scientists will carry out research that is of high quality and high potential for scientific progress.

I wish to thank all the members of the Committee for their valuable contributions and for their insights into both the scientific and societal issues surrounding this project. The reviewers provided helpful comments that ultimately helped strengthen the report, and I thank them for

myself and on behalf of the entire Committee. I also wish to acknowledge the National Academies staff (Fran Sharples, Rick Manning, Robin Schoen, Bridget Avila, and Lynn Carleton) for their thorough and thoughtful assistance with all aspects of the preparation of this report. Kathi Hanna did a superb job in assisting with the writing of the report and was an active participant in many of our discussions. Finally, since we believe the work of NIH to be of ethical significance for both current and future generations, it is our hope that our efforts and our recommendations will stimulate a thoughtful discourse aimed at assisting NIH to move from strength to strength.

Harold T. Shapiro, Chair
Committee on the Organizational Structure of the National
Institutes of Health

ACKNOWLEDGMENTS

This report is the product of many individuals. We would like to thank all those people and organizations that provided information and opinions to the committee. A list may be found in Appendix A of this report. Some of the descriptive information in this report was based on a background paper prepared for the National Academies by Michael McGeary and Philip M. Smith. This paper has proved highly useful and we very much appreciate the work done by McGeary and Smith to help get the Committee on the Organizational Structure of the National Institutes of Health off to a good start.

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

David Baltimore, California Institute of Technology
William G. Barsan, A. Alfred Taubman Health Center
Arthur I. Bienenstock, Stanford University
Enriqueta C. Bond, Burroughs Wellcome Fund
Charles A. Bowsler, Comptroller General of the United States (former)
Steve Hyman, Harvard University
Richard D. Klausner, The Bill & Melinda Gates Foundation
David Korn, Association of American Medical Colleges
Richard A. Rettig, RAND
Leon E. Rosenberg, Princeton University
Edward M. Scolnick, Merck Research Laboratories
John Seffrin, American Cancer Society
Harold Varmus, Memorial Sloan-Kettering Cancer Center
Raymond White, University of California, San Francisco

Although the reviewers listed above have provided constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by Floyd Bloom of The Scripps Research Institute and Mary Jane Osborn of the University of Connecticut Health Center. Appointed by the National Research Council, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

Contents

Executive Summary	1
1: Introduction	15
2: The Evolution of NIH'S Organizational Structure	27
3: New Opportunities, New Challenges: The Changing Nature of Biomedical Science	43
4: The Organizational Structure of NIH	55
5: Enhancing NIH's Ability to Respond to New Challenges	67
6: Accountability, Administration, and Leadership	83
7: Putting Principles into Practice	97
References	103
Appendix A: Sources of Information Provided to the Committee	111
Appendix B: Acronyms and Abbreviations	115
Appendix C: Committee Member Biographies	117

EXECUTIVE SUMMARY

The continued growth in the number of organizational units of the National Institutes of Health (NIH) has been a cause of both concern and celebration for decades. Numerous NIH officials and external advisory committees have suggested that the continued creation of new units (institutes, centers, and programmatic offices) could impair NIH's functioning by making it unmanageable and impeding its ability to carry out its mission. Most recently, former Director Harold Varmus argued in a 2001 article in *Science* that NIH would be more effective scientifically and more manageable if it were organized into a far smaller number of larger institutes organized around broad areas of science. Others counter that the elimination of units that focus on particular problems would reduce attention to and funding for these problems and that a consolidation of units would reduce congressional and public support and might not be politically feasible. More generally, recent rapid increases in resources, fundamental shifts on the biomedical frontier, and evolving health concerns make it a good moment to review whether the organizational structure of NIH continues to be appropriate.

Clearly many changes have taken place in the world of science and in the nature of the health concerns that research must address. Since the late 1990s, the NIH budget has doubled to its current level of about \$27 billion as a result of congressional and presidential initiatives. In science, the importance of multi-institutional, multidisciplinary research that relies more and more on large infrastructural investments is ever more apparent. Demographics and the patterns of illness in society are changing, and the specter of intentional releases of harmful disease organisms by terrorists has emerged following the attacks of September 2001. The private sector's investments in some fields of research have increased to the point where pharmaceutical and biotechnology companies now spend more than NIH on research and development.

With the steady stream of change, concerns about whether NIH has become too fragmented to address effectively the most important biomedical and health challenges or to respond quickly enough to health emergencies have resurfaced in Congress and in some parts of the scientific community. NIH has never been administratively reorganized in any substantial way, only added on to, despite vast changes in the landscape of science and the nation's health concerns during the last half century.

Congressional Request

In report language accompanying the FY 2001 appropriation for the Department of Health and Human Services (DHHS), Congress directed NIH to have the National Academy of Sciences study "whether the current structure and organization of NIH are optimally configured for the scientific needs of the twenty-first century." Senate report 106-293 states:

The Committee is extremely pleased with the scientific advances that have been made over the past several years due to the Nation's support for biomedical research at NIH. However, the Committee also notes the proliferation of new entities at NIH, raising concerns about coordination. While the Committee continues to have confidence in NIH's ability to fund outstanding research and to ensure that new knowledge will benefit all Americans, the fundamental changes in science that have occurred lead us to question whether the current NIH structure and organization are optimally configured for the scientific needs of the Twenty-first Century. Therefore, the Committee has provided to

the NIH Director sufficient funds to undertake, through the National Academy of Sciences, a study of the structure of NIH.

Statement of Task

In response to the congressional request, the goal of this study was to determine the optimal NIH organizational structure, given the context of 21st century biomedical research. The following specific questions were to be addressed:

1. Are there general principles by which NIH should be organized?
2. Does the current structure reflect these principles, or should NIH be restructured?
3. If restructuring is recommended, what should the new structure be?
4. How will the proposed new structure improve NIH's ability to conduct biomedical research and training, and accommodate organizational growth in the future?
5. How would the proposed new structure overcome current weaknesses, and what new problems might it introduce?

The Committee on the Organizational Structure of the National Institutes of Health was formed to ensure that the views of the basic science, clinical medicine, and health advocacy communities were all adequately represented. In addition, the committee has members who are experienced in the management of large and complex organizations, including a former NIH director, two former NIH institute directors, a former university president, two persons with backgrounds in senior management of major industrial entities, and a specialist in organizational issues. Several Committee members also had considerable experience in government operations.

The Committee held six two-day meetings over the ten months between July 2002 and April 2003. In its initial meetings it invited past and present representatives of Congress, NIH, voluntary health groups, scientific and professional societies, and industry to provide perspectives on the issues before them (see Appendix A). In addition, the Committee met publicly with the current NIH director as well as several former directors. Committee members and staff also heard presentations from or interviewed NIH staff in the offices of policy and planning, budget, finance, and intramural research, and met with directors of 18 institutes or centers. Data about NIH programs and budgets were requested from NIH staff as the need emerged. Prior reports conducted about and for NIH were reviewed, as was the relevant literature. In addition, the Committee commissioned a background paper tracing the history and evolution of NIH and its institutes as a starting point for its deliberations (McGeary and Smith, 2002). Finally, several Committee members conducted town meetings at their home institutions and elsewhere, inviting scientists, administrators, and students to contribute their perspectives. Thus, the Committee was able to hear, consider, and discuss a diverse range of facts and opinions about the organizational structure of NIH. Its final report and recommendations are, however, based on the Committee's assessment of the information that was available and current trends in biomedical science and health.

The Committee's Response to its Charge

The goal of the study focused on the organizational structure of NIH, but it was not possible to address this issue satisfactorily without considering the mission of NIH, some of its key processes, and the scientific, social, and political environment in which NIH activities take place. Although a long series of reviews of NIH helped to inform committee deliberations, both

the nature of the charge and the 1-year period allowed for deliberations put important constraints on the development, character, and scope of the recommendations that can credibly be put forward. Most important, the committee was not asked to address NIH's research priorities or the quality and effectiveness of the wide array of research and advanced training programs that NIH undertakes or sponsors.

The Committee's view of its task was governed, first, by the desire to be of some practical assistance to all those who wish NIH to continue to be an outstanding organization. Scholars of organizational management have long recognized that there is more to organization than structure. An organization's ability to make effective changes is influenced by a multiplicity of factors, including structure, strategy, and systems, the last of which includes all the formal and informal processes and procedures that organizations rely on to function. Thus, the Committee proceeded on the premise that its task included assessing both the organizational configuration of NIH and the key processes and authorities that play roles in NIH-wide decision-making. Although the borders between structure, mission, and priorities are not well defined, the Committee tried not to take too expansive a view of its responsibilities.

Therefore, the Committee did not focus exclusively on whether or not there should be a widespread consolidation of NIH's institutes and centers. Rather, it took a more general approach, namely to inquire if there were any significant organizational changes—including the widespread consolidation of institutes and centers—that would allow NIH to be even more successful in the future. Although the Committee discussed on numerous occasions the advisability of the widespread consolidation of NIH, it eventually came to believe that this was not the best path for NIH to take at this time.

It is important to understand that the structure of any large and complex organization, such as NIH, is not the tidy result of a compact set of compelling propositions emanating from organizational theory any more than the particular organization of our complex pluralistic democracy is the result solely of the inspired thinking of political philosophers. The latter is instead the outcome of our particular form of politics and, therefore, heavily influenced by our history and evolving cultural commitments. It is very much the same way with NIH. It would be naïve to assume that NIH was or should be organized exclusively along the lines dictated either by the interests of the scientific community or the priorities of any other single set of interests with a concern about promoting health-related research and advanced biomedical training. NIH's existing structure is the result of a set of complex evolving social and political negotiations among a variety of constituencies including the Congress, the administration, the scientific community, the health advocacy community, and others interested in research, research training, and public policy related to health. Indeed the history of NIH provides clear evidence that each of these communities has always had a variety of views on the appropriate organization of NIH. From any particular point of view or for any particular set of interests, the current situation is not only imperfect, but is certainly not one that either the Congress or the scientific community would designate *ab initio*. Rather it has evolved as a very useful and largely productive outcome of a series of political and social negotiations that took place over time. This outcome is typical of the design of important social organizations in a pluralistic democracy. NIH has become an organization that balances its many interests and the Committee felt that the any major modifications at his point in time should focus directly on enhancing NIH's capacity to pursue major time-limited strategic objectives that cut across all the institutes and to acquire a special ability to pursue more high risk, high return projects. It was our view that at this moment the

widespread consolidation of institutes and centers is not the next best organizational step for NIH to undertake, as any benefits to be gained would be offset by the costs involved.

What does the Committee mean by “costs”? At a minimum, because Congress created the institutes, dissolving or merging institutes would require congressional action. Any thoughtful major reorganization would necessitate a lengthy and complex information gathering and decision making process that would include numerous congressional hearings involving members of Congress, congressional staff and a wide variety of interests in the various health advocacy and scientific communities. Our discussions, correspondence and meetings made it quite clear that there would be very little agreement among these communities on what the right way to reorganize NIH is, and there would probably be dozens of conflicting ideas in play and few clear avenues for narrowing these down. Moreover these discussions and negotiations would be long and contentious ones and with a quite uncertain outcome. More importantly the Committee is firmly convinced that many of the goals that might be achieved through large-scale consolidation of institutes could also be achieved more rapidly and effectively through other organizational and administrative mechanisms, as recommended in this report.

Nevertheless the Committee did feel that no organization as important as NIH should remain frozen in organization space and that some regular, thoughtful and publicly transparent mechanism is required to allow appropriate changes in the organizational structure of NIH to take place at appropriate times. Although the Committee does believe that the consolidation of two pairs of institutes is appropriate to consider at this time, it felt that these issues ought to have the benefit of the public process we have recommended.

The Committee was also well aware that all organizational changes, however well thought out, potentially carry both potential risks and benefits, and it has done its best to sort these out. The Committee recognized that the decentralized structure of NIH, which allows a large number of people throughout the scientific and advocacy communities to help to set priorities, has been and should continue to be an integral element in NIH’s success. The Committee also kept the enormous benefits of investigator-initiated grants, including those focused on fundamental research, firmly in mind during its deliberations. Finally, the Committee understood that it is the quality of leadership and decision-making at all levels, as opposed to administrative structures, that are central to NIH’s vitality. In the long run, the recruitment of outstanding leadership, the commitment to individual scientists as the main sources of new discoveries, and the reliance on the competitive review system for determining awards will be essential to NIH’s continuing success.

The fact that NIH has been working well does not mean that it could not work better if - in response to changes on the scientific frontier, new health concerns, or other important environmental shifts - some organizational modifications were made. The intent of this report is to assess the current organizational structure of NIH and to suggest modifications that might be appropriate to help NIH to become even more effective in supporting research essential to the long-term goal of improving human health.

Centralization of Administrative Functions

NIH is an agency of DHHS, which has recently issued instructions to consolidate administrative functions, such as personnel management, communications, congressional liaison, and travel, throughout the Department. The “One HHS” initiative has the stated goal of better integrating management functions across the Department’s operating and staff divisions. The initiative has already resulted in consolidation of some administrative functions at NIH. DHHS

has further plans for consolidating other functions at NIH, such as budgeting, finance, and procurement, and is encouraging NIH to consider outsourcing some of its administrative functions.

While the Committee believes that it is critical that government continue attempts to eliminate inefficiencies, it would not serve anyone if such initiatives result in decreasing the effectiveness of NIH as a research and training organization or damage its ability to recruit talented leaders at all levels. Centralization of certain functions can be effective, but is not always the best means to achieve increased efficiencies. At times, centralization serves everyone's interests, but at other times it serves no one's interests. The Committee believes that initiatives to centralize or outsource from NIH key science-related functions that are difficult to separate from the performance of its primary mission, such as aspects of grants management, fail to appreciate how closely these administrative functions are tied to the scientific enterprise.

Recommendation 1: *Centralization of Management Functions*

Any efforts to consolidate or centralize management functions at NIH, either within NIH or at the DHHS level, should be considered only after careful study of circumstances unique to NIH and its successes in carrying out its research and training mission. A structured and studied approach should be used to assure that centralization will not undermine NIH's ability to identify, fund, and manage the best research and training proposals and programs in support of improving health.

Organizational Structure of NIH

NIH's continuing success has been due largely to its ability to adapt to meet the ever-changing needs and challenges posed by science, medicine, and public health. Moreover, there is a perception that given the substantial increases in resources and the vast expansion of the biomedical enterprise, the addition of institutes and centers has been productive and has provided an ever broader base of support and budget success both for the specific interests involved and for NIH in the aggregate. While everyone understands that this expansion cannot and should not continue indefinitely, many see no particular difficulty with the current number of institutes and centers.

The Committee carefully considered major structural changes in NIH, including possible revisions in the number and reporting lines of institutes and centers (ICs) to the Director. The Committee considered numerous proposals for restructuring NIH in great detail. However, as laid out in this report, it did not find a compelling intellectual argument for major structural alterations at this time. Rather the Committee makes recommendations for achieving many of the goals identified by proponents of major restructuring (more authority for the NIH director, increased responsiveness, greater flexibility, and more opportunity for coordination) primarily by other means.

Many previous reports have suggested that increasing the number of ICs at NIH would make it less effective. Thus the present Committee is hardly the first to consider these problems and deliberate over potential solutions. The Committee notes, however, that little changed as a result of past studies. The trend toward continued growth in the number of units in NIH has continued to the present in the absence of an accepted process such as that suggested in the 1984 Institute of Medicine report. The Committee believes therefore that it would be useful for

Congress to consider amending the authorizing legislation for NIH to require that certain steps be taken in considering the creation, dissolution, or consolidation of organizational units.

Recommendation 2: *Public Process for Considering Proposed Changes in the Number of NIH Institutes or Centers*

Either on receiving a congressional request or at the discretion of the NIH director in responding to considerable, thoughtful, and sustained interest in changing the number of institutes or centers, the director should initiate a public process to evaluate scientific needs, opportunities, and consequences of the proposed change and the level of public support for it. For a proposed addition, the likelihood of available resources to support it should also be assessed and the burden of proof should reside clearly with those seeking to add an organizational element.

Despite the Committee's conclusion that a large-scale restructuring of the ICs would not be wise now, no organization that is expected to remain effective should have to bear the burden of a frozen organizational structure, and not all its existing units are likely to continue to have the same relevance or independence in the future. Therefore, the public, the scientific community, or the director of NIH, in concert with internal and external advisers, should be able to suggest additions, subtractions, or mergers of units to Congress at appropriate times. The Committee provides two suggestions for potential mergers for further study: the merger of the National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism and the merger of the National Institute of General Medical Sciences and the National Human Genome Research Institute. Indeed, the Committee favors these mergers, but believes that such changes should benefit from use of the process outlined above. However, because of extraordinarily persuasive arguments about exceptional needs made by a variety of groups in discussions with the Committee, it recommends merging several clinical research components of the extramural and intramural program to create a National Center for Clinical Research & Research Resources.

Recommendation 3: *Strengthen Clinical Research*

NIH should pursue a new organizational strategy to better integrate leadership, funding, and management of its clinical research enterprise. The strategy should build on but not replace existing organizational units and activities in the individual ICs' intramural and extramural research programs. It should also include partnerships with the nonprofit and private sectors. Specifically, the Committee recommends that several intramural and extramural programs be combined in a new entity to subsume and replace the National Center for Research Resources, to be called the National Center for Clinical Research and Research Resources (NCCRRR). In addition, a deputy director for clinical research should be appointed in the Office of the Director to serve as deputy director and head of the new entity.

Enhancing NIH's Ability to Respond to New Challenges

Although the Committee is not recommending a major structural reorganization of NIH's institutes and centers, it concluded that to meet the scientific and health goals of the nation, NIH needs new mechanisms for mobilizing and coordinating funding from many units for high-priority initiatives that cut across the purviews of individual ICs. Although co-funding of projects by multiple institutes occurs, it is not clear to what extent these projects are true "end-to-end"

collaborations. Thus, “multi-institute funding” should be distinguished from “trans-NIH initiatives”, in which planning and implementation of activities involves more than one institute from start to finish. The Committee believes that the best means to achieve mobilization and coordination of new cross-cutting initiatives is through the initiation via NIH-wide strategic planning of a rotating series of multiyear, but time-limited, strategic initiatives that involve all the ICs.

Recommendation 4: *Enhance and Increase Trans-NIH Strategic Planning and Funding*

a. The director of NIH should be formally charged by Congress to lead a trans-NIH planning process to identify major crosscutting issues and their associated research and training opportunities and to generate a small number of major multi-year, but time limited, research programs. The process should be conducted periodically - perhaps every 2 years - and should involve substantial input from the scientific community and the public.

b. The director of NIH should present the scientific rationale for trans-NIH budgeting to the relevant committees of Congress, including a proposed target for investment in trans-NIH initiatives across all institutes. For example, an average target of 5% of overall NIH funding in the first year, growing to 10% or more over 4-5 years, may be appropriate.

c. The appropriations committees should annually review budget justifications and testimony from the NIH director and from individual IC directors about the participation of each unit in the planned trans-NIH initiatives and the portion of their budgets so directed. Congress should include budget targets in the appropriations report language. The Committee recommends beginning with 5% of the overall NIH budget.

d. To ensure that each IC uses the target proportion of its budget for trans-NIH initiatives of its choosing, that proportion of the annual appropriation to each unit should be treated as “in escrow” until the NIH Director affirms that the unit has committed to its expenditure for the identified trans-NIH initiatives.

e. The President should include in the budget request, and Congress should include in the NIH appropriation for OD, funds to support an appropriate number of additional full-time staff to conduct the trans-NIH planning process and “jump-start” the initiatives that emerge from this process.

To carry out the responsibilities of managing, planning, and coordinating the programs of NIH's 27 ICs, the NIH director is assisted by a number of staff units collectively called Office of the Director (OD) Operations. The budget for OD Operations has not grown in proportion to NIH's research funding and is inadequate for the effective management of the organization. When unforeseen needs surface, the OD is likely to have to “pass the hat” to the ICs to gather the additional resources needed.

Recommendation 5: *Strengthen the Office of the NIH Director*

The Office of the Director should be given a more adequate budget to support its management roles or greater discretionary authority to reprogram funding from the earmarked components of its budget when necessary to meet unanticipated needs. In particular, if the director is given the responsibility and authority to conduct NIH-wide planning for trans-NIH initiatives, the director's budget will need to be amplified to take the costs of such planning into account.

The earmarking of funds by Congress for the establishment and continuation of programmatic offices in OD sometimes limits the director's flexibility and fluidity of resources, as well as his or her ability to effect change across the organization. It is difficult to ascertain whether the programmatic offices within OD have achieved their intended goals. The time may be right to assess the effect that the programmatic offices in OD have had, including their role in the NIH director's policy and planning processes, whether the programs have clear goals, and whether there is a need to "sunset" an office once it achieves its goals. The Committee believes that the process recommended in Chapter 4 for evaluating the merits of proposed additions to or subtractions from the list of ICs should also be applied to the creation of new offices in OD itself.

Recommendation 6: *Establish a Process for Creating New OD Offices and Programs*

The public process recommended in Chapter 4 (Recommendation 2) for evaluating a proposal to create a new institute or center or to consolidate or dissolve an institute or center should also be used for a proposal to create, consolidate, or dissolve an office in OD. The process should be used to evaluate the scientific needs, opportunities, and consequences of the proposed change, the likelihood of resources being available to support it, and public support for it.

The pressures that exist in organizational environments such as NIH's may make it difficult to undertake high-risk research—even though such research may offer potentially high payoff. The Committee also believes that there is a need for a Director's Special Projects Program that is outside the budgets of the ICs and is funded as an OD line item. The goal of the program would be to provide a mechanism to augment the funding of high-risk, innovative research projects. In a broad sense, the Committee imagines the program to be patterned after the Defense Advanced Research Projects Agency (DARPA).

Recommendation 7: *Create a Director's Special Projects Program*

A discrete program, the Director's Special Projects Program, should be established in OD to fund the initiation of high-risk, exceptionally innovative research projects offering high potential payoff. The program should have its own leader, who reports to the director of NIH, and a staff of short-term (2-4 years) program managers to manage identified projects with advice on program content from extramural panels. The program should be structured to permit rapid review and initiation of promising projects; if peer review is deemed appropriate, the program should use peer review panels created specifically for it and charged with selecting high risk, high potential return projects. Congress should be prepared to provide new funding in the amount of \$100 million, growing to as much as \$1 billion per year for this endeavor, and commit to support it for at least 8-10 years so that a sufficient number of projects can reach

fruition and a full assessment of program efforts can be made. A program review should be conducted during the fifth year to provide mid-course guidance.

The Committee is convinced that the Intramural Research Program (IRP) of NIH should not be merely an internal extension of the extramural community but rather should be doing distinctive research that the extramural community cannot or will not undertake. The Committee believes that too little weight has been placed on potentially distinctive contributions of the IRP and that both uniqueness and quality should be essential justifications of the IRP.

Recommendation 8: *Promote Innovation and Risk Taking in Intramural Research*
The intramural research program should consist of research and training programs that complement and are distinguished from those in the extramural community and the private sector. The intramural program's special status obligates it to take risks and be innovative. Regular in-depth review of each component of the intramural program should occur to ensure continuing excellence. Allocation of resources to the intramural program should be closely tied to accomplishments and opportunities. Inter-institute and intramural-extramural collaborations should be supported and enhanced.

Accountability, Administration, and Leadership

Public accountability and leadership are key aspects of NIH's stewardship of the biomedical enterprise. The Committee has suggested several ways for NIH to enhance its public accountability and ensure the continuing vitality of its leadership.

The current deficiencies in information management methods and infrastructure to collect, analyze, and report level-of-investment data in a timely fashion must be addressed. The problem requires the development of an NIH-wide agreement on what to track and publish and of a single method for coding data that uses consistent definitions and deals with the uncertainties inherent in counting research when it is only related but not directly applicable to a specific topic. Once developed, the statistics should be kept current and their accuracy ensured through quality control. NIH must also improve its tracking and analysis of the research accomplishments of scientists trained and supported with NIH funds.

Recommendation 9: *Standardize Data and Information Management Systems*
For purposes of meeting its responsibilities for effective management, accountability, and transparency, NIH must enhance its capacity for the timely collection, thoughtful analysis, and accurate reporting of the nature and status of its research and training programs and public health advances. Data should be collected consistently across institutes and centers and submitted to a centralized information management system.

The vision of the NIH leadership regarding accountability and the procedures and structures that the leadership adopts to enhance it are perhaps the most important ingredients in the complex mix of policies and strategies that enable NIH to meet its responsibilities to all its constituents. Leadership and vision may influence particularly the extent to which accountability is reinforced and implemented at diverse levels of the NIH system, from top management through staff to individual intramural and extramural investigators. In the current NIH environment, reviews of the performance of senior members of management—a form of public accountability—are too informal and ad hoc to be effective. Moreover, the processes and criteria

for review are not obvious or well defined. These reviews should consider the extent to which the Institute/Center Director promotes the effectiveness of NIH as an overall entity, including supporting trans-NIH initiatives. By communicating, as appropriate, the results of reviews to the NIH director's advisory groups, the IC directors can demonstrate an additional level of accountability. While some aspects of a review should be held as confidential, those elements that relate directly to the mission and objectives of NIH should be made available to the director's advisors.

The committee also believes that a healthy degree of turnover in leadership is critical for sustaining the vitality of a research organization. It would provide opportunities for leading scientists across the nation to leave their positions for a set period to come to NIH as a form of public service to provide effective scientific leadership to critical elements of the nation's biomedical enterprise.

Recommendation 10: *Set Terms and Conditions for IC Director Appointments and Improve IC Director Review Process*

a. All IC directors should be appointed for 5-year terms. The possibility of a second and final term of 5 years should be based on the recommendation of the director of NIH, which should include consideration of the findings of an external review of job performance. The authority to hire and fire IC directors should be transferred from the Secretary of Health and Human Services to the NIH director.

b. The Director of NIH should establish a process of annual review for the performance of every IC director in terms of his or her effectiveness in fulfilling scientific and administrative responsibilities. The results of such reviews should be communicated, as appropriate, to the Advisory Committee to the Director and/or the Council of Public Representatives.

The committee concluded that review and revitalization of OD is an essential prerequisite for accountability and leadership. It noted that the National Science Foundation Act of 1950 creates a term of 6 years for the National Science Foundation director and concluded that this has been a good model for creating a system of accountability and periodic review that has the possibility of transcending changes in administrations.

Recommendation 11: *Set Terms and Conditions for the NIH Director Appointment*
The NIH Director, appointed by the President, should serve for a term of 6 years unless removed sooner by the President. The possibility of a second and final term of 6 years should be based on a positive external review of performance and the recommendation of the Secretary of Health and Human Services.

The committee believes that the special status granted the National Cancer Institute (NCI) by the National Cancer Act should be re-examined. Because the President appoints the NCI director and the NCI budget bypasses the NIH director, it is possible that an unnecessary rift is created between the goals, mission, and leadership of NIH and those of NCI. For scientific and administrative reasons, this special status should be reconsidered.

Recommendation 12: *Reconsider the Status of the National Cancer Institute*
Congress should reassess the provisions of the National Cancer Act of 1971, particularly as they affect the authority of the NIH director to hire senior management and plan and coordinate the NIH budget and its programs in their entirety.

Like other federal science agencies, NIH makes extensive use of advisory committees (variously known as study sections, councils, boards, etc.) of nonfederal scientists, health advocacy representatives, and others to ensure the best possible input of expertise and additional perspectives on the evaluation of programs and the development of policies and priorities. NIH had 140 chartered advisory committees as of May 2002, more than any other federal agency. The Secretary of Health and Human Services appoints 32 committees, the NIH director appoints 74, and the President appoints two. In the appointment process, the President generally follows the recommendations of the Secretary and the Secretary generally follows the advice of the NIH and institute directors in filling positions, although they add their own candidates from time to time. At times in the past, administrations have tried to exert greater control over NIH, and there has been conflict over the perceived politicization of the advisory committee appointment process. The Committee believes that it is essential that members be appointed to these advisory groups because of their ability to provide scientific or public health expertise to the review and approval of awards and policies. They should not be selected to advance political or ideological positions.

There are substantial differences among institutes in the uses and roles of advisory councils; some are actively involved in establishing institute goals, and others are restricted to *pro forma* actions, with little advice or involvement sought by institute personnel. Advisory councils should routinely and consistently be consulted in the priority setting and planning processes of an institute, have active involvement in decisions regarding issuance of program announcements and requests for applications, and work to ensure that the institute is held accountable in reaching its goals and communicating with the public. The manner in which institute directors interact with their advisory councils should be a criterion for IC director reviews.

Recommendation 13: *Retain Integrity in Appointments to Advisory Councils and Reform Advisory Council Activity and Membership Criteria*

- a. Appointments to advisory councils should be based solely on a person's scientific or clinical expertise or his or her commitment to and involvement in issues of relevance to the mission of the institute or center.
- b. The advisory council system should be thoroughly reformed across NIH to ensure that these bodies are consistently and sufficiently independent and are routinely involved in priority-setting and planning discussions. Councils should be effectively engaged in discussions with IC leadership to enhance accountability, facilitate translation of goals and activities to the scientific community and the public, and provide feedback to the IC director. To achieve sufficient independence and avoid conflicts of interest, a substantial proportion of a council's scientific membership should consist of persons whose primary source of research support is derived from a different institute or center or from outside NIH.

Although it is desirable to keep administrative and overhead costs as low as possible, appropriate funding for these costs is essential to the effectiveness of any organization, including those that sponsor research and training programs. At NIH, the resources for those functions (for example, management of extramural activities, some intramural research program costs, program development, priority setting, education and outreach, acquisition and maintenance of new information technology systems, professional development, and facilities management) flow through the Research Management and Support (RMS) budgets of the various units that make up NIH. In the early 1990s, Congress imposed limitations on RMS that restricted its growth. In the middle 1990s, RMS was reduced, and little growth has been allowed since. In FY 2001, RMS represented 3.3% of the total NIH budget, down from 4.5% in 1995. The RMS share of the total NIH budget has decreased every year since FY 1993. The committee feels that the effectiveness of NIH is now imperiled by the lack of adequate resources to provide appropriate support both for its primary research mission and for meeting its accountability responsibilities.

Recommendation 14: Increase Funding for Research Management and Support
Congress should increase the appropriation for RMS to reflect more accurately the essential administrative costs required to effectively operate a world class \$27 billion/year research organization effectively. Moreover, when additional congressional mandates are imposed on NIH through the appropriations process, they should include funds to cover necessary administrative costs.

Whether needs and opportunities will be accommodated in existing NIH units or proliferation or consolidation will occur in the near future is an issue to be addressed by future administrations, Congress, the scientific community, and the public. NIH will continue to be shaped by the dynamics of many interacting constituencies and influences. Interests will converge or conflict, depending on the issue. The degree of convergence and divergence will continue to be influenced by other important factors such as the level of annual congressional appropriations to NIH. The recommendations made in this report are intended to help NIH to continue to be responsive, accountable, and effective in its leading role in the vast international humanitarian enterprise of biomedical research aimed at a better understanding of the human condition, the prevention and relief of disease, and the promotion of good health throughout the stages of life.

Table: Summary of Recommendations

1. Assure that centralization of management functions will not undermine NIH's ability to identify, fund, and manage the best research and training.
2. Create a public process for considering proposed changes in the number of NIH institutes or centers.
3. Strengthen the overall NIH clinical research effort through consolidation of programs and creation of a new leadership position.
4. Enhance and increase trans-NIH strategic planning and funding.
5. Strengthen the Office of the NIH Director.
6. Establish a process for creating new OD offices and programs.

7. Create a Director's Special Projects Program to support high risk, high potential payoff research.
8. Promote innovation and risk-taking in intramural research.
9. Standardize level-of-investment data and information management systems.
10. Set terms and conditions for IC director appointments and improve IC director review process.
11. Set terms and conditions for the NIH director appointment.
12. Reconsider the special status of the National Cancer Institute.
13. Retain integrity in appointments to advisory councils and reform advisory council activity and membership criteria.
14. Increase funding for Research Management and Support.

INTRODUCTION

By any measure, NIH is an important component of a vast international humanitarian enterprise aimed at a better understanding of human health, prevention and relief of the burdens of disease, and promotion of good health throughout the stages of life. It is an optimistic endeavor predicated on the belief that human life can be improved through scientific investigations coupled with the rational and ethical applications of their findings. It is an enterprise full of moral relevance because it contributes to the interests of current and future generations and to the commitment to reduce health disparities.

In *Democracy in America* (1835), French statesman Alexis de Tocqueville wrote of what he perceived as the peculiarly American pursuit of good health. Although achieving that goal remains elusive for many Americans, since the middle 1900s the US government has invested generously in biomedical research,¹ believing that such activities would have great long-term benefits for the health of American citizens and others. There is broad agreement among the American people, Congress, and the Executive Branch that investing in biomedical research is socially desirable because of its health benefits, its capacity to increase understanding of the human condition, and its potential to directly or indirectly yield economic dividends. The assumption that federally funded scientific research generates economic and other benefits for the country has been fundamental to US science policy since the end of World War II (Bush, 1945). As Donald Stokes pointed out in *Pasteur's Quadrant* (1997), the American public deeply values such investment in science "not only for what it is, but what it's for."

The investment in human health improvement has paid handsome dividends. Age-adjusted rates of heart disease and stroke continue to decline, there has been a modest but encouraging decrease in cancer death rates, life expectancy continues to rise, infant mortality rates are falling, and the field of genomics has advanced to the point where promising new therapeutic agents are under development by biotechnology and pharmaceutical companies. The knowledge gained from biomedical research and the large cohorts of highly trained biomedical scientists continue to be among the nation's most valuable resources. Nevertheless, new public health concerns, chronic illnesses, emerging or re-emerging infectious diseases, and persistent health disparities constitute continuing challenges for our biomedical and health care research enterprise.

For nearly 65 years, the federal agency primarily responsible for sponsoring and conducting biomedical research has been the National Institutes of Health (NIH). NIH is one of eight agencies of the Public Health Service (PHS), which is part of the Department of Health and Human Services (DHHS).² NIH accounts for about 80% of federal funding of biomedical research and development (R&D); the Department of Defense (DOD) is the second largest supporter, at 6% (NIH, 2002). Since its formation, Congress and the Executive Branch have

¹ Biomedical research in this report includes all the following categories of research: fundamental (basic), applied, behavioral, bioengineering and biotechnology, clinical, dental, health, health services, nursing, outcomes, population-based, prevention, public health, rehabilitative, and therapeutic.

² The other seven are the Agency for Healthcare Research and Quality, the Agency for Toxic Substances and Disease Registry, the Centers for Disease Control and Prevention, the Food and Drug Administration, the Health Resources and Services Administration, the Indian Health Service, and the Substance Abuse and Mental Health Services Administration.

supported steady increases in NIH's budget. NIH is the largest public source of funding for biomedical research in the world, with an annual budget of about \$27 billion. In early 2003, Congress approved a FY 2003 budget containing a 16% increase over the previous year that completed the planned 5-year doubling of NIH's budget.

NIH, by most accounts, has long been considered one of the most effective and well-managed elements of the federal government and a centerpiece of its R&D system. From one categorical institute at the end of World War II, it has evolved into a federation of 27 major institutes and centers as of 2003 (see Chapter 2 for further discussion), each conducting and sponsoring research and related activities on aspects of human health and disease through grants and contracts to scientists in universities and other nonfederal research institutions.

To ensure its continued effectiveness, NIH must respond in a rapidly changing environment that is characterized by a renewed appreciation of the complexity of human biology; the increasing need for cooperation among biomedical and related disciplines and scientists working in different sectors; growing investments in biomedical research by the US corporate sector and other countries; the need to deal with new institutional arrangements in the broader scientific enterprise that generate additional incentives, conflicts, and constraints; and developments on the scientific frontier that, for example, require changes in the technologies used, the organization of research teams, and the active engagement of participants in clinical research. Equally important are the effective management of the rapidly expanded NIH budget and the challenge of managing the many organizational components of NIH - institutes, centers, and offices.

One Impetus for This Report

A persistent subject in discussions about the organization and future of NIH is the continued growth in the number of institutes, centers, and other programmatic and organizational components that have been mandated by congressional initiative in response to demands of various interest groups. Several NIH directors have raised concerns about such growth. Former Director James Wyngaarden, in congressional testimony arguing against the creation of another institute in 1982, pointed out that "there is virtually no end to the possibilities for creation of additional categorical institutes." From a scientific viewpoint, Wyngaarden noted the mismatch between the categorical structure of NIH and trends in research toward investigating the basic life processes that underlie all health and disease and away from the symptoms of specific diseases in isolation. From a managerial point of view, Wyngaarden raised the question of whether organizational complexity tends to be counterproductive (U.S. Congress, 1981).

Harold Varmus, the most recent NIH director to suggest that the agency is becoming unmanageable through continued proliferation, opposed the establishment of NIH's two newest units, the National Institute of Biomedical Imaging and Bioengineering (NIBIB) and the Center for Minority Health and Health Disparities (NCMHD). He argued that establishing program coordination units in the director's office was preferable to creating new institutes and centers for cross cutting fields (such as bioimaging) that should not be isolated as separate entities. He also expressed a disinclination to add to the number of units that have to be managed.³

³For example, Congress recommended that NIH establish an office of Bioimaging and Bioengineering, an idea that former NIH Director Harold Varmus welcomed. However, Varmus cautioned that establishing a new Institute of Bioengineering and Bioimaging was not a good idea because such activities benefit more by being distributed among the full range of institutes and centers at NIH (NIH, 1999).

Although he began to raise the issue in various forums during the last years of his tenure as NIH director (Dennis, 1999), Varmus laid out his analysis and proposed solution most fully in an article published in *Science* (Varmus, 2001) after his departure from NIH. He acknowledged the political advantages of establishing new institutes and centers but argued that NIH would be more effective scientifically and more manageable if it were organized into a far smaller number of larger institutes organized around broad fields of science.⁴ Consolidating the existing institutes into five entities “would organize the science in a rational way” (Dennis, 1999).

Others, including many biomedical investigators, argue that at the current time the elimination of institutes, centers, or offices that focus on particular sets of problems would mean that research on the problems would not receive sufficient attention and funding and argue that a consolidation of units would reduce congressional and public support. Those arguments were put forth by many of the organizations and individuals that wrote or spoke to the committee. Moreover, there is a perception that given the substantial increases in resources and the vast expansion of the biomedical enterprise, the addition of institutes and centers has provided for the expression of a broader set of priorities and expanded political support and budget success both for the specific interests involved and for NIH in the aggregate. While everyone understands that this expansion cannot and should not continue indefinitely, many see no particular difficulty with the current number of institutes and centers.

Many of the arguments against the formation of additional institutes and centers have focused on the adverse managerial and programmatic consequences at the NIH level (the opposite of the arguments for new institutes that stress the beneficial consequences of having one institute focused on a disease category or set of related problems) – the likelihood that a new institute or center will increase the share of the budget going to overhead because each institute has a director, senior staff, and administrative units, although some of these would be needed even if the program were kept or established in an existing unit.

Other arguments against adding institutes have had substantive grounds. In particular, there has been recurrent concern that adding an institute in a particular field could dilute, rather than concentrate, efforts in it. For example, many were concerned that the new NIBIB would reduce the commitment of other institutes to important opportunities in biomedical imaging and bioengineering. The same argument was made against creating the separate NCMHD: there was concern that establishing such a center would lead other institutes and centers to decrease their commitments to work in minority health.

All institutes and most centers are legislatively mandated, receive their own funding, and enjoy a constituency base that, given other characteristics of NIH’s environment, can reduce the organizational flexibility that less federated organizational structures give industry and many

⁴ In 2001, Varmus proposed a redistribution of NIH into six units of approximately equal sizes and budgets. Five of these would be categorical institutes, committed mainly to groups of diseases: the National Cancer Institute, the National Brain Institute, the National Institute for Internal Medicine Research, the National Institute for Human Development, and the National Institute for Microbial and Environmental Medicine. Each of these would contain several major divisions for extramural research and an intramural research program. Each would also house offices to coordinate research training, international science, minority and women’s health, and other activities, both within and among the five institutes. The sixth unit, NIH Central, would be led by the NIH director, to whom the directors of the five institutes would report. NIH Central would have responsibility for policies across NIH (e.g., on intellectual property, personnel management, or training programs), the peer-review process, scientific infrastructure (e.g., information technology, buildings and facilities, including the intramural Clinical Research Center), and thematic coordination (through links to the offices in each of the five institutes).

other government agencies, such as the National Science Foundation (NSF). In addition, as the number of institute and center directorships has increased, the recruiting and administrative burden on the NIH director has become substantial. Although some argue that NIH is becoming unmanageable, others believe that this is not the case and that substantial consolidation might not be programmatically desirable or politically feasible. In fact, some believe that the complex decentralized organization developed over the years has made NIH *more* effective in responding to research opportunities and public needs and aspirations and is an important source of its success (Congressional Budget Office, 2002).

In addition to the issues surrounding the proliferation of units, recent changes in biomedical science and how it is conducted may also raise questions beyond the narrow matter of the number of components in the organization. For example, research is becoming more interdisciplinary, more dependent on a common set of research tools and technologies (including costly large-scale infrastructure, such as supercomputers and imaging machines), and more focused on fundamental processes that underlie many diseases.⁵ Many of those developments increase the benefits of a strategic and coordinated effort among institutes and centers in some fields and may call for a more strategic NIH-wide approach to emerging challenges than has been traditional at NIH. Those emerging opportunities do not necessarily argue for a reduction in the number of units at NIH so much as for a change in the qualitative nature of the work conducted and the depth and breadth of interactions among the units.

Other trends also have caused some to believe that a review of the organizational structure of the agency is necessary. For example, demographics and patterns of illness in society are changing and investment by the private sector is growing, which has altered the terrain of some areas of research in a manner that could call for an adjustment in the role of NIH within the broader biomedical enterprise. Pharmaceutical and biotechnology companies now spend more than NIH on research and development - well over \$46 billion per year (Pharmaceutical Research and Manufacturers of America, 2001; Biotechnology Industry Organization, 2003). In addition, the Bayh-Dole Act (PL 96-517, Patent and Trademark Act Amendments of 1980) created a uniform patent policy among the many federal agencies that fund research, enabling small businesses and nonprofit organizations, including universities, to retain title to inventions made in federally funded research programs, thereby creating a new congressionally mandated responsibility of NIH to further technology transfer and commercialization of its research results by the private sector.

As a result of the steady stream of change, there have been persistent and growing concerns in Congress and in some parts of the scientific community about whether NIH has become too fragmented to address effectively the most important biomedical and health challenges or to respond quickly enough to health emergencies or economic challenges. Despite those persistent concerns, NIH has never been administratively reorganized in any substantial way, but only added to, despite vast changes in the landscape of science and the nation's health concerns during the last half century.

⁵ These trends have been cited by NIH leaders. See, for example, the remarks of Director Elias Zerhouni at a field hearing held by a subcommittee of the House Science Committee (Jenkins, 2002) and presentations by Acting Director Ruth Kirschstein (Kirschstein, 2001; Haley, 2001).

Congressional Request and Statement of Task

In report language that accompanied the FY 2001 appropriation act, Congress directed NIH to have the National Academy of Sciences study “whether the current structure and organization of NIH are optimally configured for the scientific needs of the twenty-first century.”⁶ Senate report 106-293 states:

The Committee is extremely pleased with the scientific advances that have been made over the past several years due to the Nation’s support for biomedical research at NIH. However, the Committee also notes the proliferation of new entities at NIH, raising concerns about coordination. While the Committee continues to have confidence in NIH’s ability to fund outstanding research and to ensure that new knowledge will benefit all Americans, the fundamental changes in science that have occurred lead us to question whether the current NIH structure and organization are optimally configured for the scientific needs of the Twenty-first Century. Therefore, the Committee has provided to the NIH Director sufficient funds to undertake, through the National Academy of Sciences, a study of the structure of NIH.

In response to the congressional request, the goal of this study was to determine the optimal NIH organizational structure, given the context of 21st century biomedical science. The following specific questions were to be addressed:

1. Are there general principles by which NIH should be organized?
2. Does the current structure reflect these principles, or should NIH be restructured?
3. If restructuring is recommended, what should the new structure be?
4. How will the proposed new structure improve NIH’s ability to conduct biomedical research and training, and accommodate organizational growth in the future?
5. How would the proposed new structure overcome current weaknesses, and what new problems might it introduce?

The Committee on the Organizational Structure of the National Institutes of Health was formed to ensure that the views of the basic science, clinical medicine, and health advocacy communities were all adequately represented. The Committee also included persons who were experienced in the management of large and complex organizations, including a former NIH director, two former NIH institute directors, a former university president, two individuals with backgrounds as senior managers of major industrial entities, and a specialist in organizational issues. Several Committee members also had considerable experience in government operations.

The Committee held six two-day meetings over the ten months between July 2002 and April 2003. In its initial meetings it invited past and present representatives of Congress, NIH, voluntary health groups, scientific and professional societies, and industry to provide

⁶HRpt 106-1033, “Conference Report to Accompany H.R. 4577 - Making Omnibus Consolidated and Emergency Supplemental Appropriations for Fiscal Year 2001,” December 15, 2000, endorsed the language in the Senate report calling for the NAS study of the NIH structure and asked for a report within a year of the appointment of the new NIH Director. See SRpt 106-293, “Departments of Labor, Health and Human Services, and Education and Related Agencies Appropriation Bill, 2001,” May 12, 2000.

perspectives on the issues before them (see Appendix A). In addition, the Committee met publicly with the current NIH director as well as several former directors. Committee members and staff also heard presentations from or interviewed NIH staff in the offices of policy and planning, budget, finance, and intramural research, and met with directors of 18 institutes or centers. Data about NIH programs and budgets were requested from NIH staff as the need emerged. Prior reports conducted about and for NIH were reviewed, as was the relevant literature. In addition, the Committee commissioned a background paper tracing the history and evolution of NIH and its institutes as a starting point for its deliberations (McGeary and Smith, 2002). Finally, several Committee members conducted town meetings at their home institutions and elsewhere, inviting scientists, administrators, and students to contribute their perspectives. Thus, the Committee was able to hear, consider, and discuss a diverse range of facts and opinions about the organizational structure of NIH. Its final report and recommendations are, however, based on the Committee's assessment of both the information available and current trends in biomedical science and health.

The Committee's Response to its Charge

This study focused on the organizational structure of NIH, but that cannot be addressed satisfactorily without considering the mission of NIH, some of its key processes, and the scientific and social-political environment in which NIH activities take place. Although a long series of past reviews of NIH helped inform committee deliberations, the nature of the charge and the 1-year period allowed for deliberations constrained the development, character, and scope of the recommendations that the Committee could credibly put forward. Most important, the committee was not asked to address NIH's research priorities or the quality and effectiveness of the wide array of research and advanced training programs that NIH undertakes or sponsors.

Even a relatively narrowly defined focus on the organizational structure of NIH was challenging because of the need to disentangle structure, procedure, policies, achievements, criticisms, and priorities. For example, the Committee debated whether its charge referred solely to the number of institutes and centers that can be effectively and responsibly managed or could it also assess the role and authority of the NIH director? Should the nature, role, and scope of the intramural research program be discussed because the program is a key structural element of NIH? Over the years many talented and energetic scientists have occupied various leadership positions at NIH and introduced a wide variety of innovative organizational initiatives. Many of these initiatives have been successfully implemented in individual institutes, centers, and offices, but they have not moved easily from unit to unit or survived changes in leadership. What managerial mechanisms might ensure the widespread adoption of best practices by the institutes, and how might they be adopted or strengthened in place of or in conjunction with structural reorganization? One could pose numerous additional questions in an attempt to understand and define the set of activities, processes, and procedures encompassed by the term organizational structure. And such questions cannot even be approached without considering the role and mission of NIH.

The Committee's view of those complexities was governed by the desire to be of some practical assistance to all those who wish NIH to continue to be an effective - indeed, outstanding - organization. The Committee therefore took its task to include assessing the organizational configuration of NIH—both its quantitative and qualitative aspects—and the key processes and authorities that play roles in NIH-wide decision-making. Although the borders between structure, mission, and priorities are themselves not well defined, the Committee tried

not to take too expansive a view of its responsibilities. In addition, Elias Zerhouni, the current NIH director, suggested to the committee at its first meeting that it would be useful for the committee to concentrate on and assess eight specific issues:

1. The effectiveness of governance mechanisms
2. The effectiveness of decision-making processes across and within the institutes
3. The balance between centralization and decentralization
4. The need for better management tools (NIH-wide standards and methods)
5. The development of mechanisms to allocate (or redirect) resources across NIH
6. Mechanisms for coordination of science
7. The ability of the NIH leadership to hold institutes accountable
8. The need for strategic human resources policies

Based on the advice it received from former and current NIH directors as well as its conversations with congressional staff, throughout its deliberations the Committee kept a number of broadly conceived organizational ideas in mind. First, scholars of organizational management (e.g., Waterman, Peters, and Phillips, 1980) have long recognized that there is more to “organization” than structure. An organization’s ability to make effective changes is influenced by a multiplicity of factors beyond the number of units or shape of its organizational chart, for example strategy, structure, systems, staff capabilities, shared values, and behavior. “Systems” refers to all the formal and informal processes and procedures that organizations rely on to function. The word “organized” calls the question: Organized to do what? The answer typically is: Organized to build new institutional capability or new skill— in this case, for example, the institutional skill to adapt research and training programs to the new demands of science. To respond to change, an organization must work out its *strategy*—preferably mixed strategies—and, if necessary, *restructure* in order to implement those strategies. Also it will have to change other dimensions of the way it organizes itself to respond. In line with these views, the Committee believes that many potential changes in aspects of NIH other than the number of blocks on its organizational chart could improve its overall effectiveness and help it to stay at the cutting edge of biomedical research.

Therefore the Committee considered numerous proposals for restructuring NIH in great detail⁷ but did not focus exclusively on whether or not there should be a widespread consolidation of NIH’s institutes and centers. Rather, it took a more general approach, namely to inquire if there were any significant organizational changes—including the widespread consolidation of institutes and centers—that would allow NIH to be even more successful in the

⁷ In their background paper prepared for this Committee, McGeary and Smith (2002) summarized the published responses to the Varmus proposal and the results of their interviews on this topic. In addition, at its inaugural meeting, July 30-31, 2002, the Committee heard from Bernadine Healy, NIH director from 1991 to 1993, who suggested grouping NIH in four quite different “clusters”: 1) federal laboratories and the clinical center to deal with emergency issues; 2) health and disease institutes; 3) medical and scientific institutes; and 4) a national research capacity (e.g., NCCR, NLM, large clinical trials capability). Dr. Healy was not opposed to forming more institutes—she even suggested two new units for nutrition and rehabilitation. She noted, however, that abolishing institutes is easier said than done. This was reiterated by former Illinois Representative and House Appropriations Subcommittee Chair John Porter, who told the group that any attempt to eliminate individual institutes will likely meet strong political resistance. He urged the committee to think of ways to eliminate duplication and increase consolidation and accountability.

future. Although the Committee discussed on numerous occasions the advisability of the widespread consolidation of NIH, it eventually came to believe that this was not the best path for NIH to take at this time.

It is important to understand that the structure of any large and complex organization, such as NIH, is not the tidy result of a compact set of compelling propositions emanating from organizational theory any more than the particular organization of our complex pluralistic democracy is the result solely of the inspired thinking of political philosophers. The latter is instead the outcome of our particular form of politics and, therefore, heavily influenced by our particular history and evolving cultural commitments. It is very much the same way with NIH. It would be naïve to assume that NIH was or should be organized exclusively along the lines dictated either by the imperatives of the scientific agenda or the priorities of any other single set of interests with a concern about promoting health-related research and advanced biomedical training. Rather NIH's existing structure is the result of a set of complex evolving social and political negotiations among a variety of constituencies including the Congress, the administration, the scientific community, the health advocacy community, and others interested in research, research training, and public policy related to health. Indeed the history of NIH provides clear evidence that each of these communities has always had a variety of views on the appropriate organization of NIH. From any particular point of view or for any particular set of interests, the current situation is not only imperfect, but is certainly not one that either the Congress or the scientific community would designate *ab initio*. Rather it has evolved as a very useful and largely productive outcome of a series of political and social negotiations that took place over time. This outcome is typical of the design of important social organizations in a pluralistic democracy. NIH has become an organization that balances its many interests and the Committee felt that any major modification at this point in time should focus directly on enhancing NIH's capacity to pursue major, but time limited, strategic objectives that cut across all the institutes and to acquire a special ability to pursue more high risk, high return projects. It was our view that at this moment the widespread consolidation of institutes and centers should not be a high priority as the benefits to be gained would not sufficiently offset the costs involved, particularly when there are other available options that could achieve the same benefits.

What does the Committee mean by "costs"? At a minimum, because Congress created the institutes, dissolving or merging institutes would require congressional action. Any thoughtful major reorganization would necessitate a lengthy and complex information gathering and decision making process that would include numerous congressional hearings involving members of Congress, congressional staff and a wide variety of interests in the various health advocacy and scientific communities. Our discussions, correspondence and meetings made it quite clear that there would be very little agreement among these communities on what the right way to reorganize NIH is, and there would probably be dozens of conflicting ideas in play and few clear avenues for narrowing these down. Moreover these discussions and negotiations would be long and contentious ones and with a quite uncertain outcome. More importantly the Committee is firmly convinced that many of the goals that might be achieved through large-scale consolidation of institutes could also be achieved more rapidly and effectively through other organizational and administrative mechanisms, as recommended in this report.

Nevertheless the committee did feel that no organization as important as NIH should remain frozen in organization space and that some regular, thoughtful, and publicly transparent mechanism is required to allow changes to take place at appropriate times. Although the

committee does believe that the consolidation of two pairs of Institutes is appropriate at this time, it felt that this issue ought to have the benefit of the public process it has recommended.

Thus, as laid out in this report, the Committee did not find a compelling intellectual argument for widespread consolidation of institutes and centers at this time. It did, however, identify numerous opportunities for organizational change to improve the agency's responsiveness and flexibility and makes several suggestions for adopting an array of strategies to better accomplish NIH's research mission.

The committee was aware that all organizational changes, however well thought out, carry both potential risks and benefits, and it has done its best to sort these out. It also recognized that the decentralized structure of NIH, which allows many people throughout the scientific and advocacy communities to help to set priorities, has been and should continue to be an integral element in NIH's success. The current structure of NIH allows the public to see its many faces. The Committee believes that this has been a very useful organizational response to a complicated set of scientific and political influences. The Committee was particularly mindful of the need to sustain the coalition that has made NIH the success that it is today. In addition, the Committee kept the enormous benefits of investigator-initiated grants, including those focused on fundamental research, firmly in mind during its deliberations. Finally, the Committee understood that the quality of leadership and decision-making at all levels, as opposed to administrative structures, is central to NIH's ongoing vitality. In the long run, the recruitment of outstanding leadership, the commitment to individual scientists as the main sources of new discoveries, and reliance on the competitive review system for determining awards will continue to be essential to NIH's continuing success.

That NIH has been working well does not mean that it could not work better if - in response to changes on the scientific frontier, to changes in health concerns, or to other important environmental shifts - some organizational changes were made. The intent of this report is to assess the current organizational structure of NIH and to suggest modifications that might be appropriate to make NIH even more effective in supporting research essential to the long-term goal of improving human health.

General Principles by Which NIH Should Be Organized

NIH accomplishes its objectives through the design, organization, administration, and management of extramural and intramural research and training programs and the provision of specialized research facilities that support the programs. In broad scope, NIH's priorities focus on scientific research that is most likely to shape the understanding, diagnosis, treatment, and prevention of society's most important health challenges. That focus includes strong support of fundamental scientific research that is aimed at improving our understanding of organisms, processes, biological systems, and individual and societal risk factors broadly believed to be relevant to human health. It also embraces support of graduate and postgraduate training needed to ensure an adequate supply of scientists to continue to study those important health concerns.

An evaluation of NIH's priorities requires explicit recognition of a number of interrelated factors. Most important in this respect is an understanding of the evolving nature of the scientific enterprise, which includes not only the changing nature of science itself but also the evolving role of other institutions and other disciplines, both here and abroad, that have generally similar aims and the changing nature of our health concerns. Recognition of the global nature of medical and health problems and their relevance to the interests and health of the people of the United States warrants special mention. Finally, and perhaps most obvious, the level of resources

available to NIH clearly will affect the profile and extent of NIH's activities. Effective management of its resources is especially challenging now because of the pace of scientific developments, new health priorities, the changing institutional structure of the biomedical research enterprise, and recent rapid budget growth.

In going about its task, the Committee first addressed the opening question in its statement of task: "Are there general principles by which NIH should be organized?" Only by arriving at an early determination of NIH's principal overall function and the mechanisms in place to achieve its mission could the Committee adequately address the other items in its charge. Thus, an overarching mission and the mechanisms needed to meet it became the basis of the remainder of the committee's tasks. The recommendations developed by the Committee focus on modifications in basic policies and organizational structure that are designed to assist NIH in performing its primary function.

The success of NIH in meeting its various challenges and, in particular, fulfilling its mission to improve health through the use of science to develop new knowledge has been outstanding. All those who have contributed to the creation and dynamic evolution of the NIH—the institutions it has supported, the scientists and health professionals who have created so much knowledge and understanding, and the American people and their elected representatives—have helped to reduce humankind's burden of disease, disability, and premature death. NIH has also been successful in catalyzing changes at the frontiers of science. Those changes and the recent doubling of NIH's budget make this an appropriate time to consider whether the organizational structures that have served NIH and the world so well in the past remain appropriate for its future roles.

The charge to this Committee is worded in the form of a series of questions about whether there are general principles around which NIH should be organized. In the context of evaluating NIH's organizational structure, the Committee decided to describe the principles as they relate to NIH's overall mission and the basic policies, structural and otherwise, adopted to achieve it. In the end, the Committee agreed that articulating its view of the mission of NIH would provide the appropriate foundation to guide its deliberations:

NIH's principal mission is to serve as a mechanism for efficiently and effectively deploying federal resources across a wide array of institutions and individuals in the nation's scientific community to advance the scientific frontier and ensure research and training in fields of special relevance to human health needs.⁸

Some might view this mission as stopping short of the goals of public health, that is, not including the goal to directly improve human health. The Committee was cognizant of the tension that exists among the scientific, medical, patient, and political communities about expectations of NIH. It concluded, however, that improving health—as much as it is critically dependent on accurate and adequate science—is a goal that also involves health providers, industry, and policy makers and is influenced by social and economic factors that range far from the research mission of NIH. Moreover, NIH is but one of eight DHHS agencies charged with a health-related mission. The other agencies - Agency for Healthcare Research and Quality, the

⁸ NIH states its mission as "science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability (NIH, 2001).

Centers for Disease Control and Prevention, the Agency for Toxic Substances and Disease Registry, the Food and Drug Administration, the Health Resources and Services Administration, the Indian Health Service, and the Substance Abuse and Mental Health Services Administration - also focus on health and complement the research mission of NIH. There is no question that these agencies must work together even more effectively to ensure that there is a continuum of federal effort and concern regarding improved health for all Americans.

Based on its view of NIH's mission, the Committee agreed that there follows from this fundamental charge a list of subprinciples or basic policies and approaches that, if adhered to, would allow NIH to achieve its mission:

1. The NIH research and training portfolio should be broad and integrated, ranging from basic to applied and from laboratory to population-based, in support of understanding health and how to improve it for all populations. The portfolio should reflect a balance between work in existing highly productive domains or disciplines and high-risk, groundbreaking, potentially paradigm-shifting work. The portfolio should be especially responsive whenever scientific opportunity and public health and healthcare needs overlap.
2. NIH should support research that cuts across multiple health domains and disease categories. This might require special efforts to integrate research across NIH components.
3. The NIH research and training portfolio should make special efforts to address health problems that typically do not attract substantial private-sector support, such as prevention, some therapeutic strategies, and many rare diseases.
4. The standards, procedures, and processes by which research and training funds are allocated should be transparent to applicants, Congress, voluntary health organizations, and the general public. Moreover, a wide variety of constituencies should have input into the setting of broad priorities.
5. Extramural research should remain the primary vehicle for carrying out NIH's mission. Open competitive peer review should be the usual mechanism guiding extramural funding decisions.
6. The intramural program is a federal resource that enhances NIH's ability to fulfill its mission. The program should seek to play a unique and distinctive role in the nation's scientific enterprise.
7. As a world-class science institution, NIH should have state-of-the-art management and planning strategies and tools. A key need is the ability to retrieve comprehensive and interpretable NIH-wide data related to its various objectives.
8. There should be appropriate mechanisms to ensure the continuing review, evaluation, and appointment of senior scientific and administrative leaders at all levels of NIH.

9. Proposals for the creation, merger, or closure of institutes, centers, and offices should be considered through a process of thoughtful public deliberation in which potential costs, benefits, and alternatives are addressed.

Organization of the Report

To place the Committee's analysis and recommendations in context, Chapter 2 provides background information about the evolution of the structure and organization of NIH. Chapter 3 focuses on examples of how new discoveries are changing the conduct, review, and evaluation of science and addresses whether the NIH structure is suitably configured to adapt to these changes and to promote them.

In Chapter 4, the Committee focuses on the NIH structure itself and processes for merging, consolidating, or expanding the number of its components, including a proposal to revitalize and integrate clinical research.

Chapter 5 provides ideas and suggestions for reorganization that could facilitate the conduct of increasingly important trans-NIH scientific research and enhance NIH's ability to maintain itself at the leading edge of scientific progress. The chapter proposes changes that would enhance the NIH director's authority, particularly as related to trans-NIH initiatives that should begin to constitute a larger proportion of NIH activities, mechanisms for fostering high-risk research, and the intramural research program.

Chapter 6 discusses issues related to NIH's need to be publicly and financially accountable through its advisory and review processes, data systems, leadership, and administrative efficiency, including the budgetary and administrative issues related to managing a large research organization.

Chapter 7 summarizes the recommendations made in the report in the context of their consistency with the principles and basic policies elucidated in this introduction.

Summary

NIH will continue to be influenced both by scientific developments and by a changing political landscape and growth in the numbers and sophistication of scientific and health advocacy groups. Interests will converge or conflict depending on the degree to which issues are influenced by such factors as the state of the economy and the federal budget. It may seem easier to innovate and cooperate when the budget is increasing, but rapidly increasing budgets can also overwhelm good planning and long-term strategic thinking. In any case, it is clear that when budget growth slows, especially in an era of great opportunity and need, difficult decisions arise and priorities are affected.

Independently of budget issues, NIH is increasingly called on to perform in a coordinated way to address key research subjects that involve multiple institutes and to respond to immediate public health needs. An important question is whether NIH's federated and decentralized structure, as currently configured, can respond adequately and in a timely manner to those challenges. This report makes a series of recommendations aimed at increasing and enhancing NIH's ability to accomplish its mission.

THE EVOLUTION OF NIH'S ORGANIZATIONAL STRUCTURE

The National Institutes of Health (NIH) began as a modest set of federal research laboratories supporting the public health mission of the Public Health Service. As a result of the nation's steady determination to increase its commitment to research in the biomedical and related sciences, NIH has evolved into a large and complex decentralized organization that sponsors research throughout the United States and at some sites abroad. NIH now consists of 20 institutes (including the National Library of Medicine, NLM), seven centers, and four programmatic offices in the Office of the Director (OD) that are intended to coordinate activities in specific fields across NIH (Figure 2.1). Only institutes and some centers have authority to award research grants; the Clinical Center, Center for Information Technology, and Center on Scientific Review do not award research grants. The 20 institutes and four of the seven centers have their own appropriations.⁹ More than 40 unit heads report directly to the NIH director: the directors of the 27 institutes and centers, 12 staff offices, and four program offices.

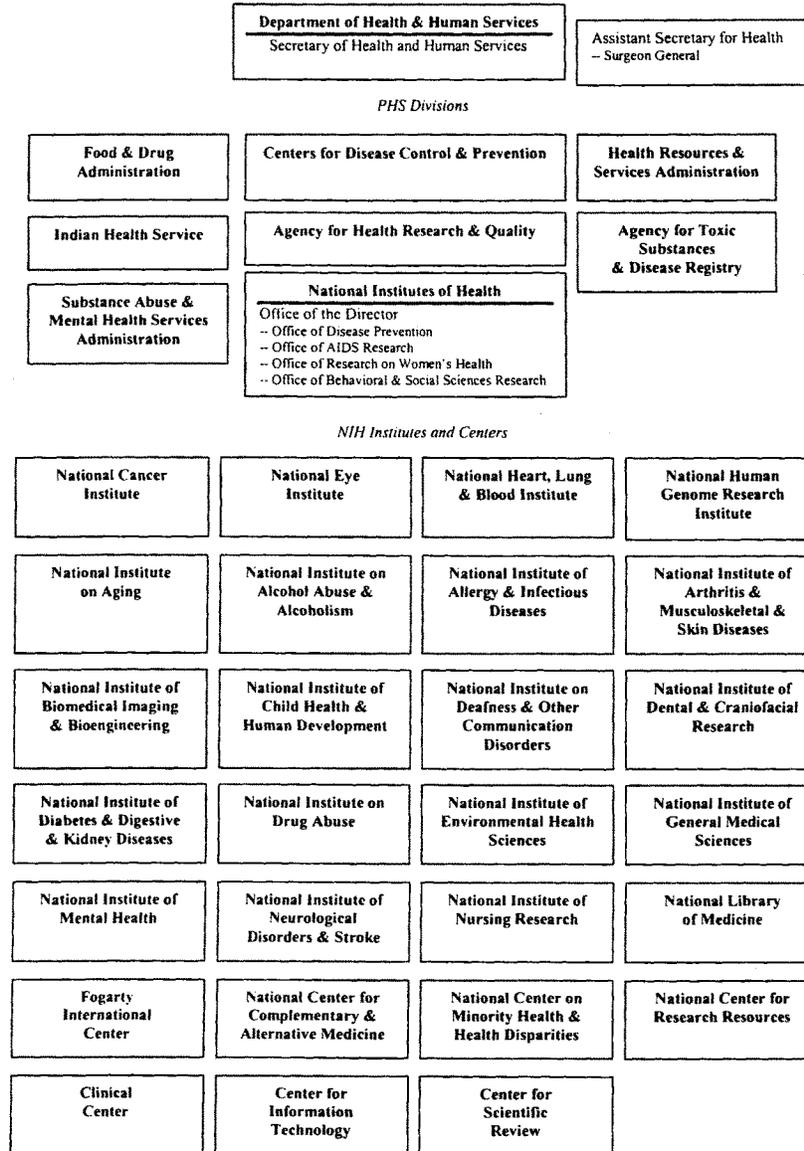
The size and expanse of the agency are impressive. In FY 2002, NIH's budget funded 43,600 research grants and 1,600 contracts in universities, medical schools, and other research and training institutions in the United States and abroad and supported 16,700 full-time training positions.¹⁰ NIH employs about 17,700 full-time personnel. The intramural research program consists of more than 2,000 research projects conducted by more than 9,000 government scientists and technical support staff. The agency occupies 75 buildings on more than 300 acres in Bethesda, MD, including laboratories and a 267-bed clinical research facility. One of the institutes, the National Institute of Environmental Health Sciences (NIEHS), is in North Carolina. Additional facilities are in Baltimore, Frederick, and Poolesville, MD; Hamilton, MT; and other locations. NIH supports about 50,000 researchers at 2,000 universities and colleges, health professional schools (medicine, dental, public health, pharmacy, and nursing), teaching hospitals, independent nonprofit research institutes, and industrial laboratories in all 50 states and some other countries.

There have been unsuccessful efforts to bring other health research agencies under the NIH umbrella. For example, the National Institute for Occupational Safety and Health and the National Center for Health Services Research (now the Agency for Healthcare Research and Quality) have, at times, been considered good candidates for integration into NIH, but they were perceived as too far removed from the biomedical research mission of NIH.

⁹ In addition, there are appropriations for the Office of the Director and for Buildings and Facilities, for a total of 26 separate appropriations for NIH in the Labor/Health and Human Services Appropriations Act.

¹⁰ These figures are based on the President's budget request for FY 2003 to the Labor/Health and Human Services/Education Appropriations committees. NIH also receives some funding under the Department of Veterans Affairs and Housing and Urban Development appropriation (\$76 million is requested for environmental research in FY 2003) and the Balanced Budget Act of 1997 (\$97 million for type 1 diabetes research is requested in FY 2003). See on-line table at <http://www4.od.nih.gov/officeofbudget/CJ2003/Mechanism%20-%20Total%20Proposed%20Law.PDF>.

Figure 2.1 Current Organization of NIH



Institutes

The institutes are highly varied and reflect not only their particular foci and budgets but also the varied circumstances of their creation, how long they have been in existence, the nature of the scientific opportunities available, the strength of support by their advocates, and the priorities of the administration and of Congress. They are broadly similar to each other in their relationships with the NIH director, Congress, and the other institutes and centers.

The NIH institutes can be thought of as being in five general categories, although there is no optimal taxonomy for this purpose. Some are organized by disease (for example, cancer; mental health; diabetes and digestive and kidney disorders; arthritis and musculoskeletal and skin disorders; neurological diseases; allergies and infectious diseases; deafness and other communication disorders; and drug and alcohol abuse). Some are organized by organ system (for example, heart, lung and blood; and eye); some by life stage (child and human development and aging); some by field of science (for example, general medical sciences, environmental health sciences, and the human genome); and some by profession or technology (nursing, dental, biomedical imaging and bioengineering) (Morris, 1984).¹¹ Those institutes organized by life stage have complex relationships to those organized by disease group or organ system with extensive, indeed near overlap with the missions of other institutes; for example, the National Institute of Child Health and Human Development (NICHD) overlaps in nearly all of its research with other categorical institutes and in many ways serves as an institute for the profession of pediatric research and to some extent obstetrics research. Such overlaps can create tensions among institutes—some that are likely to be beneficial and some that are likely to be detrimental, depending on how they are acknowledged and responded to.

The most common mechanism of origin of the institutes has been the Congressional mandate responding to the health advocacy community. Some, however, have developed in their own special circumstances. The National Human Genome Research Institute was established by NIH around a particular scientific objective. NIEHS, which focuses on the health effects of environmental exposures, was organized around a health problem, but not at the urging of health advocacy groups. NICHD and the National Institute on Aging (NIA) were organized around population groups (in 1962 and 1974); more recently, units focused on the health of women and minority groups were established in the 1990s and may be candidates for eventual elevation to institute status. The National Institute of Nursing Research was organized around a professional group—nurses—in 1993, and the establishment of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) was authorized in 2000 after a 5-year advocacy campaign by radiologists and bioengineers.

Each institute except for the National Cancer Institute (NCI) has a director with a research background who is appointed by the Secretary of Health and Human Services. (The director of NCI was made a presidential appointee by the National Cancer Act of 1971; see Box 2A.) Each institute has a national advisory council to advise the institute director on policies and priorities and to provide a second level of review for extramural grant applications recommended for funding. All but one of those councils are appointed by the Secretary of Health and Human Services. (The National Cancer Advisory Board and the President's Cancer Panel of NCI are appointed by the President.) All institutes but one (the National Institute of General Medical

¹¹ The categories and assignments through 1984 follow Morris, 1984:67. The last category, for nursing, dentistry, and imaging, has been added.

Sciences) have intramural programs that perform basic and clinical research at the Clinical Center, in laboratory facilities on the NIH Bethesda campus, or elsewhere. Boards of Scientific Counselors advise each institute director on and oversee the performance of the intramural program and its researchers. Until recently, each director had a staff that mirrored the staff of the NIH director, including deputies for intramural and extramural research and offices for budget, administration, communications, legislation, and personnel. (Some of these functions have been or may be consolidated under the One HHS initiative discussed below.) The extramural grant programs of the institutes receive the largest share of their budgets. As measured by their budgets, institutes have grown at different rates over time. Starting from a small base, new institutes tend to receive large percentage budget increases in their early years.

Box 2A: The National Cancer Act of 1971 [P.L. 92-218]

- Outgrowth of the report of the National Panel of Consultants on the conquest of Cancer (the Yarborough Commission)
- Elevated and expanded certain authorities of the National Cancer Institute director, including appointment by the President and preparation and submission of the annual budget estimate (Bypass Budget) directly to the President
- Established the President's Cancer Panel and the National Cancer Advisory Board
- Initiated the National Cancer Program under Sec. 407 of the PHS Act as follows: "(a) The Director of the national Cancer Institute shall coordinate all of the activities of the National Institutes of Health relating to cancer with the National Cancer Program. (b) In carrying out the National Cancer Program, the director of the National Cancer Institute shall: (1) With the advice of the National Cancer Advisory Board, plan and develop an expanded, intensified, and coordinated cancer research program encompassing the programs of the National Cancer Institute, related programs of the other research institutes, and other Federal and non-Federal programs."
- Authorized the first cancer centers
- Established cancer control programs as necessary for cooperation with state and other health agencies
- Established an information dissemination program
- Established the International Cancer Research Data Bank

Centers

There are two types of centers. Some do not fund or conduct research, but rather provide operational support to the rest of NIH. The Center for Scientific Review (CSR), for example, is concerned solely with coordinating the activities of the set of scientific peer review panels called study sections, which review and score applications submitted to NIH for research grants and fellowships and recommend the most promising ones to the institutes for funding. Other centers conduct or support research and have been established as a result of legislation, for example the Fogarty International Center.

Office of the Director

To carry out responsibilities that include planning, coordinating and managing the programs of the 27 institutes and centers, the NIH director is assisted by units in OD known collectively as OD Operations. In addition, several offices and programs in OD address problems that the director or Congress believe need high-level NIH-wide attention. In all, 12 staff offices and four program offices report to the Director,¹² in addition to the 27 institute and center directors.

The 1980s and 1990s saw the development of program offices in OD to help to promote and coordinate activities that are not solely in the portfolios of any of the individual institutes (Table 2-1). The Office of Disease Prevention, which includes the Office of Rare Diseases (ORD), the Office of Dietary Supplements (ODS), and the Office of Medical Applications of Research, was created in 1985 as a response to a congressional desire to increase disease prevention research. It is headed by an associate director for disease prevention. The Office of AIDS Research was established in 1988 to coordinate AIDS research and is also headed by an associate director. The Office of Research on Women's Health and the Office of Behavioral and Social Sciences Research were created in 1990 and 1995 respectively. Two program offices also created in the 1990s (alternative medicine and minority health) have since been elevated to center status, which gives them national advisory councils and the authority to award research grants. The Office of Bioengineering and Bioimaging has become an institute, NIBIB. Funding for OAR is specified in the appropriation act, and the funding of several other offices is earmarked in the OD appropriation in the conference committee report, for example, \$10.4 million for ORD and \$17.0 million for the ODS in FY 2002.

The NIH director reports directly to the Secretary of Health and Human Services. Although the NIH director has considerable influence with Congress and the Administration with respect to the overall budget of each institute and center, he or she does not have strong formal authority with respect to the operation of the institutes. Institute and center directors have considerable autonomy, but they probably recognize the benefits of having a strong NIH director in securing increased support from Congress and the Administration. Ideally, the NIH director is not only a distinguished scientist and a person with compelling ideas, but also an able leader with the ability to recruit other effective leaders and work well with the Secretary of Health and Human Services, other members of the Administration, and Congress. The director has a small (\$10 million) discretionary fund and, in principle, the authority to transfer up to 1% of an institute's or center's appropriation to another unit as long as the transfer does not increase any one appropriation by more than 3%. The federal budget and appropriation process, which culminates in a set of appropriations to NIH and its various institutes and centers, is the most important management tool available to the NIH director, who may use it to influence priorities and ensure that NIH is responding to opportunities and problems as he or she sees them develop. The budget and appropriation process, which begins internally, ultimately involves substantial interaction with the Department of Health and Human Services (DHHS), the Office of Management and Budget (OMB), and, on rare occasions, the President. Because of the central and historically generous role of Congress in the appropriations process, health advocacy groups are most likely to direct their lobbying efforts at the legislature.

¹² See OD organization chart at <http://www1.od.nih.gov/oma/manualchapters/management/1123/nih.pdf> and "Organization and Functions, NIH, OD" at <http://odeo.od.nih.gov/about/org/tocodo~1.htm>.

Office	Year Established	<i>Major Focus</i>
Office of AIDS Research	1988	Planning, coordination, evaluation, and funding of all NIH AIDS research and support of trans-NIH coordinating committees in areas of AIDS research
Office of Research on Women's Health	1990	Focal point for women's health research at NIH, including establishment of a research agenda; inclusion of women as participants in NIH-supported research; and support of women in biomedical careers
Office of Disease Prevention, which includes the Office of Rare Diseases (1993), Office of Dietary Supplements (1995), and Office of Medical Applications of Research (1977)	1985	Coordination of disease prevention activities, advice to director on disease prevention research; promotion and coordination of NIH-wide research on rare or orphan diseases and on the role of dietary supplements in health; work with institutes and centers to assess, translate, and disseminate results of biomedical research that can be used in delivery of health services
Office of Behavioral and Social Sciences Research	1995	Stimulation of behavioral and social science research throughout NIH and its integration with other research conducted or supported by NIH

The Budget Process

To understand how NIH has evolved, it is important to understand its funding environment and budget process (see Figure 2.2). NIH's statutory authority comes from the Public Health Service Act (PHSA) of 1944, as amended (42 U.S.C., et seq.). Some institutes and several programs (training and facilities construction) are subject to time and dollar authorizations that require periodic renewal by Congress.¹³ The last authorization, the NIH Revitalization Act of 1993, lapsed in 1996 (P.L. 103-43); the effort to renew the authorization in 1996 failed because of conflict over provisions about the use of fetal tissue in research. There have been no further efforts to pass a general reauthorization of NIH.¹⁴

Since 1996, NIH has operated on the basis of annual appropriation bills, although technically appropriations amounting to nearly half of NIH's funding are unauthorized. In the absence of authorizations, the appropriation committees, in their legislation and report language, have provided guidance that is similar to the guidance that authorizing committees enact. From time to time, bills to make specific changes in the PHSA are introduced; sometimes they are passed, such as the one that established NIBIB in 2000 (P.L. 106-580) and the one that established centers of excellence for research on the muscular dystrophies in 2001 (P.L. 107-84).

¹³ The War on Cancer Act of 1971 was the first to impose time and dollar limits on an institute.

¹⁴ The 1994 authorization for the National Institute of Mental Health, the National Institute on Alcohol Abuse and Alcoholism, and the National Institute on Drug Abuse (P.L. 102-321) has also lapsed. See Congressional Budget Office, 2002.

NIH, DHHS, OMB, and Congress manage the NIH appropriation primarily through a mechanism budget, that is, a set of budget functions that aggregate similar types of expenditures across NIH. Most of the budget (more than 80%) funds extramural activities, including research, training, and construction of facilities.¹⁵

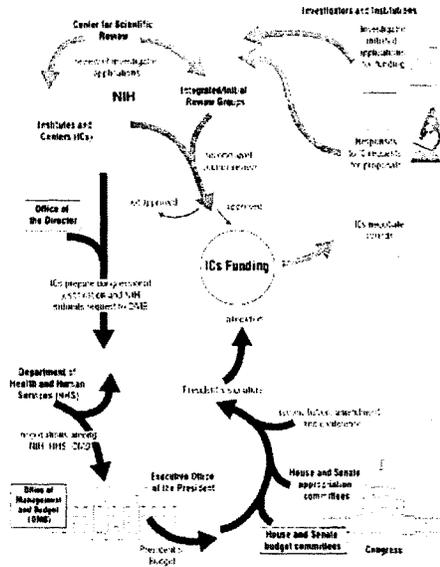
Six congressional committees affect NIH funding: the authorizing and appropriating committees for DHHS in each house and the House and Senate Budget Committees. Officially, the Budget Committees set targets for NIH appropriations in the DHHS budget. The role of the authorizing committees is to set a level of funding that the appropriations committees may not exceed, although historically NIH has benefited from having an open-ended authorization, that is, Congress authorized "such sums as may be necessary" without a time limit. During a period of conflict between the President and Congress in the 1970s, Congress began to exert tighter control over some institutes by imposing time and dollar limits in the authorizing legislation. Currently, NCI, the National Heart, Lung, and Blood Institute, NIA, the National Institute of Mental Health (NIMH), the National Institute on Drug Abuse (NIDA), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), NLM, and the National Research Service Awards (training and fellowship programs) are subject to time-and-dollar limits. As noted above, those programs have been operating with unauthorized appropriations since 1996, which underlines the fact that currently the appropriations committees exert the most influence on NIH. The authorizing committees can and do originate specific pieces of legislation affecting the organization of NIH, such as the law creating NIBIB. But the appropriations committees are not required to fund mandates in authorizing legislation.

The appropriations committees tend to have substantial influence on all aspects of NIH, including its organization, because of the rather open-ended grants of authority by the authorizing committees. Although they do not put much detail into law - usually just the total for each appropriation - they can use the reports that accompany bills to mandate NIH actions, including establishment of new organizational units. Report language does not have the force of law, but agencies try to follow it because they know that they will be before the appropriations committees again each year.

The main impact of the congressional budget process on NIH has been to reinforce the autonomy of the institutes and centers through their separate appropriations. That means that the NIH director has no formal role in the budget *execution* stage, except for the seldom-used authority to transfer up to 1% of each institute's appropriation.

¹⁵ The extramural share of the NIH budget is a little larger than the 80.9% accounted for by research grants, training awards, research and development contracts, and extramural construction in FY 2002 because the National Library of Medicine, Cancer Prevention and Control, and Office of the Director budgets also include some extramural support.

Figure 2.2: The Annual Budget Process for NIH Compared with its System for Allocating Funds



Caption for Figure 2.2: This figure illustrates the complex processes involved in NIH's budget. To begin the process, the institutes and centers work with the NIH director to develop their budget requests using guidance from OMB and HHS. The resulting budget is submitted through HHS and OMB to the President, and then appropriated by Congress, although numerous changes may be negotiated at many points along the way. After the institutes and centers receive their funding allocations, money is awarded to individual investigators and institutions through the peer review system under the administration of individual institutes and centers. Investigators may initiate proposals for funding on topics of their own choosing or may submit proposals in response to solicitations on specific topics from the institutes and centers.

Advisory Committees

Like other federal science agencies, NIH makes extensive use of advisory committees (see Box 2B). The committees are composed of nonfederal scientists, health advocates, and laypersons to ensure that scientific expertise and public input are considered in making policies and evaluating programs. Advisory committees also foster a broader understanding of public concerns by the scientific community and increase public understanding of the scientific and technical impediments to research progress (NIH, 2001). NIH had 140 chartered advisory committees as of May 2002 - more than any other federal agency.¹⁶ In total these advisory groups have 4,298 members, of whom 75% are members of the scientific review groups that evaluate applications for research funding. All the groups operate under the guidelines of the Federal Advisory Committee Act of 1972, as amended.

NIH uses advisory committees for initial and second-level peer review of applications for research grants and for policy and program advice. The overall purpose of the committees is to help to ensure that NIH programs are responsive to both scientific opportunity and health needs. The system of advisory committees is also an important mechanism for coordination and management. They include the Advisory Committee to the Director (ACD), the director's Council of Public Representatives (COPR), and the advisory councils established by law for each institute. The director's level advisory groups and ad hoc groups appointed to address particular issues provide NIH leaders with external views and advice on overall research needs and program priorities. The national advisory councils to the institutes, which include scientists and laypeople, provide a similar function to institute directors.

Box 2B: NIH Advisory Committees

NIH uses four types of advisory committees. Two are directly involved in reviewing grant applications, through what NIH calls a "dual review system."

Integrated/Initial Review Groups and Special Emphasis Panels - provide scientific and technical merit review which is the first level of peer review of research grant applications and contract proposals. These groups can be located in CSR or created and used by individual institutes who choose not to use CSR for review of particular initiatives. Within CSR, these groups comprise the study sections.

National Advisory Councils and Boards - perform the second level of peer review for research grant applications and offer advice and recommendations on policy and program development, program implementation, evaluation, and other matters of significance to the mission and goals of the respective institutes or centers. They also provide oversight of research conducted by each Institute's or Center's intramural program.

Thus, in the first level of review, grant applications are peer-reviewed by the integrated/initial review groups and the special emphasis panels primarily for their scientific value and technical merit. In the second level of review, grant applications are reviewed by a national advisory council (or board), which is composed of both scientists and lay representatives noted for their active involvement and expertise in an area of health. The council recommends

¹⁶ See overview and list of committees by appointing officials at <http://www1.od.nih.gov/cmo/about/index.html>.

applications for funding to the institute (or center) director based not only on scientific merit but also on the relevance of the proposed project to the institute's mission and priorities.

The dual review system, which separates the scientific assessment of proposed projects from policy decisions about scientific areas to be supported and the level of resources to be allocated, permits a more objective evaluation than would result from a single level of review. The dual system of review provides the responsible NIH officials with the best available advice about scientific as well as societal values and needs (NIH, 1992b).¹⁷

The two other types of advisory bodies are:

Boards of Scientific Counselors - review and evaluate the research programs and investigators of the intramural laboratories.

Program Advisory Committees - provide advice on specific research programs, future research needs and opportunities, and identify and evaluate extramural initiatives.

The President appoints two committees: the National Cancer Advisory Board and the President's Cancer Panel. The Secretary of HHS appoints 32 committees, including the national advisory councils of the institutes and centers, Board of Regents of NLM, the ACD, and the Office of AIDS Research advisory council. The NIH Director appoints 74, although about half of them are the initial review groups and special emphasis panels in CSR and the institutes and centers. The Director also appoints advisory committees to program offices in OD (except OAR), boards of scientific counselors (except NCI), COPR, and for certain research areas (e.g., sickle cell disease, sleep disorders, recombinant DNA, medical rehabilitation research). Some are appointed by institute directors, especially the NCI Director under the authority of the National Cancer Act of 1971.

The President generally follows the recommendations of the Secretary of Health and Human Services in appointing advisory committee members, and the Secretary generally follows the advice of the NIH and institute directors in filling positions, although they add their own candidates from time to time. During the 1972-1974 period, when the Nixon Administration was trying to exert greater control over the NIH budget, there was a great deal of conflict with the scientific community over the perceived politicization of the advisory committee appointment process. This issue re-emerges from time to time, and is of current concern.

Peer Review System

If the institutes and centers are the public face of NIH, the study sections and peer review system are its scientific face. The fact that the research proposed by extramural scientists must pass muster with experts in their field and that all extramural awards, which account for more than 80% of NIH expenditures, are peer reviewed has been and continues to be central to NIH's success. The peer review system is not perfect but it is the best guarantee we have that scientists will carry out research that is of high quality and has high potential for scientific progress. The state of scientific understanding and the potential for near-term progress are always difficult to assess and may vary considerably across disciplines and diseases. At any given time, some areas of research are riper for progress than others. The interaction of the two systems—institute-based assessment of need on the one hand and the study section/peer review system on the other—enables NIH to reconcile the sometimes conflicting goals of addressing the most important

¹⁷ Contracts are subjected to a similar peer review process, except the second level of review is by senior institute staff.

health needs through research and funding the best science. Although the categorical nature of the institutes helps policy makers to allocate funding among broad areas of health research (such as cancer, heart disease, arthritis, brain disorders, child development, and genomics), the structure and process of peer review are intended to ensure that research that is likely to be the most productive is funded.

The intramural program uses a retrospective process for reviewing the research of NIH's own scientists rather than the prospective peer review described above. The intramural program has been the subject of several reviews (Institute of Medicine, 1988; NIH, 1994).

CSR was established in 1946 to administer the review and evaluation of proposals for the rapidly expanding grant program and peer review has been the centerpiece of this operation. Like institutes and centers, study sections established by CSR proliferated over the years, from 20 in 1946 to more than 100 in 1994, plus many ad hoc and special emphasis panels. By that time, it became apparent that the peer review system needed restructuring to respond to changes in the way science is conducted. According to CSR, more and more applications address complex biological problems with broad, multidisciplinary research programs that are collaborative, multi-investigator, and multi-center, thus calling for a greater breadth of expertise. "There are also more trans-NIH initiatives that involve extensive collaborations within and across disciplines and institutions. The CSR peer review system, designed many years ago with a focus on individual investigator-initiated research, may no longer provide the one size that fits all. More flexible ways of operation are likely required..." (CSR, 1999 and 2000a).

By the mid 1990s, pressure for a comprehensive reexamination of the structure of the study sections and the organization of CSR had grown. In 1998, the Panel on Scientific Boundaries for Review recommended a substantial change in the structure of review groups. The panel suggested that as much science as possible be reviewed on an organ-system or disease basis, rather than discipline-related study sections. It called for grouping study sections into 24 clusters called Integrated Review Groups (IRGs), most of them addressing basic, translational, and clinical research within the context of the biological problem being addressed, such as a particular disease or physiological function (CSR, 2000b).¹⁸

"This recommendation acknowledges the advent of molecular medicine, where biochemistry, genetics, molecular and cellular biology have become tools applied to virtually all fields of health-related research. Molecular medicine applications will be reviewed in the context of the biological questions addressed rather than lumped in discipline-related study sections where they will compete against each other." (CSR, 2000c).

The panel also recommended IRGs for basic scientific discovery and methods development not associated with a particular disease, and clusters addressing crosscutting fields such as aging and development. Of the 24 IRGs, 7 were recently reorganized and will be retained as is, 6 will be new, and 11 will be modified from existing IRGs.¹⁹

In addition, when the Alcohol, Drug Abuse, and Mental Health Administration's three institutes—NIHM, NIDA, and NIAAA—were reintegrated into NIH in 1993, the number of institutes with large neuro- and behavioral science research portfolios increased to five. This

¹⁸ See the CSR website for detailed information about the restructuring of CSR and the peer review process at <http://www.csr.nih.gov/about.htm>. Also at <http://www.nih.gov/archives/renamed.htm>.

¹⁹ See <http://www.csr.nih.gov/events/implementplan.htm>.

necessitated the complete restructuring of neuroscience and behavioral science review in 1996, which involved substantial participation by the extramural research community.

In the second phase of the restructuring, which began in February 2001, external advisory teams were brought in to assess and recommend changes in the study group structure of each IRG.²⁰ Currently there are 159 study sections, an average of 8, but ranging from 3 to 12, per IRG. After the process of reviewing and restructuring the study sections is completed in 2003, ad hoc external advisory groups will review each IRG every five years. Periodic evaluation is intended to keep the structure of study sections current with the changing landscape of science and is an important development. If the plan for regular review is carried forward, it should prevent the need for a major overhaul in the future of the kind that is being undertaken by CSR at present. The Committee commends NIH for proceeding with these ongoing reforms.

Historical Forces Behind Organizational Complexity

The establishment of NCI in 1937 began the long history of creating categorical institutes that organized research in the context of particular diseases. Citizen advocacy for NIH funding and growth grew in scale and sophistication after World War II and changed national health policy. The wartime experiences of leading government scientists and the success of the Office of Scientific Research and Development brought about wide acceptance of a broad federal role in supporting research in our nation's universities. In addition, military recruitment and mobilization produced greater recognition of the roles of health and disease in determining the physical fitness of American military personnel. For example, during the early 1940s about 21% of the 2 million potential military recruits could not meet Selective Service dental requirements. This observation led President Truman to sign legislation that created the National Institute of Dental Research (NIDR) on June 24, 1948. At that time, NIH consisted of three institutes—cancer, heart, and dental.

From the middle 1940s to 1974, health advocates were successful in persuading Congress to establish additional institutes, often against the wishes of administrations, which generally opposed creation of new categorical institutes. Elizabeth Drew (1967) described the interactions among the NIH leadership, congressional committees, and voluntary health associations. The philanthropist Mary Lasker, her associates, Florence Mahoney and Mike Gorman, and her friends in the medical research community, including Sidney Farber and Michael DeBakey, played an enormous facilitating role. Drew called Lasker, Mahoney, and their allies “noble conspirators”.

Substantial post-Watergate changes in the political organization of Congress in the 1970s changed the relationships between the executive and legislative branches and marked a new era in activism generally. Congress assumed more oversight of executive agency programs - an oversight that often resulted in highly specific instructions regarding organizational details. The changes in Congress also eroded the traditional strong roles of committee chairs and dispersed power to subcommittee chairs and members. That enabled the health advocacy groups to lobby more widely and successfully for the creation of new organizational units at NIH.

In the 1980s, mass advocacy techniques pioneered by AIDS activists inspired other groups to organize at the grass roots as well as at the national level, creating an even more effective way to influence politicians in Washington. Some of the groups have continued the long established pattern of pushing for creation of named entities at NIH to create focal points

²⁰ As of May 16, 2002, meetings had been held and proposed guidelines posted for 10 IRGs at <http://www.csr.nih.gov/PSBR/IRGComments.htm>.

for developing more research funding for particular diseases. That has often resulted in the establishment by Congress of a named program at the office level. Through continued pressure, offices may then be elevated to centers and, in some cases, to institute status. In addition, the practice of pressing for increased funding for specific diseases in existing institute programs, such as Parkinson's and Alzheimer's, became more prevalent in the 1990s.

Public need and scientific opportunity are not necessarily compatible or congruent. In the face of good intentions, some consider it risky to invest in research on a disease if the science is not ready and the ability to make progress is unclear. It is possible to argue that the tension between disease-based advocacy and scientific opportunity has been productive and has led to more funding for basic research while making scientists more sensitive to public expectations of reducing the burden of disease by investing tax dollars in research. Achieving the appropriate balance between need and opportunity is difficult, however, and results in understandable tensions among the scientific community, health advocacy groups, NIH management, the Executive Branch, and Congress about who should determine NIH priorities.

Over the last 25 years, the scientific community—largely through professional and university associations—has also become a part of the dynamic that drives the growth of the NIH budget. As a result, the political environment has become a quadrilateral relationship among scientific associations, voluntary health organizations, Congress, and administrations—all with an interest in improving health through research. But they do not always agree on how, or on how much relative to other national needs. The activism of scientific societies generally focuses on appropriations and on specific programs or problems, such as the need for informatics support or specific fundamental research initiatives. The scientific societies have generally opposed the creation of new units and pressed for increasing the numbers and amounts of grant awards, training programs, and improvements in the operation of the study section system.

NIH and the Department of Health and Human Services

During the course of the Committee's work, several other independent activities focusing on administrative aspects of NIH were underway, most of which are related to NIH's responsibilities as an agency of DHHS.

Over its history, NIH has rarely been directed to add new organizational units by an administration. Indeed, most often DHHS, OMB and other parts of the Executive Office of the President oppose creating new institutes and centers, and OMB, in its institutional oversight role, usually attempts to enforce this. At the departmental level, the same desire to rationalize and order the subcomponents of the department apply. Over the years, DHHS secretaries and NIH directors have generally not favored expansion.

Given this history, it is not surprising that DHHS Secretary Tommy Thompson has issued instructions to consolidate administrative functions, such as personnel management, communications, congressional liaison, and travel, throughout HHS. The "One HHS" initiative has the stated goal of better integrating DHHS management functions across its operating and staff divisions. The initiative has already resulted in consolidation of some administrative functions. Although all the operating divisions of DHHS are involved, NIH is especially affected because of its highly decentralized structure. Of 40 personnel offices in HHS, for example, NIH previously accounted for 27. These have now been consolidated into one for NIH and three for the rest of the department (DHHS, 2001).²¹

²¹ The plan contains several principles, including "managing HHS as one department".

Plans to consolidate the communications, legislative, and congressional affairs offices of NIH have been only partly carried out because of objections from Congress. Many of those offices, which focus on outreach to the public and Congress, were established in the institutes and centers by statute and therefore may be less subject to departmental consolidation policies. DHHS has plans for consolidating other functions at NIH, such as budgeting, finance, and procurement, and is encouraging NIH to consider outsourcing some of its administrative functions (for example, grants management), citing the goals of the President's Management Agenda (OMB, 2002). Late in its deliberations, the Committee Chair was able to meet with DHHS officials to discuss centralization. Also in early 2003, the House Energy and Commerce Committee and the House Oversight and Investigations Subcommittee initiated examinations of how NIH manages and polices its research portfolio, particularly how it reviews and manages grants (Ochs, 2003).

While the Committee believes that it is critical for initiatives to eliminate inefficiencies to continue, centralization of administrative functions is not always the most effective way of proceeding, especially when these functions are difficult to separate from the performance of the primary mission (Sclar, 2000). It would not serve anyone's interests if well meaning efforts to increase efficiency undermined the effectiveness of NIH's programs and its ability to recruit talented leaders at all levels. Assembling the Nation's best talent to work on the biomedical frontier is both very challenging and a qualitatively different operation than hiring for more routine and common administrative tasks. The Committee believes that initiatives to centralize or outsource from NIH key science-related functions, such as aspects of grants management, fail to appreciate how closely this so-called administrative function is tied to NIH's primary mission. Treating crucial science management functions as general administrative services could do great harm to the NIH research enterprise. Moreover, the Committee finds the prospect of mandatory centralization of some administrative aspects of NIH's scientific mission contrary to a stated intent of the President's Management Agenda, which is "Freedom to Manage":

Federal managers are greatly limited in how they can use available financial and human resources to manage programs; they lack much of the discretion given to their private sector counterparts to do what it takes to get the job done. Red tape still hinders the efficient operation of government organizations; excessive control and approval mechanisms afflict bureaucratic processes. Micro-management from various sources—Congressional, departmental, and bureau—imposes unnecessary operational rigidity.

Recommendation 1: *Centralization of Management Functions*

Any efforts to consolidate or centralize management functions at NIH, either within NIH or at the DHHS level, should be considered only after careful study of circumstances unique to NIH and its successes in carrying out its research and training mission. A structured and studied approach should be used to assure that centralization will not undermine NIH's ability to identify, fund, and manage the best research and training proposals and programs in support of improving health.

In response to DHHS and OMB administrative efforts to reduce duplication and overlap and to ensure resource redirection toward mission-critical areas, NIH senior management announced the formation of the NIH Administrative Restructuring Advisory Committee in April 2003. The Advisory Committee will include broad NIH representation and focus on trans-NIH

proposals to change NIH administrative management functions (NIH, 2003a). The Committee believes that NIH is being responsive to justifiable concerns about improved efficiencies and encourages DHHS to work with the NIH Advisory Committee as it conducts its work.

NIH's Location in the Federal Government

The Committee also briefly discussed one other recurrent issue surrounding NIH's place in the Executive Branch. Since 1952, NIH has been housed in the equivalent of DHHS. However, as the structure of the Department has changed and as NIH's budget and prominence have grown, the appropriateness of NIH's placement has been questioned by some. NIH is now responsible for over 50% of federal nondefense R&D expenditures. Moreover, other large science-supporting agencies, such as the National Science Foundation (NSF) and the National Aeronautics and Space Administration, enjoy independent agency status. That status enables them to interact more directly with the leadership of the Executive Branch, including OMB and the rest of the Executive Office of the President, and with appropriate committees of Congress. Some argue that the fact that NIH is subsumed in DHHS and therefore unable to have such direct interactions potentially compromises its ability to carry out its mission most expeditiously and effectively.

Those who oppose making NIH independent of DHHS argue that it is important to keep NIH embedded in the Department because the NIH mission of health research is an integral part of the DHHS mission and is analogous to the arrangement in other departments, such as the collocation of the Defense Advanced Research Projects Agency and other defense R&D organizations with the service organizations in DOD. Independent agency status for NIH would also risk eroding the strong political support that it enjoys in Congress and among the voluntary health organizations and might upset the productive relationships that exist among NIH's various constituencies, which may be very difficult to reestablish under new circumstances. Furthermore, many feel that NIH needs more, not less, connection with the Food and Drug Administration, the Centers for Disease Control and Prevention, and other PHS agencies.

Although not clearly in the purview of this study, the issue of NIH's location in the Executive Branch was raised by a few people during the Committee's deliberations. The concern deserves more extensive consideration than could be provided by this Committee.

Summary

NIH is a distinctive organization that is best thought of as a federation of units tied together by common processes and overall objectives. The processes are those for deploying federal research funding across a wide array of institutions and individuals to mobilize the nation's best scientific capabilities to focus on NIH's priorities. The overall objectives are to advance the scientific frontier and to support research training in fields of special relevance to the nation's health needs.

Despite the similar processes and shared goal of its components, however, NIH is highly decentralized, and its priorities are influenced by a wide variety of key constituencies concerned with health and the vitality of the nation's biomedical research and development system. As a result, NIH's scientific portfolio is spread across a very large number of topics and fields among which it may be difficult to discern overall strategic goals or distinctive functions.

In chapters 4 through 6, the Committee addresses the implications of this highly decentralized structure both in terms of the strengths it brings to certain endeavors and the

obstacles it can raise for others. The next chapter addresses the changing landscape for biomedical research and how this might affect NIH's organizational structure.

Chapter 3
NEW OPPORTUNITIES, NEW CHALLENGES: THE CHANGING NATURE OF
BIOMEDICAL SCIENCE

The frontier of biomedical science has rarely been as exciting and as full of spectacular opportunities as it is today. From basic science through clinical research to health services research, the opportunities made available through the impressive advances of recent decades in the biomedical as well as the physical, computational, and behavioral and social sciences —have brought us to a frontier of unprecedented opportunity. Those developments have also begun to transform the conduct of both large and small-scale biological and biomedical research in rather dramatic ways. Although traditionally structured laboratory and clinical investigations are still its most essential components, several technical and scientific breakthroughs have altered how research is conducted. For example, high-throughput technologies are enabling rapid accumulation of unprecedented amounts of biological and health-related information. Nucleic acid and protein databases are revolutionizing some of the ways in which the structure and function of biomolecules and cells are studied. Databases and biological repositories have become ever more essential resources for scientists, and biocomputing and bioinformatics are indispensable tools in new types of investigations that are based on these vast amounts of data. Moreover, in some fields the scientific enterprise is characterized by the increased importance of large-scale and complex projects. All those additions to the traditional research paradigm are placing new demands on approaches to research funding and management because some parts of the scientific frontier require the creation of larger-scale products, significant new infrastructure investments,²² or the mobilization of interdisciplinary research teams, sometimes involving large numbers of investigators at many institutions. More strategic planning and coordination of investigators on the part of the National Institutes of Health (NIH) as a whole are required if it is to make the most effective use of its resources.

Increasingly, investigators will need to integrate knowledge gained from high-throughput molecular research and high-powered imaging studies with knowledge from population-based epidemiological studies and clinical trials to learn what works and what does not work, what is safe and what is not safe. It seems clear, for example, that there will be a greater need for research on interactions among genetic variation, cell dynamics and behavioral, metabolic, nutritional, environmental, and pharmaceutical variables. And greater prominence must be given to research in the behavioral and social sciences, to health services research that is related to the more effective treatment of diseases and improvement of quality of life, and to the continuing evaluation of preventive interventions. Growing awareness of the association between socioeconomic status and health and health disparities provides new challenges as well as opportunities for research. The opportunities and needs raise the issues of setting research priorities and defining appropriate boundaries for NIH research, but they also raise questions about whether NIH's current institutional structure facilitates or limits the adaptability of its programs.

Finally, international and economic factors are changing the nature of science. First, a greater sense of urgency permeates some fields of research, given the threat of bioterrorism,

²² At the same time that the present committee was conducting its work, the National Cancer Policy Board of the National Academies was preparing a report, *Large-Scale Biomedical Science: Exploring Strategies for Future Research* (Institute of Medicine, 2003a). Some of the material in this chapter was gathered by the National Cancer Policy Board during its deliberations.

persistent and emerging infectious diseases, and the complexity of the international environment for science with its pressing health needs. Second, private industry and foreign governments have substantially increased their funding of biomedical research and development (R&D) (National Science Foundation, 2002). Third, the increasingly global nature of science raises new challenges to the NIH structure with respect to international collaboration, capacity-building, and training.

An overview of how biomedical science has developed in the last decade and where it might be leading is helpful in determining whether NIH's current organizational structure is best suited to address emerging scientific opportunities and partner effectively with other federal agencies and the private sector. This chapter presents a snapshot of certain aspects of the current research environment with some speculation as to how it is changing.

Clinical Research Needs

Clinical research informs and stimulates fundamental science; conversely, basic laboratory and epidemiological research inform and stimulate clinical research. As defined broadly by NIH in a report of a task force chaired by David G. Nathan (National Institutes of Health, 1997a),²³ clinical research includes

- Research conducted with human subjects or on material of human origin (tissues, specimens, and cognitive phenomena) in which an investigator interacts directly with human subjects. This research includes mechanisms of human disease, therapeutic interventions, clinical trials, and development of new technologies.
- Epidemiologic and behavioral studies.
- Outcomes and health services research.

Others might define clinical research more broadly to include some aspects of drug screening, and development of diagnostics and gene therapy—all laboratory-based activities but nonetheless patient-focused forms of research.

The research community recognizes a social compact with the public to help improve health by advancing knowledge along all relevant parts of the scientific frontier. At the same time, the translation of discoveries in fundamental and applied science into useful clinical and public health interventions and uses of such interventions to reduce disability, morbidity, and health disparities are the ways the public measures the success of its investments in biological and behavioral research.

Yet for nearly 25 years there have been persistent concerns about the health and future of our national efforts in clinical research (Wyngaarden, 1979). Reviews of its status and recommendations for improvement have been conducted previously and in a far more thorough manner than could this Committee. Most recently, the NIH Director's Panel on Clinical Research was commissioned in the spring of 1995 by Harold Varmus, the Director of NIH, because the "perception of crisis in clinical research that had simmered for decades had intensified by a funding shortage induced by managed care and new restrictions on the Federal budget" (National Institutes of Health, 1997a). More recently, members of the Clinical Research Roundtable of

²³ NIH's definition excludes *in vitro* studies that use human tissues but do not deal directly with patients. That is, clinical, or patient-oriented, research is research in which it is necessary to know the identity of the patient from whom the cells or tissues under study are derived.

IOM published a review of the challenges facing the national clinical research enterprise (Sung et al., 2003).

NIH sponsors a large set of programs in clinical research and training through its institutes' and centers' extramural and intramural research programs; the agency is the largest sponsor of clinical research in the world. NIH spent \$7.6 billion on clinical research in FY 2002, estimates it will spend \$8.4 billion of its \$27 billion budget in FY 2003 and projects spending \$8.7 billion in FY 2004. A large portion of the clinical research supported by NIH occurs extramurally in hospitals and clinics affiliated with medical schools, independent research institutes, and health departments throughout the United States. A smaller but vitally important portion of NIH's clinical research portfolio is conducted through the intramural research programs of the institutes and at its Clinical Center.

The clinical research programs sponsored by NIH differ from most of those supported by the private sector in that NIH-sponsored clinical research focuses most heavily on increased understanding of disease prevalence, disease mechanisms, and long-term outcomes of therapies. Appropriately, most clinical research sponsored by the private sector (such as pharmaceutical, biotechnology and medical device companies) focuses on testing the efficacy and safety of new drugs and devices before their approval by the Food and Drug Administration (FDA). Both types of clinical research are essential to advance human health, and they depend on one another.

Clinical research is often conducted on a large-scale at multiple institutions across the country or even around the world. For example, in 1991, NIH launched the Women's Health Initiative (WHI) with the broad goal of investigating strategies for the prevention and control of some of the most common causes of morbidity and mortality among postmenopausal women, including cancers, cardiovascular disease, and osteoporotic fractures.²⁴ Congress provided special funding, totaling \$213 million over 4 years, through the Office of the Director. The WHI has functioned as a trans-NIH consortium and is one of the largest studies of its kind ever undertaken in the United States, involving more than 40 centers nationwide and 162,000 women. The first results from the WHI have been reported, for example, the rates of cancers, heart disease, and osteoporosis in women taking hormone replacement therapy (Pradhan et al., 2002). The findings have had a large and prompt impact on medical practice and on the ways physicians prescribe such therapy for their patients.

Another example is the Collaborative Programs of Excellence in Autism, launched in 1997.²⁵ At the request of Congress, NIH formed the Autism Coordinating Committee (ACC) to enhance the quality, pace, and coordination of NIH efforts to find a cure for autism, and the ACC has been instrumental in the research into, understanding of, and advances in autism. Five institutes (the National Institute of Child Health and Human Development, National Institute of Environmental Health Sciences, National Institute of Mental Health (NIMH), National Institute of Neurological Disorders and Stroke, and National Institute on Deafness and Communication Disorders) are members of the ACC. In addition, representatives of the National Institute of Allergy and Infectious Diseases and the National Center for Complementary and Alternative Medicine participate in ACC meetings, as do representatives of the Centers for Disease Control and Prevention (CDC), FDA, and the US Department of Education.

Because many major diseases have common risk factors, broad-based, potentially large-scale, and trans-NIH projects are sometimes required to share information and show linkages more precisely. For example, smoking, high-fat and low-fiber diets, physical inactivity, and

²⁴ See http://www.nhlbi.nih.gov/health/public/heart/other/whi/wrn_hlt.htm

²⁵ See <http://www.nichd.nih.gov/autism/nihacc.cfm>

exposures to exogenous and endogenous toxins are all likely to contribute to the development and progression of numerous diseases that are within the purview of multiple institutes. But despite a growing list of successful trans-NIH collaborations, NIH officials told the Committee that NIH has for decades had a notably difficult time in funding clinical, let alone population-based, studies that involve major diseases that belong to multiple institutes, such as cancers, heart disease, pregnancy outcomes, and duodenal ulcers related to smoking. In addition to studies of causation, trials seeking reduction of lung cancer and heart disease with other agents (such as beta-carotene in the 1980s and 1990s and other antioxidants now) have been difficult to fund across institutes.²⁶ Generally, one institute has had to be willing to fund the whole study, but this often results in less than fully efficient investigations of diseases that fall outside the institute's mandate (such as heart disease in trials supported by NCI or cancer in trials supported by NHLBI) or in passing up the opportunity to broaden the benefit of a trial at a modest cost.

Evidence-Based Medicine and Health Services Research

An increasingly important extension of the value of clinical trials is in research to enhance evidence-based medicine, which aims to take the best available information from clinical trials and observational studies and apply it in clinical practice. For example, despite a rich evidence base for management of cardiovascular disorders, study after study has demonstrated disconcertingly low rates of compliance with widely disseminated evidence-based treatment guidelines for managing such common cardiovascular conditions as coronary heart disease, congestive heart failure, and high blood pressure. The difficulty in translating the results of clinical trials into clinical practice suggests the presence of multiple barriers to implementation. Although there is substantial overlap, the barriers are in four general domains related to science, the health profession, the patient, and the health system. Even very well-designed randomized clinical trials may fail to examine all the relevant risk factors and patient and cultural variables.

Barriers related to the health profession include lack of knowledge of the best current evidence, time constraints, and the overriding desire to avoid iatrogenic complications. Patient-related barriers include managing multiple prescriptions for multiple chronic conditions, time and financial constraints, and difficulties in engaging in health-modifying behaviors such as smoking cessation, exercise, and dietary modification. Barriers related to the health system include lack of sufficient insurance, lack of integrated approaches to the care of chronic illness, and the high cost of health care. The complexity of issues involved mandates a comprehensive and collaborative approach involving physicians and other health care professionals, patients and their families or other support systems, and the health care system itself if the myriad barriers to implementing evidence-based care are to be overcome (Rich, 2002). Indeed, much of the complexity is not fully understood and requires further research.

Health services research is within the mission of NIH. Some institutes, such as the National Institute on Aging, National Cancer Institute (NCI), NIMH, the National Institute on Drug Abuse, and the National Institute on Alcohol Abuse and Alcoholism, have substantial portfolios, even whole divisions, that focus specifically on health services research. Another Department of Health and Human Services agency, the Agency for Healthcare Research and Quality (AHRQ), takes the lead in some aspects of health services research and recommends strategies for monitoring and improving quality of care, but it cannot fully address the demand

²⁶ These and related issues concerning trans-NIH initiatives were raised repeatedly during Committee interviews with NIH senior management.

for the full array of such research. Furthermore, health services research is closely related at the disease or health-dimension level to treatment research, as well as to much more basic behavioral science (such as social psychology theory or organizational theory). Thus, there are many reasons to support health services research in multiple institutes. In fact, NIH estimates that it spends about \$800 million per year on health services research compared with \$300 million per year for the entire AHRQ budget (Sung et al., 2003; Helms, 2002). Clearly, more coordination across NIH and between NIH and other agencies, such as AHRQ, the Department of Veterans Affairs, and the Centers for Medicare and Medicaid Services, would advance this developing field.

Increasing Urgency in Some Fields of Research

In the last few years, the United States has become increasingly and uncomfortably aware of its vulnerability to bioterrorist threats. Concerns about vaccine supplies, efficacy and safety of older vaccines, and the documentation for handling and storing materials that pose biological, chemical, and radioactive hazards have reopened discussions about public health research in general and about openness and secrecy in scientific communication (Omenn, 2003). The role of NIH in rapid response to research needs arising from bioterrorism—especially in areas where there is little incentive for private investment—has been the subject of recent analyses; some have questioned the agency's ability to be flexible and responsive (National Research Council, 2002).

New infectious diseases (West Nile virus and Severe Acute Respiratory Syndrome [SARS]) and reemerging infectious diseases (malaria in Virginia and tuberculosis worldwide), increasing antibiotic-resistance in pathogenic bacteria, and the threat of bioterrorism have caused renewed interest in infectious disease agents, epidemiology, and surveillance of potentially exposed populations (Omenn, 2003). Those research subjects require reaching across public health, agriculture, ecology, and other fields in ways that might not be typical or easy with NIH's current structural configuration. Beyond NIH, greater collaboration with the intelligence community, emergency workers, law enforcement, and the pharmaceutical, communications, and information industries will be required (National Research Council, 2002). The sudden spread of SARS in China and several other countries also highlights the need for rapid detection, identification, and response; working with CDC and international health organizations, NIH can play a pivotal role in improving scientific knowledge of the coronavirus that will be important in developing vaccines and treatments.

Addressing Health Disparities

Increasing attention is being directed to the biological, genetic, and socioeconomic basis of health and whether all Americans are benefiting from health-related research advances. The life expectancy of members of many minority groups in the United States is still much shorter than that of white Americans. Recent years have seen gains in longevity and lessening of the impact of chronic diseases, but minority populations have not benefited as much as the white population. The disparities have many causes (Institute of Medicine, 2002).

The influence of racial bias is not limited to access to health care. Racial prejudice and discrimination can be sources of acute and chronic stress that have been linked to such conditions as cardiovascular disease and alcohol abuse (Cooper, 2001; Yen et al., 1999). Discrimination can restrict people's educational, employment, economic, residential, and partner choices, affecting health through pathways linked with what psychosocial scientists refer to as

human capital. Environmental influences of industry, toxic waste disposal sites, and other geographic characteristics linked with poverty and minority status can result in serious disadvantages to minority groups' health (Institute of Medicine, 1999).

The increasingly recognized links among genetics, health, socioeconomic status, and macroeconomics emphasize the importance of research to examine and decrease the magnitude of health disparities. In 2000, the National Center on Minority Health and Health Disparities was established by the passage of the Minority Health and Health Disparities Research and Education Act of 2000 (PL 106-525), reflecting a concern among policymakers that NIH was not paying sufficient attention to this issue.²⁷

The Growth of Large-Scale and Discovery-Driven Science

Most federally-supported biomedical research has been conducted through small independent projects initiated by individual investigators working in relatively small research groups. Such research is typically hypothesis-driven, that is, aiming to address specific biological questions. That approach to research remains essential, but developments on the scientific frontier have encouraged scientists to consider also the increased importance of carefully selected broader and larger-scale projects, for example, to develop extensive pools of data and other research tools that can then facilitate the more conventional approach to research. This approach, often called "discovery" science, is based on the assumption that the analysis of a complete data set collected across the breadth of a biological system (for example, an entire genome) is likely to yield clues and patterns on which to base hypotheses about the relationships of important biomolecules operating in the system.

The Human Genome Project: An Important Additional Paradigm in Basic Biology

The biggest and most visible large-scale, discovery-driven research project in biology is the Human Genome Project (HGP), an international effort to map and sequence the entire human genome. When it was first proposed, many scientists opposed the project on the basis of its cost and size and the fact that it was managed science; they assumed it would take funding away from other, more important projects. It was also viewed by many as a forced transition away from hypothesis-driven science to a directed, hierarchical mode of "Big Science" (Cook-Deegan, 1994). Many argued that it was technically infeasible. Proponents of the HGP won out, especially as the Department of Energy began on its own, and NIH secured designated funds that allowed it to make its first awards in 1988. A draft sequence of the entire human genome was completed in 2000, and the full sequence in April 2003 (Pennisi, 2003). The data from the HGP constitute a vast and rich resource for biomedical research for many years to come.

The next challenge lies in identifying the functions of the genes and the complex regulatory dynamics of the cell to understand the mechanisms that lead to the creation of proteins and their functions (Burley, 2000). Sequences from the genome project are being analyzed with improved understanding of cell dynamics to help to identify protein families. Structural genomics uses computational analyses with structural determinations of the protein products to advance the study of protein function. Proteomics permits simultaneous examination of changes

²⁷ In particular, see July 26, 2000 hearing of the Senate Health, Education, Labor and Pensions (HELP) Committee's subcommittee on Public Health on health disparities of minorities, women and under-served populations, and NIH's role in addressing them. Witnesses were also asked to comment on the proposed Health Care Fairness Act, S. 1880 and H.R. 3250.

in expression levels and modifications of structure and function in health and disease. The resulting data must be assessed against a background of population-based studies entailing the generation, storage, and analysis of enormous quantities of epidemiologic, genotypic, and phenotypic data. The process of hunting for disease-related mechanisms that seem to be directly related to genetic material—once an expensive and arduous undertaking conducted by individual laboratories and investigators—has become rapid and highly automated; it is limited primarily by the incompleteness of our understanding of cell regulation, the unexpected complexity of many diseases, and the lack of a rich information base regarding many nongenetic risk factors in the relevant human populations. Despite the spectacular discoveries of recent decades there remain large gaps in our understanding of how genetic information is transformed into biological meaning. The challenge of this task has led some to warn of the prospect of a bottleneck between genome-based scientific advances and translation to clinical improvement (Nathan and Varmus, 2000).

The Mounting Importance of Biocomputing, Bioinformatics, and Clinical Informatics

As a result of the HGP, associated projects, and imaging research, biologists and clinical investigators are faced with more opportunity and data and a greater need to organize the data in a meaningful, coherent, and public manner than ever before. For example, automation has allowed fewer people to accomplish more sequencing in shorter periods. The immense amount of information generated by this class of projects is stimulating new collaborations among clinical medicine, biology, chemistry, physics, and the fields of bioinformatics, computer science, and mathematics. Large amounts of computational expertise are a necessity. To understand the similarities and differences among organisms of the same and different species, sophisticated comparisons must be conducted, and many of them cannot be conducted effectively solely with traditional tools. Using appropriately designed databases and powerful computers, bioinformatics is providing a view of the relationships among organisms that are sometimes separated in evolution by many millions of years. Computers can display patterns and periodicities that would rarely be found if searched for with traditional approaches and techniques (Hood, 2003). Thus, in many ways, biology is becoming an information science (Botstein, 2000). The creation and development of such databases and database technologies (methods for storing, retrieving, sharing, and analyzing biomedical data) are becoming more important in all biomedical fields. As more information from clinical trials becomes available, the need for standardization and interoperability of clinical databases will increase. Coordinating knowledge gained from a large and growing set of clinical trials with new insights from genetic research could appreciably advance knowledge about the treatment of disease. A system of interoperable databases would allow clinical researchers to track more efficiently any finding back to its basic scientific roots; conversely, a research scientist might track forward to postulate from hypotheses through potential applications on the basis of innovative uses of existing data (NIH, 1999b). Similarly, linkages between genetic databases or clinical databases and environmental exposure databases will be essential for understanding and modifying gene-environment interactions (National Research Council, 2002).

Other Large-Scale and Trans-NIH Science Initiatives

As a result of the success of the HGP, there is considerable interest in developing other larger scale projects with broad potential benefits. One well established example in cancer research is the Cancer Genome Anatomy Project (CGAP) of NCI. The goal of the CGAP is to

develop gene-expression profiles of normal, pre-cancerous, and cancer cells, which could be used by many investigators to search for new methods of cancer detection, diagnosis, and treatment. In addition to the CGAP, the number of large-scale initiatives in genomics involving multiple institutes has grown. The successful initiation of many of them depended on the institutional leadership at the time combined with growing budgets, according to Francis Collins, director of the National Human Genome Research Institute. In his presentation to the Committee, Collins described other plans for large-scale, trans-NIH projects that include building libraries of small molecules and tools for screening; longitudinal cohort studies to connect genotype, phenotype, and environmental risks; highly annotated databases of gene and protein structures and function; development of a computational model of the cell; and large-scale efforts in imaging and other population-based studies.

Recently, 18 institutes co-funded a bioengineering nanotechnology initiative, 12 co-funded initiatives in structural biology of membrane proteins, and 16 institutes and centers supported an effort in methods and measurement in the behavioral and social sciences.

The examples cited above indicate that there is some flexibility in NIH's administrative and priority-setting procedures to respond to new developments and allow for the initiation of large-scale research endeavors. However, recent funding patterns indicate that institutes with the largest budgets, such as NCI, the National Institute of General Medical Sciences (NIGMS), and the National Heart, Lung, and Blood Institute) are more likely to initiate and support large-scale research projects. Smaller institutes do not have enough funds or flexibility in their budgets to begin such projects although they often leverage their resources through a larger institute's investment. It is not clear to what extent these projects are true collaborations in the sense that the participating institutes identify a challenge or an opportunity, work together toward developing a project, co-fund investigators and/or institutions, and manage and oversee the ongoing work. Thus, "multi-institute funding" should be distinguished from "trans-NIH initiatives," with the latter referring to activities that involve more than one institute in planning and implementation from start to finish.

Unanticipated fluctuations in annual congressional allocations and the appropriations process (which provides separate budgets for each IC) make strategic planning for new long-range, large-scale, or trans-NIH projects more difficult. In years in which the budget remains flat, new projects, especially large-scale new projects, are especially difficult to initiate. Moreover, because large-scale science is costly, it has the potential to reduce the funding available for the critical, but smaller, investigator-initiated projects. It is a bit more complicated for small research groups to initiate larger-scale projects because of the requirement that applicants for RO1 grants >\$500,000 per year in direct costs obtain institute or center agreement at least six weeks prior to the anticipated submissions deadline before they can apply.²⁸ Thus, these requests require special budgetary and program planning in addition to scientific merit and budget justification. Applications submitted in response to NIH PAs or Requests for Applications (RFAs), which include their own specific budgetary limits, are not subject to the same limits.

In addition to cost considerations, NIH management told the committee that true collaborations across institutes and centers can be made more difficult for a number of administrative reasons, such as: lack of clear support from leadership about the importance of such work; insufficient rewards for work conducted beyond the purview of an institute's specific mission; placement of "available" staff on such projects rather than individuals with the most

²⁸ NIH Notice for Acceptance for review of unsolicited applications that request more than \$500,000 in direct costs, Effective June 1, 1998; see <http://grants.nih.gov/grants/guide/notice-files/not98-030.html>. Notice updated October

appropriate skills or background; and insufficient financial resources and office space dedicated to get the work done.

New Resource Requirements: Patient Databases and Specimen Banks

Other trends in biomedical science are influencing the importance of some kinds of data. For example, collections of archived patient information - including clinical data, family history, and risk factors - and such human biological materials as tissue, blood, urine, and DNA samples are essential for studying the biology, etiology, and epidemiology of diseases, especially if the diseases are linked. Such data can also be used to examine the long-term effects of medical interventions.

In 1999, the National Bioethics Advisory Commission estimated that more than 282 million specimens of human biological materials were stored in the United States and that they were accumulating at a rate of more than 20 million cases per year (NBAC, 1999). Maintenance, cataloging, and storage of these specimen banks and related data in a format that is widely accessible to the research community would require a long-term investment. Ensuring the quality and usefulness of specimen banks after the project-based funding ends is an unresolved issue now managed on a case-by-case basis.

The capacity to link medical records of individuals with family histories and disease phenotypes is an important point of departure for genetic analysis. Investigators at centers that have developed the capability and permission to search their patient database for informative patients and families will be well positioned to compete for the increasing proportion of federal and industrial research resources that will be devoted to genetic research, especially if non-genetic variables can be measured and be linked (Silverstein, 2001; Omenn, 2000). Electronic medical records could make the work of specialists in one discipline widely accessible to specialists in many disciplines. If appropriate protocols can be developed, these records could be used to integrate the work of clinicians with that of researchers and administrators, and could permit better and more rapid assessments of the health of the public in general and of individual patients in particular (Silverstein, 2001). It is important to note, however, that such electronic medical records would be available only in carefully reviewed and controlled circumstances under the federal Health Insurance Portability and Accountability Act and provisions of the Common Rule (45 CFR 46).

Electronically accessible medical records also could be used to track the health of the public in real time, for example, vaccine use or occurrence of hypertension, bacterial and viral pneumonias, cardiac arrhythmias, and sexually transmitted diseases. This would require substantial new federal money for equipment, personnel, and infrastructure and the expertise and resources of agencies other than NIH (Silverstein, 2001). In addition, the widespread use of the records raises a whole set of new ethical issues concerning privacy and confidentiality that must be adequately addressed if the public is to maintain its support for biomedical research. Non-clinical database links will be essential to address environmental, dietary, and behavioral interactions with genetic predispositions (Omenn 2000).

One issue that is common to all large-scale projects that generate research tools or databases is accessibility. Concerns are often raised regarding intellectual property rights, open communication among researchers, public dissemination of data and assuring protection of privacy and confidentiality. Explicit understanding must be negotiated and must be included in informed consent documents.

The Growing Need for Interdisciplinary Research

Many of the projects described above are interdisciplinary. However, smaller-scale studies in the biological and biomedical sciences are also requiring more organized collaboration among disciplines. For example, data assessment, technology development, and a deeper understanding of science increasingly necessitate the involvement of non-biologists, such as engineers, physicists, and computer scientists. Recognition of the value of interdisciplinary research is not new. Indeed, the history of medicine demonstrates that many important advances have come from an interdisciplinary approach, for example, laser surgery involved ophthalmologists, anatomists, and physicists; and gene discovery, such as the cloning of the gene associated with Huntington disease, required the input of epidemiologists, neurologists, psychologists, sociologists, and geneticists. In fact, some of the newer fields in science are hybrid or trans-disciplinary efforts, such as bioinformatics, neuroscience, and health services research. The HGP has relied on the combined expertise of biologists, chemists, computer scientists, mathematicians, and engineers. In the behavioral sciences, psychologists increasingly use artificial intelligence, brain imaging, and molecular biology to map behaviors (Institute of Medicine, 2000). And psychiatric researchers long ago turned to epidemiologists and geneticists for help in identifying risk factors.

What is changing is the recognition that the need for interdisciplinary research is likely to grow. Some of the most persistent and chronic causes of disease, disability, and death are proving to be vexingly complex. Elaborate and sometimes subtle relationships among genes, environment, behavior, and disease and treatment interventions underlie HIV/AIDS, heart disease, autoimmune diseases, cancers, and substance abuse. Those conditions rarely lend themselves to the model of the single investigator working in isolation in their own discipline.

Most scientists would agree that the collective framing of research questions often leads to better answers. At the very least, most scientists are recognizing that the variables of interest and the tools of other disciplines might be useful in their own work. However, the organization of science and research administration, in academia and funding agencies, often presents challenges to interdisciplinary work. In 2000, an Institute of Medicine committee examining the need to foster interdisciplinary science in the brain, behavioral and clinical sciences wrote that “long-held biases, beliefs, educational practices, and research funding mechanisms have created a system in which it is easier to conduct unidisciplinary than multidisciplinary work” (Institute of Medicine, 2000). The committee concluded that the creation of environments in which interdisciplinary research and training occur will probably require many changes and multiple integrated approaches. Creating a new breed of interdisciplinary scientists requires rethinking of the training process, including redesigning research training programs and funding mechanisms to support interdisciplinary training, research, and practice.

In 1999, NIGMS initiated a new funding mechanism referred to as glue grants, intended to provide the resources to bring together and retain scientists from multiple disciplines to focus on a research topic. In 2003, the Fogarty International Center announced a similar program. NIGMS’s goal was to address problems that are beyond the reach of individual investigators who already held funded research grants related to a proposed topic of study. The RFA stated:

Biomedical science has entered a new era where these collaborations are becoming critical to rapid progress. This is the result of several factors. First, not every laboratory has the breadth to pursue problems that increasingly must be solved through the application of a multitude of approaches. These include the involvement of fields such as

physics, engineering, mathematics, and computer science that were previously considered peripheral to mainstream biomedical science. Second, the ability to attack large projects that involve considerable data collection and technology development require the collaboration of many groups and laboratories. Finally, large-scale, expensive technologies such as combinatorial chemistry, DNA chips, high throughput mass spectrometric analysis, etc., are not readily available to all laboratories that could benefit from their use. These technologies require specialized expertise, but could lend themselves to management by specialists who collaborate or offer services to others.

NIGMS originally conceived of the large-scale glue grants after consultations with leaders in the scientific community who emphasized the importance of confronting intractable biological problems with the expertise and input of large, multifaceted groups of scientists. Applicants are asked to consider what it would take to solve a problem if a team of investigators already funded were to coordinate and integrate their efforts and what approaches might be possible with the grant that cannot be achieved with just R01 support. Efforts to disseminate information are required, for example, meetings of participating investigators, newsletters, and Web sites. Materials produced as a result of glue grants are to be made available to the wider community as is reasonable. One important objective of the glue grant program is to benefit a broad scientific community (beyond those named in the application).

Trends in Public-Private Sector Research and Collaboration

Changes in the financing, organization, and performance of R&D and technological innovation have altered how industry, research performers, and governments in the United States and elsewhere invest in research. According to Pharmaceutical Research and Manufacturers of America (PhRMA), in 2001 member companies spent over \$30 billion on research to develop new treatments for diseases - an estimated 17% of sales, a higher R&D-to-sales ratio than any other US industry. An additional \$17 billion was spent on R&D by the biotechnology industry. (Pharmaceutical Research and Manufacturers of America, 2001; Biotechnology Industry Organization, 2003).

Many initiatives - such as the SNPs Consortium, the mouse genome project, the structural genomics consortium, and the more general Small Business Innovation Research Program - have involved close collaborations between public funding agencies and private industry. Furthermore, numerous NIH institutes have started specific projects and grants that have been directed at enhancing public-private collaboration. Those experiments promise to deliver benefits to patient care. At the same time, they have raised important issues about intellectual property, ethical conduct of research, and conflict of interest that need to be addressed. The development of new products, processes, and services often entails gaining access to firm-specific intellectual property and capabilities.

Firms and research performers have responded to these developments by outsourcing R&D and by forming collaborations and alliances to share R&D costs, spread market risk, and obtain access to needed information and know-how. Alliances, cross-licensing of intellectual property, mergers and acquisitions, and other tools have transformed industrial R&D and innovation. Universities have moved to increase funding links, technology transfer, and collaborative research activities with industry and government agencies. Government policies have supported these developments through changes in

antitrust regulations, intellectual property regimens, and initiatives in support of technology transfer and joint activities (NSF, 2002a).

In addition, numerous strategic research and technology alliances among a variety of institutions and enterprises, many involving international partners, have been created over the last two decades. Universities are important partners in these research joint ventures, participating in 16% of them from 1985 to 2000 (NSF, 2002a).

Increasing International Research

The decline of global political blocs, expansion of convenient and inexpensive air travel, and advent of the Internet have facilitated scientific communication, contact, and collaboration. Data collected by NSF (2002) show that the expansion of R&D efforts in many countries is taking place against a backdrop of growing international collaboration in the conduct of R&D. More R&D collaborations can be expected to develop with Internet-facilitated innovations such as virtual research laboratories and the simultaneous use of distributed virtual data banks by investigators around the globe.

In many countries, foreign sources of R&D funding have been increasing, and this underlines the growing internationalization of industry R&D efforts. In Canada and the United Kingdom, foreign funding has reached nearly 20% of total industrial R&D; it stands at nearly 10% for France, Italy, and the European Union as a whole. US firms are also investing in R&D conducted in other locations. R&D spending by US companies abroad reached \$17 billion in 1999; it rose by 28% over a 3-year span. More than half that spending was in transportation equipment, chemicals (including pharmaceuticals), and computer and electronics products (NSF, 2002).

A particularly notable international collaboration is the Human Proteome Organization (HUPO), which has launched international initiatives in characterization of proteins in plasma, liver, and brain and in underlying technologies, antibody resources, and bioinformatics (Hanash and Celis, 2002). NIH Director Zerhouni's Roadmap exercise identified proteomics as a leading enabling technology for new discoveries. NIH and FDA are closely involved with the not-for-profit HUPO, and several individual institutes have mounted their own proteomics workshops.

Summary

Multiple trends are changing the nature and environment of biomedical research, including the persistent need for better approaches to clinical research, health services research, and evidence-based medicine; continuing concerns about health disparities; the looming threats of emerging infectious diseases and bioterrorism; the increased need for large-scale and trans-NIH projects that require longer-term strategic planning and commitments; the emergence of discovery-driven science and its attendant informatics and data requirements; the need to add new infrastructure elements to the nation's biomedical enterprise; the essential role of interdisciplinary research in many diseases; and expanding relationships between the public and private sector and between the United States and the rest of the world in research.

THE ORGANIZATIONAL STRUCTURE OF THE NATIONAL INSTITUTES OF HEALTH

A critical focus of the Committee's attention was the growing perception that the proliferation of the National Institutes of Health's (NIH's) institutes and centers (ICs) poses numerous problems for the agency, its leadership, and the overall effectiveness of its research and training portfolio in light of the new opportunities and challenges described in Chapter 3. As discussed briefly in Chapter 1, the Committee deliberated extensively on a variety of proposed responses to the changing nature of the biomedical frontier. Some observers have suggested maintaining the current array of ICs but grouping them in some way into "clusters," each of which would report to a deputy director, who in turn reports to the NIH director. That arrangement would maintain the existence of individual ICs and might encourage strategic planning within each cluster while reducing the number of subordinates with whom the NIH director must negotiate on strategy and direction. But the creation of a new management layer between the NIH director and the individual IC directors would, in effect, make the ICs divisions of larger organizations and might decrease the status, independence, and attractiveness of IC directorships and compromise the potential of the NIH director to provide appropriate strategic leadership.

Others, such as Varmus (2001), have suggested consolidating all existing institutes into say, five larger institutes of about equal size, whose leaders would report to the NIH director. Such a solution might well simplify some aspects of NIH management and some have suggested it might improve the overall effectiveness of the research portfolio. But it could also risk losing the support of many of the congressional, health advocacy, and public coalitions that have contributed so much to NIH's success. As noted in Chapter 1, the Committee believes that the development of NIH's current organizational structure has been a useful response to a set of complicated scientific and political influences. The Committee does not find the conceptual or practical case for a wholesale reorganization sufficiently compelling to outweigh its potential adverse consequences or risks. Rather, as laid out in this and subsequent chapters, the Committee makes recommendations for achieving many of the goals identified by proponents of major restructuring (more authority for the NIH director, increased responsiveness, greater flexibility, and more opportunity for coordination) primarily by other means.

The Committee is aware that many previous reports have recommended the adoption of a presumption against the continual addition of units to NIH. For example, the Special Committee on Medical Research, chaired by Cyril Norman Hugh Long in 1955 (NSF, 1955), concluded in its report that the seven institutes then in NIH were sufficient. Similarly, the President's Biomedical Research Panel stated in 1976 (Department of Health, Education, and Welfare, 1976), when there were 11 institutes, that "the creation of additional Institutes is not likely to make the NIH more effective; it might well make it less so. Therefore, if new programs are to be established, or existing programs strengthened, this should be accomplished through the present Institutes rather than through the creation of new ones." In the same year, the report of a Congressional panel chaired by Representative Paul Rogers (US House of Representatives, 1976) noted that the "categorical" structure of the institutes was a key to the success of NIH because it had given the public, Congress, and the administration a way to understand and identify with the mission of each institute. The Rogers report also noted, however, that NIH was

facing pressure for too much categorization from advocacy interests not represented by name in the institute structure; “with eleven institutes, the problem of fragmentation becomes very real.”

In 1984, an Institute of Medicine (IOM) committee chaired by James Ebert concluded that the current organizational structure of NIH was appropriate and effective (IOM, 1984). No new institutes had been created since 1974, but in the intervening decade, three institutes – the National Cancer Institute (NCI), the National Heart, Lung, and Blood Institute (NHLBI), and the National Institute for Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) – had been elevated to “bureaus”, giving their directors more authority and the flexibility to create separate divisions to house major subunits of these institutes (NIH, 1976).²⁹ These changes were to accommodate health advocates’ concerns, but pressures from outside groups were once again building for a separate institute for arthritis and a new institute for nursing. The 1984 IOM committee argued that “NIH is now at a stage where there should be a presumption against additions at the institute level because such changes (1) fragment the scientific effort and diminish effective communication with key scientists in other institutes, (2) add to the burden and difficulty of effective program coordination by the NIH Director and his top staff, and (3) add to administrative costs without ensuring increased appropriations.” Because there might be circumstances in which organizational change would be necessary and it would be important to recognize such circumstances, the 1984 committee recommended that there be a formal process to assess proposed major organizational changes in NIH, and it articulated five criteria for evaluating organizational proposals:

1. “The activity of a new institute or other organizational entity must be compatible with the research and research-training mission of NIH. If a major emphasis of the proposed new entity is in regulation, the delivery of services, or other non-research activities, it is not appropriate for incorporation in NIH.
2. “It must be demonstrable that the research area of a new institute or other major organizational entity is not already receiving adequate or appropriate attention.
3. “There must be reasonable prospects for scientific growth in a research area to justify the investment in a new institute or other major organizational entity.
4. “There must be reasonable prospects of sufficient funding for a new institute or other major organizational entity.
5. “A proposed change in the NIH organizational structure should, on balance, improve communication, management, priority setting, and accountability.”

²⁹ As a result of the War on Cancer Act of 1971, NCI was elevated to a bureau with a greatly expanded budget and special authorities. NHLBI also became a bureau after the National Heart, Blood Vessel, Lung, and Blood Act of 1972 expanded its programs and budget; Congress added blood to the name of the institute in 1976. The NIADDK was raised to the bureau level in 1982, and separate divisions for diabetes, arthritis, digestive diseases, and kidney diseases were established. This was to respond to a report by the National Commission on Arthritis and Related Musculoskeletal Diseases that found the combination of topics under this institute’s umbrella “incongruous”. The bureau title has since been done away with (Cohen, 1993). See McGeary and Smith, 2002, for additional details.

Thus the present Committee is hardly the first to consider these problems and deliberate over potential solutions. The Committee notes, however, that little changed as a result of past studies. The trend toward proliferation of units in NIH has continued to the present in the absence of an accepted process such as that suggested in the 1984 report.

NIH's continuing outstanding success has been due largely to its ability to adapt its programs and structure to meet the ever-changing needs and challenges posed by science, medicine, and public health. As already noted, the Committee carefully considered in multiple meetings major structural changes in NIH, including possible revisions in the number and reporting lines of ICs to the director and concluded that a wholesale consolidation of NIH's ICs into a much smaller number of units is likely to generate more disadvantages than advantages. Nevertheless the Committee believes that a thoughtful process should be in place to respond to restructuring concerns as they arise to enable NIH to modify its structure as the situation warrants and NIH's continuing vitality demands. Because NIH is a public institution, the American public has a stake in its success and should be welcomed into decisions about its continued vitality and growth. A broad array of people and interests should be able to engage in thoughtful and balanced discussions about changes in NIH's institutional structure to address present and emerging issues even more effectively.

In line with that view, the Committee believes many changes in NIH's organizational structure and practices other than the number of ICs could potentially improve its effectiveness and help it to secure its continuing role in biomedical research. The Committee presents its recommendations on them in Chapters 5 and 6. The remainder of this chapter focuses specifically on issues surrounding the number of units (institutes, centers, and offices) in NIH and on the need to establish a more systematic process to address future needs for adding, consolidating, or dissolving structural units in response to changing scientific, health, or societal pressures.

Process for Creating New Units or Dissolving or Consolidating Existing Units

The Committee believes that it would be useful for Congress to consider amending the authorizing legislation for NIH to require that certain steps (outlined below) be taken in considering the creation, dissolution or consolidation of new institutes and centers.

Recommendation 2: Public Process for Proposed Changes in the Number of NIH Institutes or Centers

Either on receiving a congressional request or at the discretion of the NIH director in responding to considerable, thoughtful, and sustained interest in changing the number of institutes or centers, the director should initiate a public process to evaluate scientific needs, opportunities, and consequences of the proposed change and the level of public support for it. For a proposed addition, the likelihood of available resources to support it should also be assessed and the burden of proof should reside clearly with those seeking to add an organizational element.

To initiate the process, the director should consult with the Advisory Committee to the Director and should a consensus develop on the value of further exploration, the NIH director should appoint an ad hoc investigative committee, ensuring that the appropriate array of technical expertise to evaluate a particular proposal is present and that the committee has

appropriate representation of the extramural scientific and voluntary health advocacy communities.

Examples of steps it would be appropriate for the investigative committee to take include

- Inviting input from the advocates of the proposed action.
- Gathering input and opinion from the IC Directors and other scientific leaders of NIH on the need for the proposed action.
- Soliciting the views of the Council of Public Representatives and other NIH advisory bodies.
- Holding a technical forum to be attended by the scientific community to address the scientific needs and opportunities related to the proposed action and the consequences of creating, dissolving, or consolidating one or more organizational units.
- Holding a public forum to gather the views of voluntary health advocacy organizations and other stakeholders.
- Consulting interested members and committees of Congress.

After the information gathering steps, the investigative committee should synthesize a set of recommendations and report them to the NIH director. The NIH director would then deliver the investigative committee's report with his or her recommendations to Congress, indicating any important disagreements with the investigative committee. Congress should allow the process to conclude before acting to create a new unit or to consolidate or dissolve an existing unit.

Despite the present Committee's conclusion that a large-scale restructuring of the ICs would not be wise now, no organization that is expected to remain effective should have to bear the burden of a frozen organizational structure, and not all of NIH's existing units are likely to continue to have the same relevance or independence in the future. It is reasonable to suggest that the public, the scientific community, or the NIH director, in concert with internal and external advisers, should be able to suggest to Congress additions, subtractions, or mergers of units at appropriate times.

Opportunities for Mergers

After much consideration, the Committee came to the conclusion that a few ICs have overlapping missions and substantive foci and would work more effectively together than apart. The Committee suggests initiation of two careful studies to evaluate potential mergers. Those studies, however, would require time for detailed, open, and public evaluation of the issues as outlined in the process described above.

Two particular options were raised during Committee discussions as candidates for merging: the National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA); and the National Institute of General Medical Sciences (NIGMS) and the National Human Genome Research Institute (NHGRI). There are undoubtedly other mergers, additions, or closures that might be studied. The two suggested here are by no means an exhaustive list. The Committee, however, did not have the time or opportunity to review the merits of all such proposals to the extent that they deserve, which would include a thorough examination of the research and training programs of each institute under

consideration. Indeed, the Committee favors these mergers, but believes that such changes should benefit from use of the process outlined above.

A Proposed Merger of NIAAA and NIDA

NIAAA and NIDA were originally parts of the National Institute of Mental Health (NIMH). NIAAA was established by congressional action as an organizational component of NIMH in 1970. In 1974, NIAAA, NIDA, and NIMH were made autonomous institutes under the newly created Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA). With the dissolution of ADAMHA in 1992, NIMH, NIDA, and NIAAA were all transferred to NIH.

Over the years, there has been recurring interest in why the two institutes that focus on substance abuse and addiction are separate. As chair of the House Labor, Health and Human Services, and Education Appropriations Subcommittee, Representative John Porter asked the IC directors at every annual appropriation hearing why the two institutes had not been merged (Leshner, pers. comm.). More recently, questions have been raised in the Senate about the wisdom of keeping them separate,³⁰ and a National Academies study on the issue was strongly recommended in report language. To date, however, the method and implications of combining them have not been carefully investigated.

The arguments for combining the two ICs stem from overlap in their missions and substantive foci. The overlap was well described in an editorial in the *Journal of the American Medical Association* by the director of NIAAA and the acting director of NIDA (Hanson and Li, 2003):

...it is important to remember that there is a strong association among the use of tobacco, illicit drugs and the abuse of alcohol. In addition, there is a similarity of biological and social risk factors underlying vulnerability to all of these substances, including genetic and environmental factors. Lastly, there are overlapping mechanisms thought to underlie how these substances influence the brain. Hence, it would be desirable from a public health perspective to address all substances of abuse when opportunities arise.

In addition, prevention and treatment approaches are fundamentally similar for alcohol abuse and abuse of other substances.

Having two separate ICs focused on addictions has resulted in the emergence of two somewhat separate scientific communities, although some investigators receive support from both institutes. The existence of two scientific societies – the College on Problems of Drug Dependence and the Research Society on Alcoholism – and the fact that they have not convened scientific meetings together in the last 20 years provide dramatic evidence of segregation. Few studies investigate alcohol and other substances of abuse at the same time, even though few drug addicts abuse only one substance. And the exclusive focus of the two institutes on specific substances has meant that some addictions, e.g., gambling and food addictions, have received virtually no scientific attention.

³⁰ During the 107TH Congress, S. 304, the Drug Abuse Education, Prevention, and Treatment Act of 2001, as reported by the Senate Judiciary Committee on November 29, 2001, contained a provision that called for a study of a merger of NIDA and NIAAA by the National Academies. Although the bill was enacted as PL 107-273 in November 2002, the provision relating to the study was no longer included.

Arguments against merger appear to be primarily nonscientific; for example, the alcohol industry might strongly and successfully oppose such a merger to avoid being associated, even indirectly, with considerations of illegal drugs. In the Committee's view, substantive arguments against merger are not convincing. One suggests that alcohol requires a separate institute because it is unique in affecting every cell in the body; but other abused drugs studied by NIDA, such as inhalants, also affect all cells. Another argument is that alcohol is unique among abused substances in being legal, at least for adults, and thus everything surrounding the drug is unique. On the other hand, NIDA supports a large amount of research on nicotine addiction, and smoking is also legal for adults. A merger of NIAAA and NIDA would seem to offer many advantages, scientifically and with respect to improved health, and should be studied carefully. The broader scientific relationships and physical location of these two institutes with other neurosciences institutes (especially NIMH and the National Institute of Neurological Diseases and Stroke) should also be considered.

A Proposed Merger of NHGRI and NIGMS

NHGRI was born out of NIGMS to give intense focus and impetus to the sequencing of the human genome. Established originally as a center and later elevated to institute status, NHGRI has done a superb job in leading the international effort to sequence and interpret the human genome. Its efforts have extended to the sequencing of the genomes of other organisms, whose comparative study has substantial benefits for health and other fields of research. Although the sequencing efforts have involved many other ICs, particularly NCI and NIGMS, as well as the Department of Energy and the biotechnology industry, NHGRI clearly has been the leader. Many other institutes have continued work on other aspects of fundamental genetics, including the genetics of various illnesses, and biomedical genetics has emerged as an overarching NIH high-priority field and a major venue for trans-NIH collaboration. Sequencing of the human genome was declared essentially complete on April 14, 2003 at the 50th anniversary celebration of the publication of the Watson and Crick paper on the double-helix structure of DNA. Biomedical researchers are building on the information to increase understanding of the functions of genes and the proteins they generate. Genetic medicine, genomics, and proteomics are among the core biomedical disciplines for the 21st century.

The Committee considered whether there is still a compelling need for a separate genome research institute. NHGRI's initial charge has been successfully accomplished, and having a continuing discrete focal point for human genomics might be useful for maintaining momentum in the field. However, it can be argued that NHGRI no longer has an essential separate mission. Many of its activities could easily be integrated into other ICs that have advanced their research as a result of the Human Genome Project and are integrating its findings into their missions.

Among the other institutes, NIGMS has core or primary responsibility for basic biomedical research. It can be argued that the same is true for genetics and that a core responsibility for NHGRI's projects should therefore be incorporated (actually, reincorporated) into NIGMS. In recent years, NIGMS has moved decisively into larger-scale transdisciplinary research, including glue grants (see chapter 3) and other mechanisms. On balance, the Committee believes that the completion of the human genome sequencing effort offers a good opportunity to study the possibility of combining the two institutes. Moreover, ending the life of NHGRI as a separate institute would, if determined to be appropriate, provide a dramatic precedent for declaring fulfillment of a well-defined mandate.

Consolidating Clinical Research Efforts

Because of extraordinarily persuasive arguments about exceptional needs made by a variety of groups in discussions with the Committee, a recommendation is made in this section to consolidate several clinical research components of the extramural and intramural program to transform the National Center for Research Resources (NCRR) into a new entity, the National Center for Clinical Research and Research Resources (NCCRRR).

The importance of clinical research in translating the vast knowledge emanating from basic science efforts, such as the Human Genome Project, cannot be overstated. As the result of a wide spectrum of developments in the biomedical sciences, extensive research can now be done on the pathogenesis and pathophysiology of human disease. In addition, new developments in imaging provide novel approaches to understanding the health and disease states in humans. As described in Chapter 3, the challenge for clinical research is that most common diseases are complex, multi-etiological disorders in which a multiplicity of genetic and other factors interact with each other. As a result, clinical research is faced with the complex challenge of identifying the resources, intellectual capital, and large cohorts of patients with appropriate phenotypes for studies. It will take a revitalized investment in clinical research, including many large scale trials, to figure out how to tie together all the factors that contribute to particular diseases.

Clinical research has always been more of an interdisciplinary “team” effort than laboratory science, but it will increasingly require larger, multi-institute studies and a level of collaboration, sharing, and cooperation that sometimes seems at odds with the image of the lone scientist working in isolation. German pathologist Werner Kollath once lamented, “Much is known, but unfortunately in different heads.” If clinical research is to fulfill the promise of our nation’s prolonged investment in biomedical research, then a more concerted and better coordinated effort must be mounted that will make the most of all available research and training resources.

NIH already sponsors a substantial set of programs in clinical research and training through its extramural and intramural research programs. It has continued to expand efforts to support clinical research and training and attract physician-investigators, often with strong encouragement from Congress and academic leaders. For example, it has established and expanded a series of special training programs for clinical researchers collectively known as K awards. And recognizing that loans accumulated during college and medical school greatly burden young physicians and influence their choices of career paths, NIH has responded by creating competitive loan-repayment programs that offer up to \$35,000 per year for 2 years to health professionals pursuing careers in various aspects of clinical research.

The 87 general clinical research centers (GCRCs)—managed by the National Center for Research Resources (NCRR)—constitute a national network of NIH-supported clinical research sites hosted at academic health centers and teaching hospitals. They provide settings for medical investigators to conduct safe, controlled, state-of-the-art patient studies with support by the vast infrastructure of academic health centers. They also provide a crucial setting and mentorship to attract medical students, residents, fellows, and junior faculty – and patients and volunteers – into clinical research.

In addition, each institute or center with a research program supports a broad array of clinical research through individual research grants, research centers, and collaborative group funding mechanisms. Most ICs also conduct a variety of clinical research through the intramural program. As in the growing number of jointly funded extramural research programs, ICs may

cooperate in studies. Such cooperation is facilitated by the intramural program's Clinical Center on the Bethesda campus.

NIH spent \$7.6 billion on clinical research in FY 2002, estimates it will spend \$8.4 billion of its roughly \$27 billion budget in FY 2003 and projects spending \$8.7 billion in FY 2004. The figures are complicated, however, in that the 20 clinically active ICs accounted for their "clinical research" efforts quite differently. However the funding is counted, almost all NIH institutes maintain substantial clinical research programs. For example, NCI, NHLBI, NIDA, and the National Institute of Allergy and Infectious Diseases maintain extensive clinical-trial research networks. Many institutes award contracts to conduct specialized research and clinical trials of potential treatments. Some institutes, such as NCI, NIMH, and NIDA, also support extensive arrays of research centers that provide infrastructure support and specialized clinical research project support.

NIH Director Zerhouni's Roadmap for Re-Engineering the Clinical Research Enterprise (Jenkins, 2003; Metheny, 2003) outlines three pressures on the clinical research enterprise:

- the rate of growth of health care needs and expenditures requires accelerated discoveries and clinical validation;
- new clinical approaches will have to be more efficient than current ones; and
- public support and participation in clinical research are essential.

Many initiatives to bolster, support, and improve clinical research and training are under way at NIH, including public trust initiatives, the development of clinical research informatics, and planning meetings. An NIH Steering Committee on Clinical Research Infrastructure has been charged with defining the scope and purpose of clinical research informatics and ensuring sufficient external consultation to build a work plan for use of information technology in clinical trials. The plan will include data standards, core elements, model systems, and practices.

Even in light of NIH's considerable support of clinical research, the Committee sees a critical lack of coordination and standardization across NIH in its clinical research programs that cause many opportunities for collaboration and data sharing across fields to be lost. Clinical research is an expensive undertaking, requiring costly infrastructure and extensive administrative support to comply with regulatory requirements and interact effectively and efficiently in the financial and recordkeeping framework of clinical medicine. In addition, clinical databases can be sizeable and support for the necessary informatics daunting. In 2003, members of the Institute of Medicine's Clinical Research Roundtable published an article (Sung et al., 2003) characterizing the current state of clinical research as "increasingly encumbered by high costs, slow results, lack of funding, regulatory burdens, fragmented infrastructure, incompatible databases, and a shortage of qualified investigators and willing participants." The challenging and expensive enterprise of clinical research requires mastery of a broad array of skills in clinical medical fields; the application of biostatistics to clinical trial design and analysis; the principles, precedents, and procedures of bioethics; the organization and oversight of complex projects; and the communication of complex ideas to potential trial participants and peers. The roundtable described two kinds of translational blocks: from basic science to human studies and from clinical knowledge to clinical practice, health-care decisions, and population health. The length of training required, the expense and time involved, and the complex regulatory environment of clinical research have depleted the ranks of those willing to engage in clinical research, and

many feel that this trend contributes to the inability to translate basic research findings into improved health.³¹

To ensure the success of the clinical research system there must be a cadre of highly trained clinical investigators for several reasons: to discern the questions to be asked; to ensure that studies are conducted with the highest quality standards; and to ensure that there are trained clinical investigators in all medical specialties enrolling patients in trials. As basic science discoveries outstrip clinical capabilities to apply them, the lag in translating clinical research to practice will continue to lengthen. This can only be addressed by providing coordinated support for stable and rigorous academic training programs, recruiting physicians to become scientists or continue their professional development through mid-career research training, and ensuring that funds are available for clinical research proposals that seek to address significant problems in the diagnosis and treatment of human disease. For these reasons, it is critical that NIH concentrate its efforts to make the most effective use of what is already a sizeable investment.

NIH, the Association of American Medical Colleges (AAMC et al., 1999), and Sung, et al. (2003) have concluded that NIH could enhance the contribution of the biomedical research enterprise to improved health in the United States and globally in numerous ways, including

- Working to build public engagement and trust in clinical research by creating new partnerships.
- Developing with the Department of Health and Human Services' Office for Human Research Protections a national approach to standardizing and harmonizing regulations for protecting research subjects and improving standards of privacy protection.
- Supporting the development of integrated, interoperable data networks, medical record systems, and related research under a common national health-information infrastructure with standards to facilitate collection and sharing of clinical research information.
- Facilitating establishment of national and international clinical research consortia to study, standardize, and share information on disease prevention, pathophysiology, diagnosis, therapies, and outcomes.
- Strengthening the GCRC network to include more shared resources for clinical investigators.
- Creating national databases (consistent with the Health Insurance Portability and Accountability Act) that link the phenotypes, genotypes, risk factors, and multigenerational family histories of large numbers of people.
- Increasing opportunities (and funding) for clinical research training for physicians, dentists, pharmacists, public-health workers, nurses, psychologists, laboratory technicians, dieticians, computer programmers, bioengineers, and others, including education-loan repayment programs.
- Forging intergovernmental collaborations with related programs in the Department of Health and Human Services, such as the Centers for Disease Control and Prevention (CDC) and the Agency for Healthcare Research and Quality (AHRQ), as well as essential programs in the Departments of Veterans Affairs, Defense, Labor, and Agriculture

³¹ An Institute of Medicine committee is currently developing a report on the role of academic health centers in the 21st century. The committee's report is still in preparation.

The perceptions that more needs to be done to translate basic research into useful health interventions and that NIH could do more to promote and facilitate clinical and other research relating to the more effective implementation of new findings often result in calls for the creation of some new entity, whether inside or outside NIH, focused specifically on clinical research. For example, in May 2003, Senator Joseph Lieberman proposed the creation of a privately funded \$150 billion American Center for Cures, with the goal of supporting the translation of basic research discoveries into medical applications (Hawana, 2003). In the same month, the presidents of the Association of American Universities (AAU), AAMC, and the National Association of State Universities and Land Grant Colleges (NASULGC) in a letter to NCRR regarding its strategic plan, emphasized the importance of continuing to revitalize the GCRCs as a way to eliminate barriers to research progress and enhance investigator access to resources and technologies (Cohen, et al., 2003). The authors proposed merging NCRR's GCRC program with the NIH Clinical Center to form a national system dedicated to translational research.

The Committee also believes that the goals outlined above could be pursued better if the intramural and extramural clinical research programs of NIH worked more closely and collaboratively and if optimal use were made of the Clinical Center and the GCRCs, which together account for about 7-8% of the NIH budget. NIH is the ideal convener and organizer of a national clinical research enterprise and should lead a new effort throughout the biomedical research community to create and coordinate a national infrastructure for clinical research.

The Committee believes that the time is ripe for NIH to develop and implement a series of NIH-wide strategic initiatives in clinical research that engage the energies and resources of all ICs and recommends that even greater efforts be made than just merging the activities of NCRR and the Clinical Center, as proposed by AAU, AAMC, and NASULG. A concerted, proactive effort requires that someone in a leadership position—with the attention of the NIH Director and the authority to assess and coordinate efforts across NIH—systematically and routinely evaluate NIH's clinical research programs in toto. Those strategic initiatives should be aimed at facilitating the widespread incorporation of new concepts and technologies in molecular genetics, cell biology, imaging, computational biology, and information sciences into clinical research practice. Such strategic initiatives will advance the missions of all ICs and revolutionize health research. By this means, NIH's strategic investments in clinical research can have a transforming effect on the practice of medicine and public health in the United States. To achieve the goals outlined above, a more coordinated and concerted effort is needed.

Recommendation 3: *Strengthen Clinical Research*

NIH should pursue a new organizational strategy to better integrate leadership, funding, and management of its clinical research enterprise. The strategy should build on but not replace existing organizational units and activities in the individual ICs' intramural and extramural research programs. It should also include partnerships with the nonprofit and private sectors. Specifically, the Committee recommends that several intramural and extramural programs be combined in a new entity to subsume and replace the National Center for Research Resources, to be called the National Center for Clinical Research and Research Resources (NCCRRR). In addition, a deputy director for clinical research should be appointed in the Office of the Director to serve as deputy director and head of the new entity.

The Committee is well aware that there is already an Associate Director for Clinical Research at NIH who oversees the intramural Clinical Center. The new position of deputy director that we describe would, however, take responsibility for all combined intramural and extramural programs in clinical research.

The Committee gave careful thought to how to create the recommended new entity for clinical research. The most appealing option was to transform the NCRP into the NCCRRR, retaining its responsibilities for the GCRCs and K award programs and adding to these the oversight of the Clinical Center and the integration and coordination of other clinical research conducted by the ICs. The current NCRP director position would be replaced with a new position of deputy director for clinical research. Because NCRP would cease to exist, its non-clinical research programs, which are important, would have to be relocated to other venues in NIH. An attractive aspect of this option is that it does not create an additional direct report to the NIH director.

The Committee also considered other approaches, for example, moving the GCRCs, K award programs, Clinical Center oversight, and overall clinical research coordination to an institute or center other than NCRP, for example, to NHLBI. Although this option potentially could put clinical research into the hands of an entity well qualified to manage it, it could also create a lack of acceptance on the part of other institutes that might defeat the intent to improve trans-NIH integration of clinical research. Another idea was to create an entirely new center that combines the GCRCs, K award programs, Clinical Center, and coordination of IC clinical research under the direction of a newly created position of deputy director for clinical research. A major disadvantage of this option is that it would increase the number of direct reports to the director, which the Committee felt was undesirable. This could be avoided if the remaining parts of NCRP were relocated, as above, and the center was dissolved as a distinct entity.

The Committee decided that the best option is to build the new NCCRRR on the NCRP, adding to its responsibility for the GCRCs and the K awards for training and career development the oversight of the Clinical Center and coordination of clinical activities for which other ICs are responsible. If staff responsible for these critical aspects of NIH's clinical research and training portfolio report to a central office, there would be greater opportunity to enhance data sharing among clinical investigators, clarify, solidify, and standardize relevant policies, and identify and pool resources for high-cost, essential core infrastructure needs. A central location would also provide a well-informed opportunity for strategic planning. NCCRRR should have an advisory committee similar to those of other ICs (see also Chapter 6) and every effort should be made to ensure that investigators working in all aspects of clinical research have access to the services and resources of NIH and that the research agenda is not dominated by larger institutes.

The Committee understands that there is a concern about the functions of NCRP that are not related to clinical research, such as its primate centers. Those activities of the existing NCRP that are not focused on clinical research but that are nonetheless essential to the overall research enterprise should be maintained as offices or branches in appropriate other locations within NIH. The Committee believes that it should be left up to the NIH director to evaluate what current NCRP functions should be retained in the new NCCRRR and which ones to position elsewhere.

Each institute or center would continue to fund its own clinical research projects, collaborative groups, and trainees (as now through funding transfers to NCRP) and its use of the Clinical Center. Although planning at the Clinical Center emphasizes flexible cross-IC intramural use of the facility, it is envisioned that the new entity would assume a much stronger

leadership role for the entire intramural and extramural NIH clinical research enterprise and work in close partnership with the academic community and the private sector. For example, the new Center could enhance and improve relations and ongoing discussions with clinical research organizations outside NIH, such as the Office for Human Research Protections, the Food and Drug Administration, CDC, AHRQ, and the pharmaceutical and biotechnology industries.

The goal would be to extend the resources and expertise of NIH's aggregate clinical research expertise more broadly, to more fully engage the clinical research community across the country and to develop standard tools and practices to promote clinical research. For example, two key areas in which the new Center could make enormous contributions are in information technology and clinical bioinformatics. Given the great expense of clinical trials, any increased productivity achieved through automation will have a substantial impact on the number of trials that can be successfully completed and on the speed of knowledge accumulation. Another important role could be in developing, through an inclusive process with the extramural community, the area of ethical conduct of clinical research and the setting of consistent national ethical standards for NIH grantees conducting clinical research.

The Committee believes that the importance of both intramural and extramural clinical research to all the ICs requires the full time and attention of one individual and his or her office within OD. Although the current and previous NIH Directors have all strongly supported clinical research, it is just one of many missions that NIH must fulfill and thus has not received the full attention warranted, with efforts at promoting clinical research too ad hoc, too sporadic, and too subject to changes in NIH leadership. By consolidating many existing efforts into one organizational unit, clinical research would achieve maximal visibility and coordination.

Summary

The Committee's conclusion was that, at the current time, a wholesale consolidation of NIH's ICs into a much smaller number of units would generate more disadvantages than advantages; however a process to consider changing circumstances and suggestions for structural change as they arise is needed. The Committee believes that Congress should consider amending the authorizing legislation for NIH to require that either on receiving a congressional request or at the NIH director's discretion in responding to public requests for a structural change, the director should initiate a public process to evaluate the scientific, medical, financial, and public costs of the proposed change.

Some ICs have overlapping missions and substantive foci and would work together more effectively than apart, and the Committee recommends the immediate initiation of two careful studies using the recommended process to evaluate these mergers. In addition, the Committee recommends the merger of extramural and intramural functions related to clinical research.

ENHANCING NIH'S ABILITY TO RESPOND TO NEW CHALLENGES

The highly decentralized organizational structure of the National Institutes of Health (NIH) has come about through a complex process of evolution over a long period marked by substantial increases in resources and extraordinary discoveries on the biomedical frontier. The evolutionary process involved numerous events and responses to pressures from a wide variety of interested constituencies that resulted in the creation of many largely-independent organizational units. The governance of NIH has been profoundly influenced by that evolution. For example, Congress has created most additional units with their own budgets and decision-making authorities, which constrains the ability of the NIH director to influence the decisions and choices made by individual institutes and centers and makes the scientific leadership and management of NIH as a whole extremely challenging.

The Committee's view of those complexities was governed by the desire to be of practical assistance to all those who wish NIH to continue as an effective, indeed outstanding, organization, and it proceeded on the premise that its task included assessing the organizational configuration of NIH and the key processes and authorities that play roles in NIH-wide decision-making. Although the borders between structure, mission, and priorities are not well defined, the Committee tried not to take too expansive a view of its responsibilities.

On the one hand, a highly decentralized organization may be generally appropriate for a research organization because research and creativity often prosper through a bottom-up approach that encourages the flow of ideas from the widely dispersed scientific community and does not impede the role of individual investigators in choosing productive avenues of research. On the other hand, when there is a need for NIH to respond to important new health concerns or scientific opportunities—especially when inter-institute or “trans-NIH” initiatives are needed—the NIH director's authority to mobilize the needed resources is limited. There is no formal mandate for NIH to identify, plan, and implement cross-cutting strategic initiatives. In fact, the Committee has come to believe that NIH's current structure, governance, and management mechanisms have become barriers to its effectiveness in using its resources most efficiently to foster progress in large- and small-scale scientific endeavors that directly affect human health and that a more diverse set of mixed strategies for supporting research is essential.

As discussed in Chapter 4, most of what NIH does should continue to operate as usual through activities and decision structures of the institutes and centers and the peer review system. Indeed, the Committee concluded that the existing NIH structure is fundamentally healthy and should continue to pay large dividends in scientific progress and meeting the nation's health needs. However, organizational changes should be made to increase NIH's effectiveness, improve its ability to respond to new scientific needs and opportunities, and thereby enhance its vitality. In this chapter, the Committee focuses on: planning and implementation of trans-NIH initiatives, which require more authority and resources for the director; development of a new mechanism to address high-risk research; and improvement in the NIH intramural research program's ability to move quickly and flexibly to meet urgent new needs and to work more collaboratively with the extramural research community.

The Authorities of the Director and Trans-NIH Initiatives

Despite the enormous success of NIH, and in part because of that success, the changing world of biomedical science and the stewardship of this great enterprise require increased

attention to a number of critical scientific and health issues that no institute or center can address alone. In particular, as described in Chapter 3, over the last decade or more there has been growing recognition of the importance of both large and small-scale interdisciplinary science, of the importance of strategic trans-institute initiatives, and of the increasing dependence of biomedical researchers on a broad array of new infrastructure investments. NIH has responded to those forces by, for example, sponsoring and successfully carrying out a number of large-scale interdisciplinary projects, such as cancer research and the Human Genome Project. Moreover, it has become increasingly clear that there is a high payoff potential for carefully selected large- and small-scale strategic projects that require the participation of numerous organizations working in partnership. Well-planned, broad-based, trans-NIH programs will be necessary to meet most effectively scientific or public health needs or to complete a task, with the assumption that at some point particular programs will have met their intent and cease to exist in any formal way. Although NIH has been successful in putting together some initiatives in which more than one institute co-funds a research program of mutual interest, it has not been as successful in jointly planned and implemented efforts across institutes. In this respect, the decentralized, federated structure and governance patterns of NIH are a disadvantage. Furthermore, there is no formal mandate for NIH to identify, plan, and implement such crosscutting strategic initiatives.

In particular, the Committee believes that the difficulties encountered in initiating trans-NIH initiatives have been one reason why in the past some groups have called for new free-standing organizational units, which in turn has led to the proliferation witnessed over the past few decades. What might have been perceived as a lack of responsiveness on the part of NIH in some cases might have been more related to its inability to mount a sufficient response within the existing organizational framework.

The Committee suggests changes in the Office of the Director to improve the agency's agility and ability to respond to emerging scientific and health needs. These alterations would provide new mechanisms for selecting and planning strategic initiatives and would also give NIH an additional set of strategies for managing science—an approach the Committee concludes is not only appropriate, but also desirable.

The Authorities of the Director

The roles of the NIH director are to provide leadership and direction to the NIH research enterprise and to coordinate and direct important initiatives that cut across the agency. The Office of the Director (OD) is responsible for the development and management of policy for intramural and extramural research and training, the review of program quality and effectiveness, the coordination of selected NIH-wide program activities, and the administration of centralized support activities essential to the operations of the NIH. The director also oversees relationships between NIH and various other agencies in and outside the Department of Health and Human Services.

However, the NIH director has limited formal authority and OD lacks an adequate budget for its many roles. Institute and center (IC) directors have their own budgets, appropriated directly to them by Congress, which for the larger institutes, such as the National Cancer Institute (NCI) and the National Institute of Allergy and Infectious Diseases (NIAID) amount to several billion dollars. The NIH director has only a modest budget (see Table 5.1 in the section on the structure of the director's office, below) with a small discretionary fund (\$10 million) and the authority to transfer up to 1% of the IC budgets to start new initiatives. An unanticipated decision to use that transfer authority during a fiscal year can prove highly problematic. The ICs,

having typically committed their entire budgets, must cut funding for planned activities to accommodate an unexpected transfer. If a transfer is called for late in a fiscal year, the disruption to ongoing activities can be serious. Furthermore, even 1% of the budget might not be adequate for high-priority new initiatives. The reality is that the NIH director cannot mobilize important trans-NIH efforts to address new strategic goals because the authority for doing so is absent and he or she must rely largely on persuasion and goodwill to make even relatively modest changes.

The execution of current Director Zerhouni's "Roadmap" initiatives illustrates the problem well. Zerhouni has won much praise for his ambitious exercise to plan major new trans-NIH research projects, but their long-term future is by no means clear. Zerhouni has given notice that he intends to use the director's 1% transfer authority in FY 2004, and the President's budget request for FY 2004 contains an extra \$35 million (0.1 percent of the NIH budget) for OD to implement the Roadmap. But no major new initiative is a 1-year effort, so sources for FY 2005 funding and beyond will be needed. Moreover, the committee believes that there should be, over time, a series of such initiatives. Ideally, FY 2004 initiatives would be adopted as part of the relevant ICs' regular research programs in FY 2005 and beyond, but the director has no authority to ensure that this happens.

Strategic Planning for Trans-NIH Initiatives

Although the Committee is not recommending a major structural reorganization of the NIH ICs (see Chapter 4), it concluded that to meet the scientific and health goals of the nation, NIH needs to mobilize coordinated funding from many institutes for high-priority time-limited initiatives that cut across individual institutes' purviews. The Committee believes that the best means to achieve that is multiyear strategic planning that involves all ICs.

Scientific mechanisms, risk factors, and social and behavioral influences on health and disease cut across traditional disease categories. Many patients have multiple chronic conditions, so a patient-centered approach to health care and health promotion will sometimes require integration and synergy across ICs. For example, there have been recent calls for the establishment of an institute on obesity, which is a major public health concern. Because obesity is associated with diabetes, coronary artery disease, and arthritis, multiple NIH institutes could logically claim obesity as a critical component of their research portfolio. This is one of many potential topics that lend themselves to a strategic coordinated trans-NIH response in which multiple institutes could collaborate on a research plan that cuts across administrative structures in terms of planning, funding, and sharing and disseminating results. The Committee believes that a trans-NIH strategic initiative on obesity is a better mechanism to address this problem than the creation of a new institute. Proteomics, already cited by NIH Director Zerhouni as a critical enabling technology for discovery in the Road-Map, is another current example. Multiple institutes are independently holding workshops and considering or issuing Requests for Applications at a time when concerted trans-NIH work on the assessment of existing and emerging technology platforms and database formats utilizing reference specimens, could help to advance the whole field and guide NIH-supported studies. A trans-NIH initiative need not involve every IC and need not proceed indefinitely. But it would require dedicated funds, leadership, and scientific merit or it will not work.

NIH shared with the Committee evidence that the ICs are co-funding grants that account for about 20% of new awards, although the research topics of these awards have not been selected through NIH-wide strategic planning. It appeared to the Committee that, in many cases, these initiatives really involved only a few lead institutes that contributed the lion's share of the

budgets. NIH managers told the Committee that these multi-institute programs are difficult to administer: they require sign-off by each institute involved, with each institute maintaining its own accounts and oversight. Thus, if five institutes are involved, there are five parallel administrative and oversight efforts in place.

Other efforts to improve cooperation and collaboration among institutes have met with limited success. For example, NIH intramural scientists have formed some 70 scientific interest groups across institutional boundaries; these groups are no doubt important forums for scientific exchange but they do not set priorities, plan programs, or expend research funds. A relatively new and path-breaking attempt at trans-NIH science is the consolidation of the intramural programs of the neuroscience-related institutes in the newly constructed Porter Center on the Bethesda campus. Other cooperative attempts, such as the NIH Pain Research Consortium—although well intended—have started and faltered over many years because funding generally has not been available and research programs are dependent on the willingness of individual institutes to fund specific projects (IOM, 2003b). The Committee was told in numerous interviews with NIH leadership that past efforts by the NIH director to “raise funds” from ICs to support trans-NIH initiatives have been viewed by the ICs as intrusions on their budgets. This is a direct consequence of the federalist structure of NIH and one this Committee would like to see reformed.

The Committee expects that many IC directors would see the expansion of such collaborations through planning and disbursement of research and training funds as an opportunity for leadership and leverage on topics important to them and their constituencies. To reiterate, the Committee is convinced that trans-NIH initiatives are a more direct and effective means to address emerging scientific and health improvement opportunities than is the creation of new centers or institutes.

The Committee concluded that the NIH director’s authorities and resources must be increased to make it possible to achieve those goals. The Committee recommends that the director be given the responsibility and authority to develop and implement, with and through the ICs, a set of time-limited trans-NIH initiatives that are identified through a broad-based strategic planning process open to participation by all internal and external stakeholders and transparent to the public. Such a process should be conducted regularly, for example, every other year. The Committee envisions the process producing a sufficient breadth and diversity of initiatives to make it readily feasible for each institute and center, with the Director, to identify one or more initiatives that are compatible with its own mission and goals in which to participate. In fact, the Committee is convinced that such a requirement from Congress is likely to stimulate ICs to propose and even lead trans-NIH initiatives. In any case, each institute and center should be required to reserve a substantial portion of its budget for such participation, starting initially at a few percent, but increasing over the next 4 - 5 years to 10% or more if initial efforts prove successful. The Committee believes that the initiatives will, over time, allow each of the institutes and centers to pursue its goals and interests more effectively. The Committee envisions the strategic initiatives selected through the planning process being temporary in the sense that their status as “new initiatives” will extend only through one or a few planning cycles, after which other initiatives will take their place. However, as the work involved in these initiatives is performed, the Committee expects that at least some elements of the work will spin off into new components in the portfolios of many of the ICs that become part of their regular research agendas. In addition, many activities covered by existing grants and programs are likely to be relevant to some strategic initiative topics, and could become part of IC participation in the trans-

NIH initiatives if the NIH Director's review confirms their appropriateness for inclusion. That is, an institute or center could include aspects of existing programs in its trans-NIH obligation with confirmation from the director that they are relevant and should be counted as part of the IC's participation.

The Committee identified several options for organizing and managing a trans-NIH budgeting process:

- Sufficient funds (for example, 5% of the NIH budget would be about \$1.5 billion) could be appropriated to OD for the NIH director to make allocations to the participating ICs through the planning process.
- The target proportion of funds appropriated to each institute or center could be treated as though "in escrow" until the NIH director affirms that the unit has committed its expenditure for one or more of the identified trans-NIH initiatives of relevance to it.
- The use of the target proportion within each IC budget could be left to the IC and its director, with retrospective review by the NIH director and Congress. The annual performance review of the IC director would include attention to this element.

In the Committee's view, the second, or "escrow", option is preferred. The NIH director should have the authority to require the necessary funding commitments from the ICs for their participation in the initiatives chosen, but the committed funding should not be transferred either to the NIH director or to another IC. Rather it should be set aside to represent each unit's participation in furthering the chosen research initiatives. The initiatives should be carried out extramurally through multi-unit grant or contract programs, or as a combination of multi-unit extramural and participating unit intramural efforts.

The implementation of each of the initiatives should be overseen by special temporary task forces formed for this purpose with representation from each of the participating ICs. The commitment of the ICs should be reflected in the assignment of excellent staff to trans-NIH task forces on a full-time basis. As appropriate, NIH should also periodically sponsor scientific symposia to inform the relevant NIH constituencies and the director of progress on each trans-NIH strategic initiative.

Such a process would give NIH a capacity to respond to newly identified health needs in a coherent organization-wide manner. Together, the initiatives would have the effect of greatly expanding trans-NIH research and cooperation and breaking down barriers among IC research agendas. It might also make the NIH research enterprise more efficient and less apt to duplicate effort. Although OD would lead the process, its consensus-driven nature would incorporate the views of NIH's many internal and external constituencies and provide the potential to increase understanding and satisfaction of the external scientific and health advocacy communities.

Recommendation 4: Enhance and Increase Trans-NIH Strategic Planning and Funding

a. The director of NIH should be formally charged by Congress to lead a trans-NIH planning process to identify major crosscutting issues and their associated research and training opportunities and to generate a small number of major multi-year, but time limited, research programs. The process should be conducted periodically - perhaps every 2 years - and should involve substantial input from the scientific community and the public.

b. The director of NIH should present the scientific rationale for trans-NIH budgeting to the relevant committees of Congress, including a proposed target for investment in trans-NIH initiatives across all institutes. For example, an average target of 5% of overall NIH funding in the first year, growing to 10% or more over 4-5 years, may be appropriate.

c. The appropriations committees should annually review budget justifications and testimony from the NIH director and from individual IC directors about the participation of each unit in the planned trans-NIH initiatives and the portion of their budgets so directed. Congress should include budget targets in the appropriations report language. The Committee recommends beginning with 5% of the overall NIH budget.

d. To ensure that each IC uses the target proportion of its budget for trans-NIH initiatives of its choosing, that proportion of the annual appropriation to each unit should be treated as “in escrow” until the NIH Director affirms that the unit has committed to its expenditure for the identified trans-NIH initiatives.

e. The President should include in the budget request, and Congress should include in the NIH appropriation for OD, funds to support an appropriate number of additional full-time staff to conduct the trans-NIH planning process and “jump-start” the initiatives that emerge from this process.

Once again, the Committee believes that IC directors should view such planning as an opportunity for leadership and leverage on topics important to them and their constituencies and as a means for adapting their missions to new developments. Advocacy organizations, scientific societies, and NIH advisory bodies, including the Council of Public Representatives, likewise should see this process as an opportunity to gain synergies across the many interrelationships among diseases. If they do, the commitment to the trans-NIH task force should be reflected by the assignment of staff on a full-time basis, a career assignment viewed as a plum. The structure to accomplish the trans-NIH initiatives identified in the strategic process could take several forms depending on the size of the initiative, the number of institutes that need to be involved, and the likely time it will take to see the initiative to fruition.

The Committee recognizes that the prospects for putting new and significant trans-NIH objectives into practice will be affected by the growth of the NIH budget. If all existing programs continue to enjoy the highest priority there will likely be resistance in the early years of the initiative by institutes that claim difficulty in meeting their commitments while still offering some new grants. As a result the NIH director will have to exert superb and compelling leadership to withstand requests to release “escrowed” funds from trans-NIH projects. For these reasons, it is particularly critical that IC leadership comes to view participation in these initiatives as beneficial, and that Congress ask IC directors to report each year on the extent to which they are participating.

The Structure of the Office of the Director

More than 40 unit heads report to the director – the directors of 27 ICs, the heads of four program offices and the heads of 12 staff offices in OD. Although the FY 2002 budget of \$239 million for the OD may seem ample, the vast majority of this funding was earmarked for the support of a group of program offices and special programs, and that has been the case since 1993. (See Table 5.1) The composition of the earmarked amount has changed regularly, however, as OD has been used as an incubator for offices and programs that were established and then spun off as centers or institutes or absorbed into existing institutes. For example, the Office of Alternative Medicine became the National Center for Complementary and Alternative Medicine in 1998, the Office of Research on Minority Health became the National Center on Minority Health and Health Disparities in 2000, and the Office of Bioengineering and Bioimaging became the core of the new imaging and bioengineering institute in 2000.

	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002 (est'd)	2003 (req'd)
OD Operations	40,825	42,001	44,722	44,688	45,882	49,505	52,563	55,083	66,874	76,730	83,277
Director's Discretionary Fund	10,329	6,322	7,276	11,362	8,363	9,960	10,000	10,000	9,874	10,000	10,000
OAR	13,965	24,538	24,107	27,550	35,561	40,459	43,289	44,653	48,218	53,786	58,322
AREA Program	12,861	13,234	12,677	14,087	14,003	14,674	16,547	17,239	17,966		
Science Education	1,747	1,813	1,696	1,865	2,225	2,504	2,969	3,091	3,219	3,565	3,874
ORMH	9,037	9,794	8,923	8,920	8,825	9,839	10,741	11,367			
Minority Health Initiative	40,768	54,813	58,210	62,474	62,406	66,101	75,343	86,248			
ORWH	9,425	10,204	13,505	16,142	16,184	17,105	19,592	20,396	22,046	37,385	40,672
Loan Repayment Program			954	2,781	2,742	3,118	3,920	4,081	6,981	6,239	6,785
ORD			750	1,238	1,481	1,541	1,985	2,068	2,159	10,359	11,269
ODS				999	974	1,493	3,487	4,966	9,966	17,022	18,520
OBSSR			2,265	2,191	2,433	2,631	12,794	19,828	20,648	23,738	25,825
Foundation for the NIH					200	500	500	500	500		
OBB								200	1,970		
OAM	1,973	3,386	5,374	7,737	11,967						
LDRR	1,908	1,997	1,767	1,996	2,018						
Neurodegenerative Initiative					7,977						
Pediatric Initiative					4,976						
Women's Health Initiative	41,559	59,121	56,915	56,472							
Extramural Construction	4,949										
EARDA					1,500	1,500	1,905	1,984	2,067		
TOTAL	189,346	227,223	238,341	260,482	229,717	220,930	255,635	281,704	212,482	238,824	258,544

Source: For FY 1993-FY 2000, table provided by Office of the Budget, NIH; for FY 2001-FY 2003, table in FY 2003 NIH Congressional Justification Budget, Vol. V, p. OD-26 (DHHS, 2002), on-line at <http://odeo.od.nih.gov/intra/budget/fy03odcjrarrativefinal.pdf>. Figures for FY 2001, updated by NIH subsequent to submission of the FY 2003 budget, are used here.

To carry out the responsibilities of managing, planning, and coordinating the programs of the 27 ICs, the NIH director is assisted by a number of staff units collectively called OD Operations. A series of staff offices are headed by associate directors. They include the Office of Science Policy, the Office of Budget, the Office of Communications and Public Liaison, the Office of Legislative Policy and Analysis, several components of the Office of Management—Financial Management, Human Resource Management, and Research Services—and several other units.

The FY 2002 budget for OD Operations was less than \$80 million. Although the OD Operations offices assist the director in managing NIH, they are small and their budgets have not grown in proportion to NIH's research funding. The OD Operations budget increased by 88% from 1993 to 2002 compared with 125% for all of NIH. It amounts to 0.3% of the total NIH budget, down from 0.4% in 1993. Because of the tight budget for OD Operations, when unforeseen needs surface, as has happened recently with the development of stem cell research policies and harmonizing the rules for human subjects protection, OD is likely to have to "pass the hat" to the ICs to gather the additional resources needed. The Committee believes that the director should be given either a more adequate budget to support OD's management roles or greater discretionary authority to reprogram funding from earmarked components of the OD budget when necessary to meet emerging needs. Funding for OD Operations has not kept pace as NIH has expanded and has not grown in proportion to NIH's research budget; it is the Committee's view that it is inadequate for the effective management of the organization.

Recommendation 5: Strengthen the Office of the NIH Director

The Office of the Director should be given a more adequate budget to support its management roles or greater discretionary authority to reprogram funding from the earmarked components of its budget when necessary to meet unanticipated needs. In particular, if the director is given the responsibility and authority to conduct NIH-wide planning for trans-NIH initiatives, the director's budget will need to be amplified to take the costs of such planning into account.

In addition, the earmarking of funds by Congress for the establishment and continuation of programmatic offices in OD sometimes limits the director's flexibility and fluidity of resources, as well as his or her ability to effect change across the organization. It is difficult to ascertain whether the programmatic offices within OD have achieved their intended goals. Certainly, offices that move up and out to become centers or institutes reach the level of prominence desired by their advocates. But when the creation of an office in OD does not accomplish what the advocacy community desires, it increases the pressure for elevation of that office to a higher-level unit. The Committee believes that the process recommended in Chapter 4 for evaluating the merits of proposed additions to or subtractions from the list of ICs should also be applied to the creation of new offices in OD itself. The Committee is concerned that the creation of programmatic offices in OD could defeat the purpose of efforts to draw greater attention to important cross-cutting concerns because the creation of an issue-oriented office in OD tends to shift the responsibility for that issue to OD and away from the ICs, thereby reducing the attention that it might deserve. The time may be right to assess the effect that the programmatic offices in OD have had, including their role in the NIH director's policy and planning processes, whether the programs have clear goals, and whether there is a need to "sunset" an office once it achieves its goals.

Recommendation 6: *Establish a Process for Creating New OD Offices and Programs*
The public process recommended in Chapter 4 (Recommendation 2) for evaluating a proposal to create a new institute or center or to consolidate or dissolve an institute or center should also be used for a proposal to create, consolidate, or dissolve an office in OD. The process should be used to evaluate the scientific needs, opportunities, and consequences of the proposed change, the likelihood of resources being available to support it, and public support for it.

Fostering High-Risk, High Potential Payoff Research

To increase investment in high-risk, high potential payoff research, the Committee also believes that there is a need for a “Director’s Special Projects Program” external to the budgets of the ICs and funded as an OD line item. The goal of the program would be to fund the initiation of high-risk, innovative research projects. In a broad sense, the Committee imagines the program to be patterned after the Defense Advanced Research Projects Agency (DARPA), but with important differences.

The current peer-review mechanism for extramural investigator-initiated projects has served biomedical science well for many decades and will continue to serve the interests of science and health in the decades to come. NIH is justifiably proud of the peer review mechanism it has put in place and improved over the years, which allows detailed independent consideration of proposal quality and provides accountability for the use of funds. However, any system that focuses on accountability and high success rates in research outcomes may also be open to criticism for discriminating against novel, high-risk proposals that are not backed up with extensive preliminary data and whose outcomes are highly uncertain. The problem is that high-risk proposals, which may have the potential to produce quantum leaps in discovery, do not fare well in a review system that is driven toward conservatism by a desire to maximize results in the face of limited funding resources, large numbers of competing investigators, and considerations of accountability and equity. In addition, conservatism inevitably places a premium on investing in scientists who are known; thus there can be a bias against young investigators. The current steep decline in the growth rate of the NIH budget proposed in the President’s FY 2004 budget may make it even less likely that high-risk proposals will be funded.

The DARPA approach specifically seeks high-risk research and expects failures - a marked difference from the NIH study sections or the consensus approach of committees. DARPA’s mission is to develop imaginative and innovative ideas that have the potential for important defense-related technological impact. Such an impact is, however, by no means guaranteed. DARPA was developed specifically to foster research focused on high-risk, high potential payoff technology development. Typically, DARPA research establishes feasibility, and the results are handed off to other branches of the military services for development. The process has been successful: DARPA can claim credit for the foundational research that led to many noted and highly recognizable accomplishments, such as the Saturn rocket (1960s); the M-16 rifle (1970s); the Stealth fighter, global positioning system, and Arpanet/internet (1980s); the Predator unmanned aircraft (1990s); and the Global Hawk aircraft (2000s). Results of DARPA projects were also influential in the development of the National Science Foundation’s nanotechnology and computer sciences programs (Betz, personal comm.) It must be noted that much of the research funded by DARPA results in failure, which is the *expected* price of the quest for unusual breakthroughs.

Cook-Deegan (1996) provided examples of how real situations in the past might have been helped by the presence of a DARPA-like entity at NIH. In 1981, both NIH and the National Science Foundation (NSF) turned down a request from Leroy Hood and colleagues at Caltech for funding to automate DNA sequencing. The Caltech researchers subsequently obtained funding from the Weingart Institute instead, and by 1984 had made sufficient progress in prototype development to win NSF funding. Their method eventually became the dominant one on the market. In 1989, the National Center for Human Genome Research held a peer reviewed competition for large-scale DNA sequencing. It took about a year to develop and announce the competition and another year to review proposals and make funding decisions, but two years is a long time in a fast moving field. Ultimately the process rejected proposals from J. Craig Venter and Leroy Hood to do automated sequencing and selected a technology that was already a decade old. Hood's and Venter's subsequent successes in speeding up various sequencing efforts are well documented.

Cook-Deegan notes that many people assume that DARPA's approach is only suitable for engineering and technology development, but not pure science. "Experience suggests otherwise, however. Packet switching for electronic communication, computer time-sharing, integrated large-scale chip design, and networking were as conceptually 'basic' when DARPA was funding them as most molecular biology experiments are today." It is not difficult to identify research areas in today's biomedical science that might benefit from such an approach, for example, optics in neuroscience. Miller (2003) reported that in vitro studies of cultured neurons and brain tissue have built-in limitations for understanding how learning takes place in the brain. The "wish list" of neuroscientists includes finding a way to visualize individual neurons and track minute changes in the cells' structure and electrical activity; using two-photon microscopy to peer about half a millimeter into the brain to visualize the cortex and see into the unanesthetized brain; and finding a means to visualize deeper structures, such as the hippocampus. Fulfilling this wish list could bring about an optical revolution in neuroscience, but many of the needed techniques remain far off.

The Committee is aware that a number of alternative pathways might be used to establish a greater capability to support high risk research at NIH. NSF, for example, maintains a program of Small Grants for Exploratory Research (SGER) and allows its program officers to fund a limited number of small-scale, exploratory, and high-risk research projects at their own discretion subject only to internal NSF merit review. Such projects focus on preliminary work on untested and novel ideas, the application of new expertise or new approaches to "established" research topics, and work having extreme urgency with regard to availability of or access to data, facilities, or specialized equipment, including quick-response research on natural disasters and similar unanticipated events (NSF, 2002b). The SGERs are limited to \$100,000. As Cook-Deegan (1996) points out, this is a good idea, but there is no reason to think that innovative projects will always be small. The Committee believes that a mechanism to promote high risk research at NIH must allow for larger scale efforts to be effective. Another approach might be to experiment with the idea of a DARPA-like program with a pilot in only one or a few ICs. The Committee believes, however, that such an approach is likely to have limited success for two reasons. First, the establishment of such a program inside one or a few ICs is bound to limit its scope to the topical areas already in the ICs' portfolios, which could partly defeat its purpose. Second, locating such a program inside one or a few ICs would make it overly subject to their prevailing culture, which is already biased against high risk research. (It should be noted that DARPA was created to report to a high level Department of Defense official outside the research

organizations of the military services to protect it from the hostility of those services, which sought to eliminate it, Augustine, personal communication, 2002.) The Committee believes that the proposed Director's Special Projects Program would have its best chance for success if it were located in OD and had a leader who reports to the NIH director.

The proposed Director's Special Projects Program at NIH would, like DARPA, be designed to foster the conduct of innovative, high-risk research. Research initially funded through the program that generates useful results would be handed off after 3-5 years for further development and funding through the standard NIH peer-review mechanisms of the ICs. If positive results were not generated after a reasonable period of time, as is anticipated for much of this type of research, the projects would be terminated. The Committee expects that there would be clear missions and finite life spans for these projects and that multidisciplinary teams of investigators would perform most of them.

The heart and soul of DARPA are its program managers, the scientists and engineers who initiate and oversee the research programs. They are responsible for developing program ideas and choosing contractors to perform the research, usually at universities or in industry. (DARPA has no intramural research program.) The program managers are not permitted to spend more than 4 years at the agency. During their tenure, they have much autonomy in initiating programs and in choosing the investigators to be funded. DARPA reports to the Department of Defense's director for Defense Research and Engineering and operates in coordination with but independently of the military research and development establishment.

A cadre of talented program managers to select and manage the projects under the NIH Program could be drawn from academia, industry, and the ranks of NIH intramural scientists. Their most important feature would not be their previous affiliations, but rather that they are "idea people", capable of developing or recognizing unusual concepts and approaches to scientific problems. As at DARPA, the program managers would be appointed to strictly limited terms (such as 2-4 years) that are not renewable. The limitation on terms ensures that the programs are continually infused with fresh ideas and talent, which is thought to be a key reason that DARPA has been successful. The Committee believes that the NIH program managers should be able to accept ideas—either through unsolicited proposals or more directed responses to requests for applications or through peer review when appropriate—from the extramural and intramural scientific communities, as well as drawing on their own ideas. In addition, to allow for appropriate peer review, review panels specifically charged with selection of high risk, high potential return projects could be constituted outside the standard peer review mechanisms to assist the program managers in selecting projects for funding.

The Committee believes that such a program will have its best chance to succeed if Congress provides new funding. The Committee suggests that a budget of \$100 million for FY 2005 would be appropriate to initiate the program with a full time program director and four to six program managers. Because it is likely that it will take 8-10 years for the program to reach full maturity, a commitment to keep it going at least this long should be made. The Committee envisions the program's budget increasing over the 8-10 years to as high as \$1 billion per year.

Recommendation 7: Create a *Director's Special Projects Program*

A discrete program, the Director's Special Projects Program, should be established in OD to fund the initiation of high-risk, exceptionally innovative research projects offering high potential payoff. The program should have its own leader, who reports to the director of NIH, and a staff of short-term (2-4 years) program managers to manage

identified projects with advice on program content from extramural panels. The program should be structured to permit rapid review and initiation of promising projects; if peer review is deemed appropriate, the program should use peer review panels created specifically for it and charged with selecting high risk, high potential return projects. Congress should be prepared to provide new funding in the amount of \$100 million, growing to as much as \$1 billion per year for this endeavor, and commit to support it for at least 8-10 years so that a sufficient number of projects can reach fruition and a full assessment of program efforts can be made. A program review should be conducted during the fifth year to provide mid-course guidance.

Consistent with Recommendation 5 on sufficient funding for OD, this recommendation requires that the NIH director have the resources to hire first-rate scientists to help manage these increased responsibilities for developing programs.

The Intramural Research Program

The performance of the NIH intramural research program (IRP) has been evaluated several times in the last 25 years by advisory groups in response to administrative and legislative mandates. The evaluations included a review of NIH by the President's Biomedical Research Panel (Department of Health, Education, and Welfare, 1976), an Institute of Medicine report (IOM, 1988), a report by the Task Force on the Intramural Research Program of the National Institutes of Health (NIH, 1992a), and the report of the External Advisory Committee on the Intramural Research Program (NIH, 1994). That might seem to be an excess of scrutiny. But one might equally wonder whether the repeated calls for review reflect a continuing concern about the quality of programs and performance and a lack of response to criticism and recommendations. The IRP has faced persistent difficulties, including problems with recruitment and retention of senior scientists, expansion of a postdoctoral training program of uncertain and uneven quality, cumbersome administrative requirements, inadequately funded congressional and administrative mandates, and deteriorating facilities, in particular in the Clinical Center.

Like the extramural program, the IRP has a fragmented federated structure. The IRP, with its \$2.5 billion annual budget, comprises 19 separate intramural programs associated with the individual ICs. Just as each institute has a different legislative history and mandate from Congress, their IRPs vary widely in goals, scope, and size. Prior reviews have found this administrative structure to hinder unified or effective management of the IRP by the OD and to contribute to unevenness in quality, quality control, and productivity across NIH.

The IRP's proportion of the total budget has been reduced to only about 9 or 10 percent of the total NIH budget today and the IRP's budget growth has in recent years been deliberately slowed. Despite those reductions in the program, the question of what makes the IRP unique still recurs. In the past, the justification for the program was that it has distinctive input characteristics, including relatively long-term and stable funding of research programs, the availability of the Clinical Center's patient investigational facilities, few or no distractions from research for scientists, and a primarily retrospective, rather than prospective, review process for maintaining scientific quality.

For many years, the NIH campus was an exceptional training ground, especially for clinical investigators. Indeed, a large fraction of the senior leadership of the extramural biomedical research community received its training in the NIH IRP in the 1960s and 1970s. But the rapid growth in the NIH extramural program enabled biomedical research across the country

to expand in size and scope, providing superb opportunities for training at academic facilities elsewhere.

The most recent of the IRP evaluations, by the External Advisory Committee (EAC) of the Director's Advisory Committee, also known as the Marks-Cassell committee, originated because of concerns expressed by Congress and others regarding the quality, appropriateness, size, and cost of the NIH IRP. In its many recommendations to the NIH director, the EAC concluded that the problems plaguing the IRP, unless addressed, "may destine it to a mediocre future." The committee identified many areas of concern:

- The review process for tenured scientists and scientific directors,
- The review process for appointment to tenure,
- Postdoctoral training,
- Administrative issues affecting recruitment and retention,
- NIH-private sector collaborations,
- The process for allocating funds between the extramural and intramural programs, and
- Renewal of the Clinical Center.

The EAC recommended that each institute be subjected to an individual review along lines proposed by the EAC.

In response to the EAC report, NIH prepared and implemented a plan to address the review process for tenured scientists, a tenure-track program, and changes in postdoctoral recruitment and training. In addition, progress has been made in removing some of the administrative impediments to research and in enhancing the attractiveness of employment in the IRP through changes in the pay scale and retirement options for senior investigators. Some ICs implemented the IC-level reviews recommended by the EAC.

The present Committee, given the time and resources available for it to complete its task, did not attempt to evaluate the quality of the IRP systematically. The Committee is, however, persuaded that the significant efforts of recent years to reinvigorate the IRP and respond to various advisory committee recommendations have met with considerable success and that there has been a promising trend toward improved overall quality in the IRP. The Committee applauds the efforts of the NIH deputy director for intramural research to improve the program overall. Nevertheless, the balkanization of the IRP persists because of its multiple institutional budgetary and programmatic lines, which reinforce the "stove-piping" and continue to make it difficult for the senior management of NIH to ensure that the IRP supports NIH's overall strategies and plans. The Committee therefore suggests that it would be useful to consider mechanisms to foster interactions among the IRPs of the individual ICs, such as large-scale reassignments of space to bring similar programs in individual institutes together to create synergies. It might also be useful to explore reducing the balkanization of the IRPs by clustering programs that share common themes, approaches, and tools, similar to the approach currently being taken to integrate the neurosciences in one building.

The Committee is convinced that the IRP should not merely be an internal extension of the extramural community, but rather should be doing distinctive research that the extramural research community cannot, or will not, undertake. The Marks-Cassell committee stated that "quality – not necessarily uniqueness, should be of the highest priority in determining support for the intramural research program." The present Committee does not fully agree with that statement, especially with its implementation, which typically has ignored uniqueness. Too little weight has been placed on the need for distinctive contributions by the IRP. Uniqueness and

quality should both be essential justifications of the IRP, and it is not clear what distinguishes many of the current activities of the IRP from programs conducted by the extramural community.

Although evaluation of the quality of the clinical research protocols conducted in the Clinical Center was beyond the scope of the Marks-Cassell committee, that committee did ask the IC directors to characterize and prioritize their clinical protocols to assess their quality. The criteria used for the assessment included alignment with the NIH and Clinical Center missions, the extent to which the protocol represented cutting-edge science, whether the Clinical Center environment was uniquely appropriate for the study, whether the protocol addressed a national public health emergency, the importance of the protocol for training, whether the protocol was crucial to the institute's research program, whether the protocol was likely to contribute to patient care or patient comfort, and whether the protocol attempted to improve the efficiency or cost effectiveness of patient care. Some of the findings of the assessment – such as that only half of the protocols of NCI's Division of Cancer Therapy, the largest user of the Clinical Center, received excellent or good rankings – led to the identification of programs that were candidates for being phased out.

The present Committee believes that a similar process could be devised for the IRP as a whole to identify programs that represent neither excellent science nor science that is appropriately distinctive for the IRP. They are likely to constitute only a small fraction of the IRP's programs. The identified programs should be considered for phasing out, and the funding associated with them considered for diversion to other high priority uses, such as trans-NIH projects selected under the proposed NIH strategic planning effort. Opportunities for intramural-extramural collaboration, particularly for clinical research (see Chapter 4) and for research that is capital intensive and requires substantial investments in costly or specialized equipment should also be explored. Such collaborations would improve the IRP's ability to make distinctive contributions to research and NIH should find mechanisms for facilitating and managing them.

The Committee supports the principle that the science conducted by the IRP should be subject to standards of quality similar to those of the extramural program. As noted earlier, the peer review process used to evaluate most extramural research proposals commands widespread respect for its rigorous standards for maintaining research quality. At least some ICs are using comparable peer review for their IRPs. But the peer review process also has a tendency to enforce conservatism by discriminating against research whose outcome is highly uncertain. To evaluate research at the "cutting edge" fairly requires a culture, mindset, and process that views informative failures as the necessary price of strategic innovation. Investigators who conduct projects based on promising but unproven ideas that fail for reasons that could not be foreseen must receive credit for their work. Indeed, the special status of the IRP obligates it to take risks that might not be taken in the extramural program. Such considerations may require novel mechanisms for review, whose adoption could facilitate efforts to distinguish the IRP's role from what can be performed under the current extramural program. It should be reiterated that the Director's Special Projects Program proposed above should be open to ideas from IRP scientists.

The Committee agrees that another important aspect of the IRP is that it is capable of moving quickly and flexibly to meet urgent new needs. There is a lag of about a year while scientists outside NIH apply for and obtain funds to address new topics, but scientists in the IRP can shift focus very quickly simply by electing to do something different. In the middle 1980s, the IRP mounted a major AIDS research program a year before it was possible to award external grants. The importance of that history has again been well illustrated recently as NIAID

redirected the efforts of many of its researchers to respond quickly to the threat of bioterrorism and the need for new vaccines and countermeasures; they are also a logical leader in addressing the latest viral epidemic, SARS. NIH's Vaccine Research Center is another example of the IRP filling an important scientific need, for example, by designing a good manufacturing process pilot plant to develop and manufacture large amounts of HIV vaccine candidates for Phase I through Phase III trials. Another example is the high throughput screening program provided by NCI for cancer drug development studies, which is used extensively by academic and industrial laboratories.

Finally, the Committee heard repeatedly that there are historic and cultural factors that have stymied intramural-extramural research collaboration in general. Although there are some notable exceptions, these appear to be more through default than by design. NIH would benefit by promoting the exchange of personnel, space, and resources between the intramural and extramural communities, as appropriate, and as dictated by scientific or health needs.

Recommendation 8: *Promote Innovation and Risk-taking in Intramural Research*

The intramural research program should consist of research and training programs that complement and are distinguished from those in the extramural community and the private sector. The intramural program's special status obligates it to take risks and be innovative. Regular in-depth review of each component of the intramural program should occur to ensure continuing excellence. Allocation of resources to the intramural program should be closely tied to accomplishments and opportunities. Inter-institute and intramural-extramural collaborations should be supported and enhanced.

Summary

Although the Committee is not recommending major changes in the number or structure of NIH's institutes and centers, it concludes that the organization needs to be and can be transformed in other ways to meet its and the nation's scientific and health goals. Most important, the Committee concludes that it is time to begin to redirect, over the next 4-5 years, a small but significant fraction of the NIH budget to a series of strategic trans-NIH initiatives that will be carried out by both the intramural and extramural programs under the auspices of the individual institutes and centers working in partnership. Redirected funds will in many cases profoundly influence the core missions of ICs. This will require the formalization of a careful, open, and consensus-driven planning process under the direction of the NIH director that should be used to select strategic initiatives, assign responsibilities for them, and elicit commitments of funds from participating units. The Committee commends the current NIH director for undertaking what has been referred to the Roadmap effort. Congress should formalize the process by charging the director to lead a regular trans-NIH planning process to identify major crosscutting issues and opportunities and to generate a small number of high priority research initiatives. The process should be periodic - at least once every 2 years - and should involve substantial input from the scientific community and the public.

The Committee finds that funding for the operations offices of the NIH Director has not kept pace as NIH has expanded and has not grown in proportion to NIH's research budget. OD Operations funding is inadequate for the effective management of the organization and should be increased. The Office of the Director does not have the resources to respond to unexpected needs of NIH as a whole without appealing for support from the ICs. Programmatic offices in OD that were created with specific functions should be assessed for successes and failures and

whether these entities should be perpetuated indefinitely. The public process for evaluating proposals to create organizational units described in Chapter 4 should also be applied to programmatic offices in the OD.

Finally, to enhance the quality and innovative nature of NIH's portfolio, the Committee proposes a variety of adjustments in intramural research and the creation of a new program in OD to promote high-risk, high-payoff research.

ACCOUNTABILITY, ADMINISTRATION, AND LEADERSHIP

Public accountability and leadership are key aspects of the National Institutes of Health's (NIH's) stewardship of the biomedical enterprise because of the imperatives to maintain public trust, reassure Congress that the public's interest is being served, and ensure that NIH's tactical and strategic objectives for its research and training programs are thoughtfully selected, effectively pursued, and responsive to NIH's research mission, national health concerns, and the need to prepare the next generation of scientists.

Accountability is a critical and challenging aspect of leadership. It is especially challenging for an organization like NIH, which serves a broad array of constituencies and is devoted to research and training, in which outputs can be difficult to measure, market discipline is largely absent, and there is incomplete agreement on what metrics are the most appropriate. On the one hand, too mechanistic a system of accountability may fail to capture the nuances of scientific progress and indeed may stifle it or lead to an illusion of precision. On the other hand, too loose a system of accountability may lead not only to a potential loss of public confidence and trust but also to uncertainty about whether NIH's efforts are achieving, even in an approximate way, its objectives.

This chapter focuses on means by which NIH can enhance its public accountability and ensure the continuing vitality of its leadership, both of which are influenced by and have a capacity to alter the agency's organizational effectiveness. Specifically, the Committee focused on the need for improved NIH-wide data gathering and coordination, increased attentiveness to hiring and review of senior leaders, and better use of the advisory committee system. Important additional aspects of NIH's ability to meet its scientific and public health mission are the availability of sufficient resources in its management-support network to accomplish its goals, and the ability to direct administrative functions in the best interest of its research and training mission.

Annual Mechanisms for Public Accountability

Each year, NIH must complete two processes for accounting to Congress and the President on its progress in meeting its goals, conforming to its mission, and justifying its request for appropriations for the next fiscal year. Those processes, developing the budget and responding to the Government Performance and Results Act (GPRA) of 1993, are not sufficient to meet all accountability needs but they do provide useful starting points.

The Budget Process: Congressional Justification

Every fall, each institute or center (IC) with an appropriation must prepare a congressional justification budget (the CJ) that details accomplishments of the preceding year, current initiatives, and plans.³² The process of preparing the CJ is labor-intensive; programs in each IC are surveyed for data and material considered crucial for justifying programs and budgets. Each IC's information is submitted to the Office of the Director (OD), where it is reviewed and then compiled with all the other IC's CJs and submitted to Office of Management and Budget (OMB). The exception to this process is the National Cancer Institute (NCI), which

³² The formal title is "Justification of Estimates for Appropriations Committees." The CJ has a section for each IC, consisting of a set of tables and budget narrative (see Department of Health and Human Services, 2002).

under the National Cancer Act of 1971 develops a “bypass budget” that goes directly to the President and OMB.

The budget process is, perhaps, the most powerful accountability mechanism used by NIH, forcing the agency and its various units to justify their places in the programs of the President. It is both a planning and an accountability process. As in other federal agencies, the deadlines of the budget process drive the planning and priority setting process. In addition, the capacity to influence the congressional appropriation process is one of the major ways in which NIH leadership can coordinate activities across NIH. Thus, development of the annual CJ provides the perfect opportunity for NIH to respond to the Committee’s call for more investment in trans-NIH initiatives, as described in Chapter 5. If all ICs were required to account for trans-NIH activities in their CJs, the NIH director, the Secretary of Health and Human Services, and Congress would have a better sense of progress in this category of work.

The New Approach to the Government Performance and Results Act

Under GPRA, every major federal agency must ask itself some basic questions every year: What is its mission? What are its goals and how will it achieve them? How can it measure performance? How will it use performance results to make improvements?

GPRA forces a shift in the focus of federal agencies away from such traditional concerns as staffing and activity levels toward a single overriding issue: results. GPRA requires agencies to set goals, measure performance, and report on accomplishments annually. Every NIH IC goes through an annual process in which program managers are asked to review their portfolios for scientific accomplishments that provide evidence of meeting goals and missions.

Until 2003, NIH tracked the success of its programs through a comprehensive overview of its progress by reviewing and compiling scientific advances and external recognition of NIH-supported investigators. Starting in 2003, however, NIH is using more specific and transparent goals to measure research outcomes; the Committee supports this change.

The new framework being used by NIH characterizes goals on the basis of the likelihood that they will be attained and the time targeted for completion. For FY 2004, there are 27 goals arranged according to their likelihood of success and years to completion; the longest time line is set at 10 years (Table 6.1). According to NIH, the goals must be credible to researchers, the public, and other NIH stakeholders and should be as specific as possible to address definable problems. Goals that lend themselves to annual reporting and reports of incremental progress are encouraged. NIH goals must also coordinate with the overall Department of Health and Human Services (DHHS) plan, as well as those of the Centers for Disease Control and Prevention (CDC), the Agency for Healthcare Research and Quality (AHRQ), the Food and Drug Administration, the DHHS “Healthy People 2010” initiative, and the President’s Management Agenda.

Council of Public Representatives

NIH created the Council of Public Representatives (COPR) and Public Liaison Offices in response to an Institute of Medicine (IOM) report (IOM, 1998), which recommended that such bodies be created to formalize and systematize communication with the public at the highest levels of NIH. The scope and activities of COPR are evolving, but its charge is broad. COPR is a federal advisory committee of 21 members of the public from across the country who are chosen through an open nomination and application process. Its role is to advise the NIH director on public input and participation in NIH’s activities, research priority setting, and outreach

programs and efforts. Thus, COPR provides a formal mechanism for public input at the level of the NIH director, but there are multiple additional opportunities for public input across NIH. In addition, each institute has public relations activities with a major focus on communicating with and receiving input from diverse stakeholders.

COPR provides a relatively new opportunity for receiving public input and increasing accountability to a broad constituency. These and other institutional changes within NIH were designed to increase public accountability, although there has been no formal evaluation of the impact of these changes on indicators of public accountability. Furthermore, no criteria have been proposed to assess and monitor public accountability or the effectiveness of mechanisms to improve or assure it at different levels.

Challenges to Achieving Public Accountability

The committee heard anecdotal evidence that priority setting criteria often are not transparent to the interested public (for example, voluntary health organizations) and that efforts to follow indicators of success have been limited by lack of well-developed data systems suitable for tracking expenditures and research, training, and other NIH-sponsored activities in relation to institutional goals or priorities.

Because the American public is diverse, it is difficult to know what degree of public accountability is achievable at various levels, and how broadly public accountability should be implemented. Likewise, the public is likely to have divided views on what constitutes or fulfills public accountability. Indeed, in practice much of the monitoring of accountability may fall to advocacy organizations, which may or may not represent the diverse views of the spectrum of individuals suffering from various illnesses. Such organizations also might not advocate health research that cuts across diseases; this may lead to tensions over the accountability mechanisms used by Congress and the administration, including for example the level of appropriations for particular ICs, the formation of new ICs, NIH leadership approval, and program and project mandates included in authorizations and report language.

Given the barriers at both levels of translation (described in Chapter 3 and Sung, et al., 2003), another challenge to addressing accountability is the weak link between research results on the one hand and public knowledge and perceptions of their significance, potential impact, and NIH's role on the other. Several institute directors told the Committee that when NIH-supported extramural research results are reported, credit is given primarily to the investigators and their institutions without linking them to NIH's support. Giving credit to individual ICs may also minimize the importance of NIH's combined efforts. Thus, media acknowledgment of NIH's role is often minimal or absent, and this can create misleading impressions of NIH's public accountability. NIH officials told the committee that although there is no overarching (NIH-wide) communication plan, efforts are under way to develop one that mirrors the agency's "Roadmap", one that will review research plans from the perspectives of various audiences to determine whether NIH is communicating effectively. There is no doubt that communicating the depth and breadth of NIH's activities and missions is a challenging task, but doing so and doing so with credibility is essential to bolstering public confidence in the agency and enhancing its accountability.

Data Gathering and Reporting

A related problem in achieving accountability is that, given the large research and training portfolio of NIH, it is difficult to track NIH's many scientific contributions and make

information about them available in a manner that is understandable to all constituents. One of the most common types of questions asked by Congress and the public is how much research on specific diseases is being funded? Such data provide only an approximation of the level of effort devoted to objectives, but individuals and groups concerned about specific diseases or health problems often use them as a measure of input and effort to assess aspects of the NIH research and training portfolio of most interest to them. Even NIH officials complained to the Committee that such data are difficult to gather and are usually suspect because each IC uses its own method to estimate its investment. Although senior management at NIH has long recognized that the absence of a standard method for "coding" is a serious problem, no concerted effort to develop one has yet produced results.

NIH officials often point out that statistics on spending by disease may not be very useful precisely because there are no simple relationships between measures of the burden of disease and how NIH allocates funding. Health needs are an important factor, but there is rarely a straightforward one-to-one relationship between health needs and research funding allocations, let alone estimated incidence, prevalence, or burden of disease. Furthermore, the scientific opportunities for progress vary greatly among diseases in sophistication of the current knowledge base, promising lines of inquiry, and availability of sufficient researchers and facilities. Therefore, the amount of research support that can be linked directly to a specific disease not only is difficult to establish but is not by itself an adequate measure of how much or how well NIH is progressing against the disease. Nor does it reflect the potential relevance of basic research to multiple specific diseases (IOM, 1998) in that it is sometimes difficult to know which research is most relevant to the health problem involved.

Despite those challenges, the Committee concludes that the current lack of an information management method and infrastructure to collect, analyze, and report investment data in a timely fashion must be addressed. It is particularly important for NIH leadership to improve the quality and analysis of its data on the allocation of NIH funds by disease for planning and priority-setting purposes. The problem requires the development of an NIH-wide agreement on what to track and publish and a single method for coding data that uses consistent definitions and deals with the uncertainties inherent in counting research that is only related but not directly applicable to a specific topic. Once developed, the statistics should be kept current and their accuracy ensured through quality control. NIH information management must also be improved to meet goals in tracking scientists trained and supported with NIH funds.

NIH is currently instituting substantial upgrades in its business, grant tracking, and clinical research-protocol IT systems, but these upgrades will not address the problem under discussion here. The committee recognizes that developing an additional informatics system to gather data on the nature of NIH's diverse research and training programs consistently and uniformly is likely to be expensive and time-consuming and will require substantial resources and personnel. However, the development of such a system would provide invaluable information to all parties interested in NIH's programs—Congress, other Executive Branch agencies, the public, the research community, and the leadership of NIH itself. Indeed, the effective management of NIH's research and training programs require such a capacity and therefore would constitute a worthwhile investment. It also would provide the most reliable information for consideration of proposals to add, merge, or eliminate institutes, centers, and offices. Congress, which is likely to be one of the main beneficiaries of an improved information system, should consider the need for additional resources for this purpose in the budget process.

Recommendation 9: *Standardize Data and Information Management Systems*
For purposes of meeting its responsibilities for effective management, accountability, and transparency, NIH must enhance its capacity for the timely collection, thoughtful analysis, and accurate reporting of the nature and status of its research and training programs and public health advances. Data should be collected consistently across institutes and centers and submitted to a centralized information management system.

Building Accountability Through Leadership

The vision of the NIH leadership regarding accountability and the procedures and structures that the leadership adopts to enhance it are perhaps the most important ingredients in the complex mix of policies and strategies that enable NIH to meet its responsibilities to all its constituents. Leadership and vision may influence the extent to which accountability is reinforced and implemented at diverse levels of the NIH system, from top management through staff and to individual intramural and extramural investigators.

Although there have been performance plans for IC directors and senior scientists since Director Harold Varmus established them in the 1990s, the current administration has required a formal performance assessment for all supervisory personnel throughout the government. All supervisory personnel at NIH therefore are required to develop a “performance contract” listing the items each person is accountable for, which is the basis of an annual assessment. The NIH director must negotiate his or her performance contract with the Secretary of Health and Human Services. Likewise the NIH director negotiates a contract with each of the more than 40 people who are his direct reports.

The earlier system for performance plans was general in its approach, but the new contracts are more specific, for example, “increase the prevention and public awareness of diabetes”. Relevant items cascade down from the top; for example, the diabetes goal is in the President’s contract with the Secretary, who then delegates it to the NIH director, who assigns it to the appropriate senior staff. Thus, the performance contracts are a mechanism for senior management to convey what is important to their subordinates. Outreach and communication factors are major items in the contracts of IC directors.

IC directors are also involved in two other types of review:

- Every 5 years, IC directors are reviewed for their overall performance, including scientific leadership, management of their institute or center, and outreach and communications.
- Every 4 years, IC directors who conduct their own research are evaluated scientifically, as are all intramural scientists. That means that the Board of Scientific Counselors of the institute in which the research is performed oversees the review. Most directors conducting their own research do so in another institute to avoid conflict of interest.

Most senior government officials are in the top ranks of the government service (GS) system or in the Senior Executive Service (SES) and are covered by a variety of civil service provisions under Title 5 of the personnel law that protect them from dismissal and loss of rights without considerable effort on the government’s part. But salaries for SES personnel are capped. To be able to offer higher salaries and attract the nation’s most distinguished scientists, NIH obtained permission 10 years ago to place its senior positions under Title 42 of the law. Title 42

allows NIH to offer higher salaries, although people hired under this authority lose many of the civil service protections provided under Title 5 and must accept 5-year terms as opposed to permanent employment. Most directors chose to move into the Title 42 program, so they are, in fact, already subject to 5-year renewable terms. Under this system the Secretary of Health and Human Services retains approval authority for appointments. Thus, the NIH director can only recommend, but not appoint, senior leadership in the agency. The committee concludes that this lack of authority hinders the ability of the NIH director to form a cohesive senior leadership team to achieve NIH goals.

The committee also concludes that in the current NIH environment, reviews of leadership—a form of public accountability—are too informal and ad hoc to be effective. The processes and criteria for review are not obvious or well defined. One of the more obvious criteria for review, in addition to scientific excellence and leadership skills, should be an individual's performance in imagining and engaging in creative collaborations with colleagues in other institutes and centers, as such collaborations will be an increasingly important aspect of moving some of the most needed new NIH initiatives forward. And the informal review process has changed and depends on the particular policies and practices of the sitting NIH director and the personnel system in which a given IC director resides.

The committee also believes that a healthy degree of turnover in leadership is critical for sustaining the vitality of a research organization. It also provides the opportunity for leading scientists across the nation to leave their positions for a set period and to come to NIH as a form of public service and, in part, to provide effective scientific leadership to critical elements of the nation's biomedical enterprise.

Recommendation 10: Set Terms and Conditions for IC Director Appointments and Improve IC Director Review Process

a. All IC directors should be appointed for 5-year terms. The possibility of a second and final term of 5 years should be based on the recommendation of the director of NIH, which should include consideration of the findings of an external review of job performance. The authority to hire and fire IC directors should be transferred from the Secretary of Health and Human Services to the NIH director.

b. The Director of NIH should establish a process of annual review for the performance of every IC director in terms of his or her effectiveness in fulfilling scientific and administrative responsibilities. The results of such reviews should be communicated, as appropriate, to the Advisory Committee to the Director and/or the Council of Public Representatives.

By communicating, as appropriate, the results of reviews to the NIH director's advisory groups, the IC directors can demonstrate an additional level of accountability. While some aspects of a review should be held as confidential, those elements that relate directly to the mission and objectives of NIH should be made available to the director's advisors.

The committee concluded that review and revitalization of the OD is an essential prerequisite for accountability and leadership. The committee noted that the National Science Foundation Act of 1950 (42 U.S.C. 1861 et seq.), as amended, creates a term of 6 years for the NSF director and concluded that this has been a good model for creating a system of

accountability and periodic review that has the possibility of transcending changes in administrations.

Recommendation 11: *Set Terms and Conditions for the NIH Director Appointment*
The NIH director, appointed by the President, should serve for a term of 6 years unless removed sooner by the President. The possibility of a second and final term of 6 years should be based on a positive external review of performance and the recommendation of the Secretary of Health and Human Services.

Finally, the committee believes that the special status granted NCI by the National Cancer Act should be re-examined. The National Cancer Act of 1971, in addition to making the NCI director a Presidential appointee, created the President's Cancer Panel, composed of two scientists and one management specialist who provide progress reports to the President on the status of NCI's research. The act also replaced the National Cancer Advisory Council with an 18-member National Cancer Advisory Board composed of scientists and laypersons offering guidance and advice to NCI on all major initiatives. In addition, the act allows the NCI director to submit the institute's budget directly to the President, bypassing the NIH director in the process.

Because the President appoints the NCI director and the NCI budget bypasses the NIH director, it is possible that an unnecessary rift is created between the goals, mission, and leadership of NIH and those of NCI. NCI is by far and has been for some time the largest NIH institute (approximately 17% of the total NIH budget). It is not in the interests either of NIH's overall research and training programs, or of NCI, for the NIH director to have such limited authority. In addition, as the biological and cellular basis of cancer becomes more widely understood, the basic science underlying cancer research has direct implications for the etiology and progression of numerous other diseases, for example the autoimmune, infectious, and even cardiovascular diseases. Thus, for scientific and administrative reasons, NCI's special status should be reconsidered.

Recommendation 12: *Reconsider the Status of the National Cancer Institute*
Congress should reassess the provisions of the National Cancer Act of 1971, particularly as they affect the authority of the NIH director to hire senior management and plan and coordinate the NIH budget and its programs in their entirety.

It should be noted that the requirement that NCI prepare a bypass budget every year has some positive aspects in that the institute must undertake an annual strategic planning process. This useful exercise should not be dropped if NCI changes its administrative status as recommended above. Rather, all ICs should be required to develop an annual strategic plan, if they are not already doing so.

The Advisory Committees

Like other federal science agencies, NIH makes extensive use of advisory committees of nonfederal scientists, health advocacy representatives, and others to ensure the best possible input of expertise and additional perspectives on the evaluation of programs and the development of policies and priorities. NIH had 140 chartered advisory committees as of May 2002, more

than any other federal agency.³³ The Public Health Service Act (PHSA) authorizes appropriate scientific and technical peer review of biomedical and behavioral research grant and cooperative agreement applications, research and development contracts, and research conducted at NIH through its advisory committees.

As described in greater detail in Chapter 2, NIH uses several types of advisory committees. Those groups can be located in the Center for Scientific Review (CSR) (the study sections) or the councils and boards created and used by individual institutes that choose not to use CSR for review of particular initiatives. National Advisory Councils and Boards perform the second level of peer review for research grant applications and offer advice and recommendations on policy and program development, program implementation, evaluation, and other matters of importance for the mission and goals of the IC; and they provide oversight of research conducted by IC intramural programs. The dual review system, which separates the scientific assessment of proposed projects from policy decisions about scientific areas to be supported and the resources to be allocated, permits a more objective evaluation than would result from a single level of review. NIH can make awards only if they have been approved by a national advisory council and the Secretary, and this helps to insulate NIH from pressure by a member of Congress or the administration to fund a particular project. The national advisory councils are also charged with providing advice on policies and programs, although several studies have found that members of the national advisory councils do not always feel they play a strong role in policy-making.³⁴ The dual system of review provides the responsible NIH officials with advice about both scientific and societal values and needs (NIH, 1992b).³⁵

In the appointment process, the President generally follows the recommendations of the Secretary, and the Secretary generally follows the advice of the NIH and IC directors in filling positions, although they add their own candidates from time to time. During the 1972-1974 period, when the Nixon administration was trying to exert greater control over the NIH budget, there was conflict with the scientific community over the perceived politicization of the advisory committee appointment process; this issue re-emerges from time to time and is of current concern to the scientific and health advocacy communities (e.g., Bass et al., 2003). Moreover as a general matter, the success of any scientific enterprise is dependent on the encouragement of a wide variety of independent views. The Committee believes that it is essential that members be appointed to these advisory groups because of their ability to provide scientific or public health expertise to the review and approval of awards and policies. They should not be selected to advance political or ideological positions.

Several related issues emerged during the committee's deliberations with respect to NIH's advisory council system. First, there are important differences in the use and roles of the councils among ICs. Some councils are actively involved in setting institute goals and planning. In other cases, council actions are pro forma, with little advice or involvement sought from council by institute personnel. In still other cases, council members might also be grantees of the institute, and thus might feel constrained in expressing strong views or views that differ from

³³ They have 4,298 members, 75% of whom are members of initial review groups that evaluate applications for research funding. See overview and list of committees by appointing officials at <http://www1.od.nih.gov/cmo/about/index.html>.

³⁴ One study was conducted by the Institute of Medicine's Committee for a Study of the Organizational Structure of the National Institutes of Health in 1984. The other was conducted in the middle 1990s by a committee appointed by the NIH director. Neither report was made public. Copies are in the possession of the authors.

³⁵ Contracts are subjected to a similar peer review process, except that the second level of review is by senior IC staff.

than those held by institute or program staff. Those issues highlight a missed opportunity for NIH. Advisory councils should routinely and consistently be consulted in the priority setting and planning processes of an institute. They should have active involvement in decisions regarding issuance of program announcements and requests for applications, which often reflect an institute's priorities and responses to emerging opportunities or demands. They should be working to ensure that the IC is held accountable in reaching its goals and communicating with the public. They should understand and be supportive of relevant trans-NIH initiatives. Finally, a criterion for review of every institute director should be how he or she interacts with and uses the expertise of his or her advisory council.

Under Section 406 of the Public Health Service Act, national advisory councils have up to 18 members appointed by the Secretary and nonvoting ex officio members from NIH and other federal agencies. Two-thirds of the appointed members are to be "from among the leading representatives of the health and scientific disciplines (including not less than two individuals who are leaders in the fields of public health and/or social sciences) relevant to the activities of the national research institute" and one-third "from the general public and shall include leaders in the fields of public policy, law, health policy, economics, and management." The Committee believes that the advisory council system should guarantee that ICs receive independent and qualified advice. Their members therefore must be reasonably free of conflicts of interest. In addition, if NIH is to achieve the goal of increased trans-NIH collaborations, it will be important to have cross-fertilization of institutes through advisory council membership. For example, it would be useful to have a cancer researcher (who receives funding from NCI or the American Cancer Society) serve on the council of the National Institute of Environmental Health Sciences or the National Institute of Child Health and Human Development.

Recommendation 13: Retain Integrity in Appointments to Advisory Councils and Reform Advisory Council Activity and Membership Criteria

a. Appointments to advisory councils should be based solely on a person's scientific or clinical expertise or his or her commitment to and involvement in issues of relevance to the mission of the institute or center.

b. The advisory council system should be thoroughly reformed across NIH to ensure that these bodies are consistently and sufficiently independent and are routinely involved in priority-setting and planning discussions. Councils should be effectively engaged in discussions with IC leadership to enhance accountability, facilitate translation of goals and activities to the scientific community and the public, and provide feedback to the IC director. To achieve sufficient independence and avoid conflicts of interest, a substantial proportion of a council's scientific membership should consist of persons whose primary source of research support is derived from a different institute or center or from outside NIH.

Research Management and Support (RMS)

Although administrative or overhead costs are often suspect in the eyes of those who would like to see more money going directly to research or training, at appropriate levels they are essential to the effectiveness of any organization, including those that sponsor research and training programs. Similarly, the effectiveness of those responsible for the wide array of

necessary administrative services depends on their leadership and management capabilities and their ability to keep administrative and overhead costs deployed in a manner that best supports the primary missions of the organization.

In the case of NIH, the resources for administrative and overhead functions flow through the Research Management and Support (RMS) budgets of the various units that make up NIH. These budgets, collectively, support all the administrative costs of operating NIH, including management of extramural activities (planning, receipt, peer review, and awards), some intramural research program costs, program development, priority setting, education and outreach, acquisition and maintenance of new information technology systems, professional development, and facility management. Given the structure and funding mechanisms of NIH, the aggregate RMS budget is composed of 25 budget line items, one from each of the ICs that receive separate budget appropriations from Congress. RMS is functionally distinguished from the NIH OD, which is responsible for strategic leadership and receives a separate appropriation.

The administrative costs of NIH have been scrutinized regularly over the last few decades. In the early 1990s, congressional limitations were imposed that restricted inflationary and program growth of the RMS budget. A 1997 management study by Arthur Anderson (National Institutes of Health, 1997b) led to many management improvements, including

- Centralization and improvement of purchasing programs
- Conversion of the mail service to an outsourced performance-based contract
- Development of generic position descriptions
- Hiring of a Chief Information Officer, and
- Creation of a Central Service Review Committee to review the budgets of central service organizations (NIH, unpublished draft report).

In FY 1996, the NIH appropriation contained language that reduced RMS by 7.5% below the FY 1995 level. Despite growth in the overall NIH budget, the RMS reduction was not made up in FY 1997 nor was any growth provided; in FY 1998, an increase of only 1% was allowed. In contrast, from FY 1995 to FY 1999, the extramural program grew at a rate 7 times that of RMS. In the FY 2001 budget, RMS represented 3.3% of the total NIH budget, down from 4.5% in 1995. Since FY 1993, the RMS share of the total NIH budget has decreased every year. From FY 1984 through FY 1999, inflation, based on the Gross Domestic Product, increased 58.3%. During the same period, RMS grew 96.2%, while overall NIH grew 217.6%, more than four times the growth rate for RMS (NIH, unpublished draft).

At the same time, the growth in the NIH budget and the rise in congressionally mandated activities have increased the administrative requirements needed to operate a growing and diverse research organization; for example, GPR is a labor-intensive and expensive annual exercise required by Congress. Other new programmatic requirements have involved the establishment of centers, registries, and other funding requirements, all of which add costs for which RMS must be further stretched.

To accommodate RMS reductions, many institutes have implemented measures to reduce costs, such as introducing modular grant applications and awards, streamlining reviews, and converting to electronic-based research administration. Those are laudable goals under any circumstances, but adverse consequences of the restricted RMS budget seem to be growing. Many are concerned that the strain on the system harms the peer review system, stretches staff too thin, limits business oversight and scientific review, and hinders the ability to respond to

increasingly complex research programs and conduct trans-NIH initiatives. NIH's own assessment of the negative impact of the restricted RMS budget found 7 areas being adversely affected: stewardship of public funds; scientific advice and program development; public health education and community outreach; information technology acquisition, maintenance, and training; staffing issues; professional development; and facilities management (NIH, unpublished draft). There may have been good reason in the past to celebrate the containment of costs, but the Committee feels that the effectiveness of NIH is now imperiled by the lack of adequate resources to provide appropriate support both for its primary research mission and for meeting its accountability responsibilities.

Other groups have also suggested that RMS funding be raised to provide adequate means for accomplishing NIH's primary goals and to ensure a capacity for strategic planning and evaluation of its programs. In 1998, an IOM committee recommended that Congress "adjust the level of funding for RMS so that NIH can implement improvements in the priority-setting process, including stronger analytical, planning, and public interface capacities" (IOM, 1998). In 2001, the Federation of American Societies for Experimental Biology also recommended increasing RMS. The growing mismatch between the most essential or mandated administrative requirements and the RMS resources available to pay for them must be addressed.

Recommendation 14: *Increase Funding for Research Management and Support*
Congress should increase the appropriation for RMS to reflect more accurately the essential administrative costs required to effectively operate a world-class \$27 billion/year research organization. Moreover, when additional congressional mandates are imposed on NIH through the appropriations process, they should include funds to cover necessary administrative costs.

Summary

NIH uses resources in various ways to enhance public accountability, leadership and management efficiencies. However, improvements can be made.

First, NIH must commit to developing an improved system for gathering, managing, and reporting data to facilitate public engagement, strategic planning, management of the research and training portfolios, congressional justifications, and scientific communication.

Second, increased attention to the system of hiring and periodic and systematic review of IC directors will revitalize the leadership, invigorate the overall scientific community, and facilitate change and evolution of NIH's mission and goals. The NIH Director should have the authority to appoint IC directors, including the director of NCI, with the goal of building a team that shares a vision and a plan. Congress should revisit the special status of NCI to determine whether it continues to meet the needs of the current NIH organization and structure.

Third, leadership must make better use of the advisory committee system, which should be a consistent source of independent advice.

Fourth, in order to operate a world-class research agency, NIH must be provided sufficient resources to support its management needs.

Table 6.2 NIH GPRA Research Outcomes

SK igh	1-3 years	4-6 years	7-10 years
	<p>1a Conduct medications development with use of animal models, and begin to conduct Phase I and II trials of two potential treatments for alcoholism: cannabinoid antagonist Rimonabant and corticotropin-releasing hormone antagonist Antalarmin.</p> <p>1b By 2006, develop one or more prototypes for a low-power, highly directional hearing aid microphone to help hearing-impaired persons better understand speech in a noisy background.</p>	<p>2a By 2007, demonstrate the feasibility of islet transplantation in combination with immune tolerance induction for the treatment of type 1 diabetes in human clinical studies.</p> <p>2b By 2009, evaluate the efficacy of two novel approaches to prevent weight gain and/or treat obesity in clinical trials in humans.</p> <p>2c Develop methods that can classify at least 75% of proteins from sequenced genomes according to evolutionary origin and biological structure.</p> <p>2d By 2007, develop an HIV/AIDS vaccine.</p>	<p>3a Identify at least one clinical intervention that will delay the progression, delay the onset, or prevent Alzheimer's disease.</p> <p>3b By 2010, develop one universal antibiotic effective against multiple classes of biological pathogens.</p> <p>3c Determine the efficacy of using salivary diagnostics to monitor health and diagnose at least one systemic disease by 2013</p>
	<p>4a By 2005, develop two new animal models to use in research on at least one agent of bioterror.</p> <p>4b By 2005, develop improved animal models that best recapitulate Parkinson's Disease (PD) based emerging scientific findings of genetic or environmental influences, or interactions of genes and the environment on the development of PD.</p> <p>4c By FY 2007, identify 20 small molecules that are active in models of nervous system function or disease and show promise as drugs, diagnostic agents, or research tools.</p>	<p>5a By 2007, evaluate the efficacy of three new treatments for HIV infection in phase II/III human clinical trials in an effort to identify drugs that are more effective, less toxic, and/or simpler to use than the current recommended HIV treatment regimen.</p> <p>5b Establishing the efficacy of statins in preventing progression of atherosclerosis in children with Systemic Lupus Erythematosus (SLE or lupus).</p> <p>5c Expand the range of available methods to be used to create, analyze, and utilize chemical libraries, which can be used to discover new medicines. Specifically, use these chemical libraries to discover 10 new and unique chemical structures that could serve as the starting point for new drugs.</p>	<p>6a Identify the genes that control the risk for the development of age-related macular degeneration and glaucoma in humans.</p> <p>6b By 2011, assess the efficacy of at least three new treatment strategies for reducing cardiovascular morbidity/mortality in patients with type 2 diabetes and/or chronic kidney disease.</p> <p>6c By 2012, develop a knowledge base on Chemical Effects in Biological Systems using a "systems toxicology" or toxicogenomics approach.</p>

<p>7a By 2005, evaluate 10 commonly used botanicals for inhibition/induction of enzymes that metabolize drugs as a method of identifying potential botanical/drug interactions.</p> <p>7b By 2006, integrate nanotechnology-based components into a system capable of detecting specific biomarker(s) (molecular signatures) to establish proof of concept for a new approach to the early detection of cancer, and, ultimately, cancer preemption.</p> <p>7c By 2005, create the next generation map of the human genome, a so called "haplotype map" (HapMap), by identifying the patterns of genetic variation across all human chromosomes.</p>	<p>8a By 2007, determine the sequence of an additional 45 human pathogens and three invertebrate vectors of infectious diseases.</p> <p>8b Identify and characterize two molecular interactions of potential clinical significance between bone-forming cells and components of bone. Such interactions are defined as those having significant impact on the accrual of bone mass or the actual mechanical performance of bone (i.e., fracture resistance in laboratory animals).</p> <p>8c Build a publicly accessible Collection of Reference Sequences to serve as the basis for medical, functional, and diversity studies. A comprehensive Reference Sequence Collection will serve as a foundation for genomic research by providing a centralized, integrated, non-redundant set of sequences, including genomic DNA, transcript (RNA), and proteome (protein product) sequences, integrated with other vital information for all major research organisms.</p>	<p>9a By 2009, assess the impact of two major Institutional Development Award (IDeA) programs on the development of competitive investigators and their capacities to compete for NIH research funding.</p> <p>9b By 2010, demonstrate through research a capacity to reduce the total years lost to disability (YLDs) in the U.S. by 10 percent by: 1) developing treatment algorithms to improve the management of treatment-resistant and recurrent depression and 2) elucidating the mechanisms by which depression influences at least two comorbid physical illnesses (e.g., heart disease, cancer, Parkinson's disease, or diabetes). Major depression is now the leading cause of YLDs in the nation.</p> <p>9c By FY 2010, identify culturally appropriate, effective stroke prevention programs for nationwide implementation in minority communities.</p>
--	--	---

Source: National Institutes of Health, 2003.

PUTTING PRINCIPLES INTO PRACTICE

This study was requested by Congress because of growing concerns that the National Institutes of Health (NIH) is becoming too fragmented to be coordinated adequately to address fundamental changes in science or respond quickly enough to health emergencies. The Committee stands in a long line of bodies convened to review some aspect of NIH's administrative structure. The effectiveness of NIH's organization and the effects of having an increasing number of institutes and centers (ICs) has been a recurring concern for nearly half a century. Many of the blue-ribbon committees, panels, and commissions that have looked at NIH, beginning with the Long Committee in 1955 (NSF, 1955), have concluded that there were enough ICs and recommended against adding new ones. A 1984 Institute of Medicine (IOM) committee acknowledged that new institutes might be necessary under some circumstances but recommended a presumption against establishing them unless specific criteria were met through an orderly process. Despite the judgment of the past review groups that NIH should not add ICs, the net result of the dynamics of NIH's political support has been a steady incremental expansion in the number of major units over the years.

The same review groups have also generally found that NIH is a successful organization, whatever the number of ICs at the time - an indication that proliferation is not necessarily harmful. The importance of health problems, the rich opportunities for research progress in the biomedical and behavioral sciences, and past successes in advancing research and its applications are certainly major factors in explaining the degree of NIH's budgetary and structural growth. Although the present Committee concluded that in some ways NIH as currently structured presents some difficult management and programmatic challenges, it also concluded that, at the current time, widespread consolidation or restructuring would not necessarily be the best way to resolve those challenges. In fact, NIH has been productive in part because it is a federation of many specialized and quasi-independent units, and its complex decentralized structure, which has made NIH effective in responding to research opportunities and public needs, is an important source of its success.

Despite the strength imparted by decentralization, there are circumstances in which organizational, rather than structural, change or some form of administrative modification is desirable. Significant operational changes could improve the strength, responsiveness, vitality, and accountability of NIH, the world's greatest biomedical research agency.

The congressional request for this study set a goal of determining the optimal organizational structure for NIH in the context of 21st century biomedical research science. But the organizational structure of NIH cannot be addressed satisfactorily without considering its mission, some of its key processes, and the scientific, social, and political environments within which its activities take place. The Committee therefore interpreted its mandate to consider aspects of NIH's organizational structure beyond the number of administrative units.

In its charge, the Committee was asked to determine whether there are general principles by which NIH should be organized. As set out in Chapter 1, the Committee concluded that NIH's principal mission is to serve as a mechanism for efficiently and effectively deploying federal resources across a wide array of institutions and individuals in the nation's scientific community to advance the scientific frontier and ensure research training of special relevance to human health needs. It then provided as "principles" nine basic policies or goals that would allow NIH

to achieve its mission. Consideration of these nine policies or goals provided the framework for the Committee's response to the remaining questions contained in its charge:

- Does the current structure reflect these principles, or should NIH be restructured?
- If restructuring is recommended, what should the new structure be?
- How will the proposed new structure improve NIH's ability to conduct biomedical research and training, and accommodate organizational growth in the future?
- How would the proposed new structure overcome current weaknesses, and what new problems might it introduce?

Policies and Recommendations

Each basic policy or goal identified by the Committee was explored in the context of NIH's organizational structure to determine whether structure enhanced or impeded efforts to achieve them:

1. The NIH research and training portfolio should be broad and integrated, ranging from basic to applied and from laboratory to population-based, in support of understanding health and how to improve it for all populations. In addition, the overall portfolio should reflect a balance between work in existing highly productive domains or disciplines and high-risk, groundbreaking, potentially paradigm-shifting work. It should be especially responsive whenever scientific opportunity and public health and health care needs overlap.
2. NIH should support research that cuts across multiple health domains and disease categories. This might require special efforts to integrate research across NIH components.
3. The NIH research and training portfolio should make special efforts to address health problems that typically do not attract substantial private sector support, such as prevention, some therapeutic strategies, and many rare diseases.

The Committee made several recommendations aimed at achieving those goals. Most important, it made a case for expanding the role of the director of NIH to lead a trans-NIH planning process to identify major crosscutting issues and opportunities and generate a small number of major high priority research initiatives. In addition to continuing generous funding for investigator-initiated research projects, the Committee finds compelling the case for multiyear planning that would mobilize coordinated funding from many ICs for a strategic, but revolving set of high-priority trans-NIH projects. Planning and implementation of such initiatives should involve substantial input from the scientific community and the public, and Congress should ensure the necessary funding to conduct the process. The Committee also recommends that Congress revisit the special status granted the National Cancer Institute (NCI) to determine whether its unique position hinders coordinated planning and programmatic activities.

The Committee proposes the creation of a Director's Special Projects Program to fund the initiation of high-risk, exceptionally innovative research projects offering high potential payoff. Suggestions are made as to how the program should operate and be funded.

To improve the agility and responsiveness of NIH, the Committee recommends that the Office of the Director (OD) be given a more adequate budget to support its management roles or greater discretionary authority to reprogram funding from the earmarked components of its budget when necessary to meet unanticipated needs. The Committee concluded that the authorities of the NIH director should be increased to facilitate more overall planning and control of the NIH research agenda. Moreover, funding for OD Operations has not kept pace as NIH has expanded and has not grown in proportion to NIH's research budget. As a result, the OD is unable to respond to unexpected needs of NIH as a whole without appealing for support from the ICs. In particular, if the NIH director is given the responsibility and authority to conduct NIH-wide planning for trans-NIH initiatives, as recommended above, the director's budget will need to be increased to take the costs of such planning into account.

Finally, to enhance the quality and innovative nature of NIH's portfolio, greater attention must be paid to clinical research, with an effort to coordinate across the ICs in their intramural and extramural programs. Some clinical research efforts should be merged.

Efforts must be made to ensure that the intramural programs are of the highest quality and are open to collaboration internally and with the extramural community.

4. The standards, procedures, and processes by which research and training funds are allocated should be transparent to applicants, Congress, voluntary health organizations, and the general public. Moreover, a wide variety of constituencies should have input into the setting of broad priorities.

The Committee concludes that NIH lacks the information management methods and infrastructure needed to collect, analyze, and report data adequately, appropriately, and in a timely fashion. In particular, it is incumbent on NIH leadership to improve the quality and analysis of its data on the allocation of NIH funds by disease for planning and priority-setting purposes. NIH should enhance its capacity for the timely collection, thoughtful analysis, and accurate reporting of the nature and status of its research and training programs. Data should be collected consistently across ICs and submitted to a centralized information management system.

The Committee concluded that NIH is not making the best use of its advisory council system to improve transparency, include a broader community in planning and priority-setting, and assess the effectiveness of its programs. The Committee recommends that the advisory council system be thoroughly reformed to ensure that these bodies are consistently and sufficiently independent and are routinely involved in priority-setting and planning discussions.

5. Extramural research should remain the primary vehicle for carrying out NIH-supported research. Open competitive peer review should be the presumptive mechanism for guiding extramural funding decisions.

In general, the Committee concluded that the existing peer review system serves the extramural community well, although it has the potential to deter high-risk research outside the mainstream of scientific consensus. The Committee therefore recommends additional mechanisms to promote such research, such as a Director's Special Projects Program and other measures to increase the responsiveness of NIH when needs call for a more immediate reaction than that typically resulting from extensive peer review. However, any effort to change the

administrative procedures associated with grant management should be carefully assessed before it is implemented to ensure that changes in the name of efficiency do not thwart NIH's mission.

6. The intramural research program (IRP) is a unique federal resource that offers an important opportunity to enhance NIH's capability to fulfill its mission. It should seek to fill distinctive roles in the nation's scientific enterprise, with appropriate mechanisms of accountability and quality control.

Given the time and resources available for it to complete its task, the Committee did not attempt to systematically evaluate the quality of the IRP. The Committee is, however, convinced that the significant efforts of recent years to reinvigorate the IRP and respond to various advisory committee recommendations have met with considerable success and that there is a promising trend toward improved overall quality in the IRP. The Committee applauds recent efforts to improve the program overall. Nevertheless, the balkanization of the IRP persists because of its multiple institutional budgetary and programmatic lines, which reinforce the "stovepipes" and continue to make it difficult for NIH senior management to ensure that the IRP supports NIH's overall strategies and plans. The Committee suggests that it would be useful to consider mechanisms to foster interactions among the IRPs of the individual ICs, such as large-scale reassignments of space to bring similar programs from individual ICs together to create synergies. Another potentially productive avenue to explore would be to reduce the balkanization of the IRPs by clustering programs that share common themes, approaches, and tools.

In the committee's view, the IRP should not be merely an internal extension of the extramural community but rather should perform distinctive research that the extramural community cannot or will not undertake. The Committee recommends that each IC's IRP have research and training components that distinguish it from the extramural community while complementing extramural programs and taking advantage of the unique environment provided at NIH for intramural research. Inter-institute and intramural-extramural collaborations should be supported and enhanced.

7. As a world-class science institution, NIH should have state-of-the-art management and planning strategies and tools. A key example is the capability for retrieving comprehensive NIH-wide data related to its various objectives.

The effectiveness of NIH as a research agency depends on a wide array of administrative services, the resources for which flow through the Research Management and Support (RMS) budgets of the various NIH units. The allocation for RMS in recent years has been too low for NIH to operate a world-class \$27.3 billion/year research organization and should be increased. The Committee recommends that Congress increase RMS to reflect more accurately the essential administrative costs that are required to operate NIH effectively. Moreover, when additional congressional mandates are imposed on NIH through the appropriations process, they should include funds to cover necessary administrative costs.

The Committee recognizes that developing the appropriate systems for data collection and management is likely to be an expensive long-term undertaking that will require substantial resources and personnel. However, such a system would provide invaluable information to all parties interested in NIH's programs—Congress, other Executive Branch agencies, the public, the research community, and NIH leadership itself—and therefore would constitute a worthwhile

investment. It also would provide the most reliable information for considering any proposals to add, merge, or eliminate institutes, centers, and offices.

8. There should be appropriate mechanisms to ensure the regular review, evaluation, and appointment of senior scientific and administrative leadership at all levels of NIH.

The vision and skills of NIH leadership are perhaps the most important ingredients in the complex mix of policies and strategies that enable NIH to meet its responsibilities to all its constituents. Moreover, NIH leadership at all levels is responsible for setting goals according to mission, implementing the goals, and assessing progress toward them. Leadership and vision may influence particularly the extent to which accountability is reinforced and implemented at diverse levels of the NIH system, from top management through staff and to individual intramural and extramural investigators. It is the quality of leadership and decision-making, as opposed to administrative structures, that is central to NIH's vitality. In the long run, recruitment of outstanding leaders is essential to NIH's continuing success. The Committee concluded that more rigorous measures are needed to ensure that NIH leadership is periodically revitalized and reviewed. It developed series of recommendations regarding the review and appointment of IC directors, including terms of appointments and the NIH director's authority to make such appointments, and reassessment of the special status of the NCI director. The Committee suggests establishing 6-year terms for the NIH Director.

9. Proposals for the creation, merger, or closure of institutes, centers, and offices should be considered through a process of thoughtful public deliberation that addresses potential costs, benefits, and alternatives.

The Committee concluded that, at the current time, the costs of a wholesale consolidation of NIH are likely to outweigh the benefits. Nevertheless, NIH should have sufficient flexibility to consider additions, reductions, or consolidations of NIH administrative units. The NIH director and the public should be able to suggest additions, subtractions or mergers of units to Congress at appropriate times. However, there should be a formal process for considering proposals for additions, reconfigurations, or reductions that arise from the scientific community, advocacy groups, or Congress. It is not so much the number of units that predicts the success of NIH, but rather the justification of the existence of a given unit and its proven merit. The Committee concludes that there should be a more formal and systematic approach to making changes in NIH's organizational structure. The Committee recommends that on receiving a congressional request or at the discretion of the NIH director in responding to a public request, the director should initiate a public process to evaluate its scientific needs, opportunities, and consequences, the likelihood of available resources, and the level of public support to create a new institute, center, or office, or to consolidate or dissolve units. The Committee does not suggest criteria for making such decisions, as they are likely to change in light of scientific opportunities, fiscal constraints and opportunities, and health needs. But the establishment of an open system by which such decisions are made provides an opportunity for developing criteria case-by case.

Summary

NIH is increasingly called on to undertake research that involves multiple institutes, multiple disciplines, and complex diseases to be responsive to new challenges, such as public health emergencies and the threat of acts of bioterrorism. A key question posed to the Committee was whether NIH's decentralized structure has become too fragmented to respond adequately to those challenges or whether, on the contrary, it is well suited to respond to changes in opportunity and need. Related questions included whether, to help equip NIH for the future, the director's authorities should be increased and in what way or whether managerial mechanisms should be strengthened or new ones adopted in place of or in conjunction with structural reorganization.

The Committee's view of those complexities was governed by the desire to be of some practical assistance to all who wish NIH to continue to be an effective – indeed, outstanding – organization. Thus, the Committee proceeded on the premise that its task included assessing the organizational configuration of NIH and the key processes and authorities that play roles in trans-NIH decision-making. Although the borders between structure, mission, and priorities are themselves not well defined, the Committee tried not to take too expansive a view of its responsibilities. It concluded on the one hand that in many ways NIH is performing exceptionally well, using decentralization as a strength. On the other hand, it made multiple recommendations to enhance NIH's vitality and accountability through change, augmentation of existing structures, modifications of policies and practices, and measures that aim to transcend decentralization.

Whether needs and opportunities will be accommodated in existing NIH units or proliferation or consolidation will occur in the near future is an issue to be addressed by administrations, Congress, the scientific community, and the public. NIH will continue to be shaped by the dynamics of many constituencies interacting. Interests will converge or conflict, depending on the issue. The degree of convergence and divergence will continue to be influenced by other factors such as annual appropriations. The recommendations made in this report are intended to help NIH to continue to be responsive, accountable, and effective in its leading role in the vast international humanitarian enterprise aimed at a better understanding of the human condition, the prevention and relief of the burdens of disease, and at the promotion of good health throughout the stages of life.

REFERENCES

- Association of American Medical Colleges, American Medical Association, and Wake Forest University School of Medicine. (1999). *Clinical research: a national call to action*. Washington, D.C.
- Augustine, N. Member of Committee on the Organizational Structure of the National Institutes of Health, personal communication to Committee, November, 2002.
- Bass, G.D., Blumenthal, P.D., Corfman, P. et al. (2003). More on science and politics (letter). *Science* 299:1313.
- Betz, F. Former NSF program officer, personal communication to Gil Omenn, June, 2003.
- Biotechnology Industry Organization (BIO). (2003). *Biotechnology Industry Statistics*. Found on the BIO Internet home page at <http://www.bio.org/er/statistics.asp>
- Botstein, D. (2000). The role of the private sector in training the next generation of biomedical scientists, proceedings of a conference sponsored by the American Cancer Society, the Burroughs Wellcome Fund, and the Howard Hughes Medical Institute, Chevy Chase, MD Feb. 14-16.
- Burley, S.K. (2000). An overview of structural genomics. *Nat Struct Biol.* 2000 Nov;7 Suppl:932-4.
- Bush, Vannevar. (1945). *Science: The Endless Frontier*. Washington DC: United States Government Printing Office.
- Center for Scientific Review. (1999). "From the CSR Director's Desk," *Peer Review Notes*, Center for Scientific Review, National Institutes of Health, Bethesda, Md. (September). At <http://www.csr.nih.gov/prnotes/sep99prn.htm>.
- Center for Scientific Review. (2000a). "From the CSR Director's Desk," *Peer Review Notes*, Center for Scientific Review, National Institutes of Health, Bethesda, Md. (January). At <http://www.csr.nih.gov/prnotes/jan00prn.htm>.
- Center for Scientific Review. (2000b). Panel on Scientific Boundaries for Review, "Phase Report," Center for Scientific Review, National Institutes of Health, Bethesda, Md. (January). At <http://www.csr.nih.gov/archives/summary012000.htm>.
- Center for Scientific Review. (2000c). "From the CSR Director's Desk," *Peer Review Notes*, Center for Scientific Review, National Institutes of Health, Bethesda, Md. (May). At <http://www.csr.nih.gov/prnotes/may2000prn.htm>

Center for Scientific Review. (2000d). "CSR vs. IC Review: Similarities and Differences," *Peer Review Notes*, Center for Scientific Review, National Institutes of Health, Bethesda, Md. (September). At <http://www.csr.nih.gov/pmotes/sep00bod.htm#similar>.

Cohen, J. (1993). Conflicting agendas shape NIH. *Science* 261:1674-1679.
Congressional Budget Office. (2002). Unauthorized appropriations and expiring authorizations. <http://www.cbo.gov/showdoc.cfm?index=3266&sequence=0&from=7>

Cohen, J. J., Hasselmo, N, and Magrath, C. P. (2003). Letter re: National Center for Research Resources 2004 Strategic Plan, 68 FR 4503-4. Available at <http://www.aau.edu/research/Ltr5.9.03.pdf>.

Cook-Deegan, R. (1994). *Gene Wars*. New York:W.W.Norton & Company.

Cook-Deegan, R. (1996). Does NIH need a DARPA? *Issues in Science and Technology*, winter 1996.

Cooper R.S. (2001). Social inequality, ethnicity and cardiovascular disease. *Int J Epidemiol.* Oct;30 Suppl 1:S48-52.

De Tocqueville, Alexis. (2000). *Democracy in America*. Chicago, Illinois: University of Chicago Press.

Dennis, C. (1999) Varmus speculates on a possible reorganization of the NIH. *Nature.* 400(5 August 1999):491.

Department of Health, Education, and Welfare, (1958). *The Advancement of Medical Research and Education Through the Department of Health, Education, and Welfare. Final Report of the Secretary's Consultants of Medical Research and Education.* Washington, D.C.: Government Printing Office.

Department of Health, Education, and Welfare. (1976). *Report of the President's Biomedical Research Panel.* DHEW Publication (OS) 76-500 and related volumes. Washington, D.C.: Department of Health, Education, and Welfare.

Department of Health and Human Services. (2001). *Workforce restructuring plan.* November 9.

Department of Health and Human Services. (2002). *Justification of estimates for appropriations committee, fiscal year 2003, National Institutes of Health, Volume I.*

Drew, E. (1967). The health syndicate: Washington's noble conspirators. *Atlantic Monthly* December 1967:75-82.

Haley, S. (2001). Kirschstein tells how NIH is adapting to the evolving multidisciplinary research model. *Washington Fax*, May 7, 2001. <http://www.washingtonfax.com>.

- Hanash, S. and Celis, J.E. (2002). The Human Proteome Organization: A mission to advance proteome knowledge. *Mol Cellular Proteomics* 1.6:413-414.
- Hanson, G.R, and Li, T.H. (2003). Public health implications of excessive alcohol consumption. *Journal of the American Medical Assoc.* 289(8) 1031-1032.
- Hawana, J. (2003). Chronic disease cure center Part One of presidential candidate Lieberman's health care plan. *Washington Fax* May 23, 2003. Available at <http://www.washingtonfax.com>.
- Helms, W.D. (2002). Funding and Priorities for Health Services Research. Presentation by the President & CEO of the Academy for Health Services Research and Health Policy to the Institute of Medicine's Clinical Research Roundtable, June 12, 2002. Available at <http://www.iom.edu/iom/iomhome.nsf/pages/Clinical+Research+Roundtable+June+12+2002+Agenda?OpenDocument>
- Hood, L. (2003). Systems biology: integrating technology, biology, and computation. *Mech Ageing Dev.* 124(1):9-16.
- Institute of Medicine. (1984). Responding to health needs and scientific opportunity: the organizational structure of the national institutes of health. Washington, D.C.: National Academy Press.
- Institute of Medicine. (1988). A healthy NIH intramural program: structural change or administrative remedies? Washington, D.C.: National Academy Press.
- Institute of Medicine. (1998). Scientific Opportunities and Public Needs: Improving Priority Setting and Public Input at the National Institutes of Health. Washington, D.C.: National Academy Press.
- Institute of Medicine. (1999). Toward Environmental Justice: Research, Education, and Health Policy Needs. Washington D.C.: National Academy Press.
- Institute of Medicine. (2000). Bridging Disciplines in the Brain, Behavioral, and clinical Sciences. Washington, D.C.: National Academy Press.
- Institute of Medicine. (2002). Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care. Washington D.C.: National Academy Press.
- Institute of Medicine. (2003a). Large-scale Biomedical Science: Exploring Strategies for Future Research. Washington D.C.: National Academy Press.
- Institute of Medicine. (2003b). Discussion by NIH Panel on Chronic Pain, meeting of the Board on Neuroscience and Behavioral Health, June 2-3, 2003.
- Jenkins, S. C. (2002). NIH research strategy may trend toward putting the pieces together, Zerhouni testifies. *Washington Fax*, June 12, 2002. <http://www.washingtonfax.com>.

- Jenkins, S. C. (2002). NIH "roadmap meetings" identify trans-agency issues for proactive attention. Washington Fax, October 16, 2002. <http://www.washingtonfax.com>.
- Kirschstein, R. (2001). Speech at American Institute for Medical and Biological Engineering annual meeting. National Academy of Sciences Auditorium, Washington, D.C., March 1.
- Leshner, A., Member of the Committee on the Organizational Structure of the National Institutes of Health, currently Chief Executive Officer, American Association for the Advancement of Science, formerly director, National Institute on Drug Abuse. Personal Communication
- McGeary, M. and P. M. Smith. (2002). Organizational Structure of the National Institutes of Health: Background Paper prepared for the National Academy of Sciences.
- Metheny, B. (2002). Accelerated translation of discoveries into practice is a national priority, Zerhouni tells AAMC. Washington Fax November 13, 2002. <http://www.washingtonfax.com/>
- Miller, G. (2003). Spying on the brain, one neuron at a time. *Science* 300:78-79.
- Morris, Thomas D. (1984). "The Current Organization Structure of the National Institutes of Health," Appendix B in Institute of Medicine, *Responding the Health Needs and Scientific Opportunity: The Organizational Structure of the National Institutes of Health*. Washington, D.C.: National Academy Press.
- Nathan, D.G. and H.E.Varmus (2000). The National Institutes of Health and clinical research: a progress report. *Nat Med*. 2000 Nov;6(11):1201-4.
- National Bioethics Advisory Commission. (1999). Research Involving Human Biological Materials: Ethical Issues and Policy Guidance: Volume I, Report and Recommendations of the National Bioethics Advisory Commission. Available at <http://www.georgetown.edu/research/nrcbl/nbac/pubs.html>
- National Institutes of Health. (1976). Bureau Status for Institutes and Divisions. Memorandum from Leon M. Schwarz, Associate Director for Administration, November 22, 1976. Bethesda, Maryland.
- National Institutes of Health. (1992a). Report of the Task Force on the Intramural Research Program of the National Institutes of Health, transmitted April 13, 1992, to Dr. Bernadine Healy, Director, National Institutes of Health, from Richard D. Klausner, M.D., Chief, Cell Biology and Metabolism Branch, National Institute of Child Health and Human Development, NIH.
- National Institutes of Health. (1992b). Orientation handbook for members of scientific review groups. Division of Research Grants. Bethesda, Maryland.
- National Institutes of Health. (1994). The Intramural Research Program: Report of the External Advisory Committee of the Director's Advisory Committee and Implementation Plan and Progress Report. Office of the Director, Bethesda, Maryland

National Institutes of Health. (1997a). Report of the NIH Director's Panel on Clinical Research. Report to the Advisory Committee to the NIH Director. Clinical Research Program, Bethesda, Maryland. Available at <http://www.nih.gov/news/crp/97report/index.htm>.

National Institutes of Health. (1997b). Review of NIH Administrative Structure and Costs, Final Report. Arthur Andersen Government Services.

National Institutes of Health. (1999a) Proceedings of the 79th meeting of the advisory committee to the director, December [Http://www.nih.gov/about/director/dec99min.htm](http://www.nih.gov/about/director/dec99min.htm).

National Institutes of Health. (1999b). The biomedical information science and technology initiative. Working Group on Biomedical Computing Advisory Committee to the Director, Bethesda, Maryland.

National Institutes of Health. (2001). Setting Research Priorities at the National Institutes of Health. Originally prepared by the NIH Working Group on Priority Setting, 1997, revised October 2001. Available at <http://www.nih.gov/about/researchpriorities.htm#overview>.

National Institutes of Health. (2002). Federal Obligations for Health R&D, by Source or Performer, Fiscal Years 1985-2000. On-line table at <http://grants2.nih.gov/grants/award/research/sourfund.htm>.

National Institutes of Health. (2003a). Memorandum from Acting Director, Executive Secretariat to IC directors, April 10, 2003: IC Directors' Meeting Highlights. Available at <http://www.nih.gov/icd/od/foia/icdirminutes/icdir041003.htm>

National Institutes of Health. (2003b). Government Performance and Results Act, FY 2004 Annual Performance Plan. Bethesda, Maryland.

National Institutes of Health. Unpublished draft report of the NIH Research Management and Support Exploratory Committee, *Illuminating the Black Box*. Bethesda, Maryland. NEED DATE

National Research Council. (2002). Making the Nation Safer: The Role of Science and Technology in Countering Terrorism. Washington, D.C.: National Academies Press.

National Science Foundation. (1955). Medical Research Activities of the Department of Health, Education and Welfare. Report of the Special Committee on Medical Research Appointed by the National Science Foundation at the Request of the Secretary of Health, Education and Welfare. Washington, D.C.: National Science Foundation.

National Science Foundation. (2002a). Science and engineering indicators -- 2002. National Science Board, Arlington, Virginia:(NSB-02-1).

National Science Foundation. (2002b). Guide to Programs FY 2003 -- NSF funding opportunities. Available at <http://www.nsf.gov/pubsys/ods/getpub.cfm?gp>.

- Ochs, N. (2003). Reps. Tauzin and Greenwood launch examination of NIH management/oversight. Washington Fax. March 17, 2003. <http://www.washingtonfax.com>.
- Office of Management and Budget, Executive Office of the President. (2002). The President's Management Agenda, Fiscal Year 2002. Available at http://www.whitehouse.gov/omb/budintegration/pma_index.html
- Omenn, G.S. (2000) Public health genetics: an emerging interdisciplinary field for the post-genomic era. *Annual Rev Pub Health*. 21:1-13.
- Omenn, G.S. (2003). Science and technology policies concerning the life sciences. In Nelson S., Lita S. (eds). *AAAS Science & Technology Yearbook* (in press).
- Pennisi, E. (2003). Human Genome: Reaching Their Goal Early, Sequencing Labs Celebrate. *Science* 300(5618): 409.
- Pharmaceutical Research and Manufacturers of America. (2001). *Pharmaceutical Industry Profile 2001*. Washington, D.C.: Pharmaceutical Research and Manufacturers of America.
- Pradhan, A.D., J.E. Manson, J.E. Rossouw, D.S. Siscovick, C.P. Mouton, N. Rifai, R.B. Wallace, R.D. Jackson, M.B. Pettinger, and P.M. Ridker. (2002). Inflammatory biomarkers, hormone replacement therapy, and incident coronary heart disease: prospective analysis from the women's health initiative observational study. *JAMA*. 288: 980-987.
- Rich, M.W. (2002). From clinical trials to clinical practice: bridging the GAP. *JAMA*, 287(10): 1321-3.
- Sclar, E. (2000). *You Don't Always Get What You Pay For: The Economics of Privatization*. Ithaca, New York: Cornell University Press,
- Silverstein, S.C. (2001). Perspectives from genomics and informatics to medical practice. *Issues in Science and Technology*, NAS, NAE. Fall:37-41.
- Stokes, Donald. (1997). *Pasteur's Quadrant*. Washington, D.C.: The Brookings Institute.
- Sung, N.S., W.F. Crowley, M. Genel, P. Salber, L. Sandy, L.M. Sherwood, S.P. Johnson, V. Catanese, H. Tilson, K. Getz, E.L. Larson, D. Scheinberg, E.A. Reece, H. Slavkin, A. Dobs, J. Grebb, R.A. Martinez, A. Korn, and D. Rimoin. (2003). Central Challenges Facing the National Clinical Research Enterprise. *J. Amer. Med. Assoc.* 289:1278-1287.
- U.S. Congress. (1981). National Institute on Arthritis and Musculoskeletal Diseases—Establishment of, Hearing before Senate Committee on Labor and Human Resources, 97th Congress, 2nd Session, on S. 1939, To amend the Public Health Service Act to establish a National Institute on Arthritis and Musculoskeletal Diseases, July 20. Serial 98-079. Washington, D.C.: U.S. Government Printing Office.
- US House of Representatives. 1976. Investigation of the National Institutes of Health, report prepared by the staff of the Committee on Interstate and Foreign Commerce and its

Subcommittee on Health and the Environment, 94th Congress, 2nd Session. Washington DC:
U. S. Government Printing Office.

Varnus, H. (2001). Proliferation of the National Institutes of Health. *Science* 291:1903-1905.
Waterman, Jr., R.H., Peters, T.J., and Phillips, J.R. (1980). Structure is not organization.
Business Horizons. 23:14.

Wyngaarden, J.B. (1979). The clinical investigator as an endangered species. *N Engl J Med*.
301(23):1254-9.

Yen, I.H., Ragland, D.R., Greiner, B.A., Fisher, J.M. (1999). Workplace discrimination and
alcohol consumption: findings from the San Francisco Municipal Health and Safety Study. *Ethn
Dis*. Winter. 9(1): 70-80

Appendix A: Sources of Information Provided to the Committee**Organizations:**

Alliance for Aging Research
 American Academy of Allergy, Asthma, and Immunology
 American Academy of Head and Neck Surgery
 American Academy of Ophthalmology
 American Academy of Optometry
 American Academy of Orthopaedic Surgeons
 American Association for Dental Research
 American Autoimmune Related Diseases Association, Inc.
 American College of Allergy, Asthma, and Immunology
 American Dental Association
 American Dental Education Association
 American Diabetes Association
 American Heart Association
 American Obesity Association
 American Optometric Association
 Arthritis Foundation
 Association of American Medical Colleges
 Association for Research in Vision and Ophthalmology
 Association of Schools of Public Health
 Association of University Professors of Ophthalmology
 College on Problems of Drug Dependence, Inc.
 Epilepsy Foundation
 Federation of American Societies of Experimental Biology
 Friends of the NIDCR
 Institute of Ophthalmology and Visual Science, New Jersey Medical School
 International Longevity Center
 National Alliance for Eye and Vision Research
 National Foundation for Ectodermal Dysplasias
 National Mental Health Association
 Ohio State University Health Sciences Center
 Research Society on Alcoholism
 Sjogren's Syndrome Foundation
 Society for Women's Health Research
 The Ohio State University College of Optometry
 The Smith Kettlewell Eye Research Institute
 Vision Share

Individuals:

Sarah Caddick, Steven and Michele Kirsch Foundation
 Robert Core and James O'Rourke, University of Connecticut Health Center
 William Crowley, Academic Health Centers' Clinical Research Forum
 Cedric Garland, University of California, Sand Diego, School of Medicine
 Morton Goldberg, The Wilmer Ophthalmological Institute

Frederick Goodwin, former director, NIMH and ADAMHA
 Sandra Hanneman, Texas Medical Center
 Bernadine Healy, former director, NIH
 Stephen Lippard, Massachusetts Institute of Technology, Department of Chemistry
 John Porter, former US Representative
 Bob Roehr, Council of Public Representatives at NIH
 Louis Sullivan, Morehouse School of Medicine
 Thomas W. Stone, Retina and Vitreous Associates of Kentucky
 Harold Varmus, former director, NIH
 Max Harry Weil, USC School of Medicine and Northwestern University Medical School
 Robert D. Wells, Texas Medical Center

Department of Health and Human Services

- Robert Wood, Chief of Staff
- Laura Lawlor, Deputy Chief of Staff

NIH Officials - Office of the Director, NIH

- Elias Zerhouni, Director, NIH
- Wendy Baldwin, Deputy Director for Extramural Research
- John Burklow, Office of Communications and Public Liaison
- Stephen Ficca, Associate Director for Research Services
- John Gallin, Director, Clinical Research Center
- Michael Gottesman, Deputy Director for Intramural Research
- Robin Kawazoe, Director, Office of Science Policy and Planning
- Raynard Kington, Director, Office of Behavioral and Social Sciences Research
- Ruth Kirschstein, Deputy Director
- Charles Leasure, Deputy Director for Management
- Donald Poppke, Acting Associate Director for Budget
- Belinda Seto, Acting Deputy Director for Extramural Research Director
- Lana Skirboll, Director, Office of Science Policy

NIH Officials - Institute and Center Directors

- Ellie Ehrenfeld, Director, Center for Scientific Review
- Andrew von Eschenbach, National Cancer Institute
- Paul A. Sieving, Director; Jack A. McLaughlin, Deputy Director; and Michael P. Davis, Associate Director for Science Policy and Legislation, National Eye Institute
- Claude Lenfant, National Heart, Lung, and Blood Institute
- Francis Collins, National Human Genome Research Institute
- Raynard Kington, Acting Director, National Institute on Alcohol Abuse and Alcoholism
- Anthony Fauci, National Institute of Allergy and Infectious Disease
- Richard Hodes, National Institute on Aging
- Steve Katz, National Institute of Arthritis and Musculoskeletal and Skin Diseases
- Duane Alexander, National Institute of Child Health and Human Development
- James Battey, National Institute on Deafness and Other Communication Disorders
- Allen Spiegel, National Institute of Diabetes and Digestive and Kidney Diseases

- Glen Hanson, National Institute on Drug Abuse
- Ken Olden, National Institute of Environmental Health Sciences
- Richard Nakamura, Acting Director, National Institute of Mental Health
- Audrey Penn, Acting Director, Eugene Major, Acting Deputy Director, and Constance Atwell, Director, Division of Extramural Research, National Institute of Neurological Disorders and Stroke
- Patricia Grady, National Institute of Nursing Research

Other Government Officials

- Anthony J. Tether, Director, Defense Advanced Research Projects Agency
- Michael Goldblatt, Director, Defense Sciences Office, Defense Advanced Research Projects Agency

Appendix B: Acronyms and Abbreviations

AAMC	Association of American Medical Colleges
AAU	Association of American Universities
ACC	Autism Coordinating Committee
ACD	Advisory Committee to the Director
ADAMHA	Alcohol, Drug Abuse, and Mental Health Administration
AHRQ	Agency for Healthcare Research and Quality
AIDS	Acquired immune deficiency syndrome
ARAC	Administrative Restructuring Advisory Committee
CDC	Centers for Disease Control and Prevention
cDNA	Complementary DNA
CGAP	Cancer Genome Anatomy Project
CIT	Center for Information Technology
CJ	Congressional Justification Budget
COPR	Council of Public Representatives
CSR	Center for Scientific Review
DARPA	Defense Advanced Research Projects Agency
DHHS	Department of Health and Human Services
DOD	Department of Defense
EAC	External Advisory Committee of the Director's Advisory Committee
FDA	Food and Drug Administration
FIC	Fogarty International Center for Advanced Study in the Health Sciences
FY	Fiscal Year
GCRC	General Clinical Research Center
GPRA	Government Performance and Results Act
GS	Government Service
HGP	Human Genome Project
HIPAA	Health Insurance Portability and Accountability Act
HUPO	Human Proteome Organization
IC	Institutes and centers
IOM	Institute of Medicine
IRG	Integrated/Initial Review Group
IRP	Intramural Research Program
MGC	Mammalian Gene Collection
NASULGC	National Association of State Universities and Land Grant Colleges
NCI	National Cancer Institute
NCCAM	National Center for Complementary and Alternative Medicine
NCMHD	National Center on Minority Health and Health Disparities
NCRR	National Center for Research Resources
NEI	National Eye Institute
NHLBI	National Heart, Lung, and Blood Institute
NHGRI	National Human Genome Research Institute
NIA	National Institute on Aging
NIAAA	National Institute on Alcohol Abuse and Alcoholism

NIADDK	National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases
NIAID	National Institute of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB	National Institute of Biomedical Imaging and Bioengineering
NICHD	National Institute of Child Health and Human Development
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDCR	National Institute of Dental and Craniofacial Disorders
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIDA	National Institute on Drug Abuse
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIH	National Institutes of Health (National Institute of Health 1930-1948)
NIMH	National Institute of Mental Health
NINCDS	National Institute of Neurological and Communicative Disorders and Stroke
NINDB	National Institute of Neurological Diseases and Blindness
NINDS	National Institute of Neurological Disorders and Stroke
NINR	National Institute of Nursing Research
NIOSH	National Institute for Occupational Safety and Health
NLM	National Library of Medicine
NSF	National Science Foundation
OAM	Office of Alternative Medicine
OAR	Office of AIDS Research
OBB	Office of Bioengineering and Bioimaging
OBSSR	Office of Behavioral and Social Sciences Research
OD	Office of the Director
ODP	Office of Disease Prevention
ODS	Office of Dietary Supplements
OMAR	Office of Medical Applications of Research
OMB	Office of Management and Budget
ORD	Office of Rare Diseases
ORMH	Office of Research on Minority Health
ORWH	Office of Research on Women's Health
PA	Program announcement
PhARMA	Pharmaceutical Research and Manufacturers of America
PHS	Public Health Service
PHSA	Public Health Service Act
P.L.	Public Law
R&D	Research and development
R01	Traditional individual investigator research grant
RFA	Request for application
RMS	Research Management and Support
SARS	Severe Acute Respiratory Syndrome
SEP	Special Emphasis Panel
SES	Senior Executive Service
SGER	Small Grants for Exploratory Research
WHI	Womens' Health Initiative

Appendix C: Committee Member Biographies

Harold T. Shapiro, PhD, Princeton University (IOM)

Harold T. Shapiro is President Emeritus of both the University of Michigan and Princeton University. He is currently Professor of Economics and Public Affairs, Department of Economics and the Woodrow Wilson School of Public and International Affairs, Princeton University. His research interests include bioethics, the social role of higher education, hospital/medical center administration, university administration, econometrics, statistics, and economics. Shapiro's professional activities include memberships in the Conference Board Inc. and The Bretton Woods Committee. A trustee of the Alfred P. Sloan Foundation (where he is chair of the board), the University of Pennsylvania Medical Center, the Universities Research Association, and the Educational Testing Service, he also serves as a director of the Dow Chemical Company. He is a member of the Institute of Medicine and chaired its 1988 study on "A Healthy NIH Intramural Program: Structural Change or Administrative Remedies?" He is also a member of the American Philosophical Society and a fellow of the American Academy of Arts and Sciences. In July 1996, Shapiro was appointed by President Clinton to chair the National Bioethics Advisory Commission, which issued the report "Cloning Human Beings" in June 1997. From 1990 to 1992, he was a member and vice chair of President Bush's Council of Advisors on Science and Technology. He chaired the Institute of Medicine's Committee on Employer-Based Health Benefits whose report, "Employment and Health Benefits: A Connection at Risk", was published in March 1993. He earned a PhD in economics from Princeton University.

Norman R. Augustine, PhD, Lockheed Martin (NAE)

Norman R. Augustine retired in 1997 as Chair and CEO of the Lockheed Martin Corporation and previously served as Chair and CEO of the Martin Marietta Corporation. Upon retiring he served on the faculty of the Department of Mechanical and Aerospace Engineering at Princeton University. Earlier in his career he had served as Under Secretary of the Army and prior to that as Assistant Director of Defense Research and Engineering. Augustine has been Chairman of the National Academy of Engineering, President of the Boy Scouts of America and served nine years as Chairman of the American Red Cross. He has also been President of the American Institute of Aeronautics and Astronautics and served as Chairman of the "Scoop" Jackson Foundation for Military Medicine. He has been a Trustee of MIT, Johns Hopkins and Princeton. He has served on the President's Council of Advisors on Science and Technology and is a former Chairman of the Defense Science Board. He is a member of the American Philosophical Society and is a fellow of the American Academy of Arts and Sciences. His corporate board memberships are Black and Decker, Lockheed Martin, Procter and Gamble and ConocoPhillips. He has been presented the National Medal of Technology and the Department of Defense's highest civilian award, the Distinguished Service Medal, five times. Mr. Augustine holds an MSE in Aeronautical Engineering from Princeton University and has authored and co-authored four books.

J. Michael Bishop, MD (NAS, IOM)

J. Michael Bishop is the Chancellor of the University of California, San Francisco. He won the Nobel Prize together with UCSF colleague Harold Varmus for their discovery of the cellular origin of retroviral oncogenes. Their research has had significant influence on contemporary

knowledge about tumor development and the systems that govern cell growth. Bishop is a professor in the departments of microbiology and immunology and biochemistry and biophysics at the University of California at San Francisco. In 1996, he chaired a committee that reviewed the intramural program of the National Cancer Institute. He is a member of the National Academy of Sciences and the Institute of Medicine.

James R. Gavin, III, MD, PhD, Morehouse School of Medicine

Dr. Gavin is President of Morehouse School of Medicine in Atlanta, Georgia. Prior to his presidency, Dr. Gavin was the senior scientific officer at the Howard Hughes Medical Institute (HHMI) and director of the HHMI-National Institutes of Health Research Scholars Program. He earned his PhD in biochemistry from Emory University in Atlanta in 1970 and his MD from Duke University School of Medicine in 1975. Prior to joining the senior staff of HHMI, he was on faculty at the University of Oklahoma Health Sciences Center as a professor and as chief of the Diabetes Section, acting chief of the Section on Endocrinology, Metabolism and Hypertension, and William K. Warren Professor for Diabetes Studies. He previously served as associate professor of Medicine at Washington University School of Medicine in St. Louis. He was a lieutenant commander in the U.S. Public Health Service (USPHS) from 1971-73 and continues to serve as a reserve officer in the USPHS. Dr. Gavin belongs to a number of organizations, including the Institute of Medicine, the American Diabetes Association, the American Society of Clinical Investigation, the American Association of Physicians, the Alpha Omega Alpha Medical Honor Society, the Association of Black Cardiologists, Omicron Delta Kappa Honorary Society and the Sigma Pi Phi Leadership Fraternity. He is a past president of the American Diabetes Association (ADA) and was voted Clinician of the Year by ADA in Diabetes in 1991. He has served on many advisory boards and on the editorial boards of the American Journal of Physiology and the American Journal of Medical Sciences. He is on the board of trustees for Duke University, Microislets, Inc., the Robert Wood Johnson Foundation, and is chairman of the board of the Equidyne Corporation. He is national program director of the Minority Medical Faculty Development Program of the Robert Wood Johnson Foundation. He has published more than 180 articles and abstracts in such publications as Science, Journal of Applied Physiology, Diabetes, and the American Journal of Physiology. Among the many honors Dr. Gavin has received are the Daniel Hale Williams Award, the E.E. Just Award, the Herbert Nickens Award, the Daniel Savage Memorial Award, the Emory University Medal for Distinguished Achievement, the Banting Medal for Distinguished Service from the American Diabetes Association, the Distinguished Alumni Award from the Duke University School of Medicine, and the Internist of the Year from the National Medical Association.

Alfred G. Gilman, MD, PhD, University of Texas Southwestern Medical Center (NAS, IOM)

Alfred G. Gilman is Professor and Chairman of the Department of Pharmacology at the University of Texas Southwestern Medical Center. His research focus is in biochemistry and pharmacology. He won the Nobel Prize in Physiology and Medicine with Martin Rodbell for their discovery of G-proteins and the role of these proteins in signal transduction in cells. He received his MD and PhD in pharmacology from Case Western Reserve University.

Martha Hill, RN, PhD, FAAN, Johns Hopkins University School of Nursing (IOM)

Martha N. Hill, is Dean and professor at the Johns Hopkins University School of Nursing. She

holds joint appointments in the Bloomberg School of Public Health and the School of Medicine. Dr. Hill, the 1997-1998 president of the American Heart Association, is a Fellow in the American Academy of Nursing and a member of the Institute of Medicine. She served as the Co-vice chair of the recently released IOM Report *Unequal Treatment: Confronting Ethnic and Racial Disparities in Health Care*. Dr. Hill received her Bachelor of Science degree in nursing from Johns Hopkins University, her masters degree from the University of Pennsylvania, and her doctoral degree in behavioral sciences from the Johns Hopkins University School of Public Health. Dr. Hill is internationally known for her work and research in preventing and treating hypertension and its complications among underserved blacks, particularly among young, urban black men. She is an active investigator and consultant on several NIH funded clinical trials. She has published extensively and serves on numerous review panels, editorial boards, and advisory committees including the Board of Directors of Research!America and the Executive Council of the American Society of Hypertension. Dr. Hill has also consulted on hypertension and other cardiovascular-related issues outside of the US including Scotland, Israel, Australia, and South Africa.

Debra Lappin, JD, Princeton Partners, Ltd.

Debra Lappin served on the NIH Director's Council of Public Representatives from 1999 to 2003. While on the COPR, she chaired its working group on Human Research Protections, served on ad hoc advisory committees addressing NIH Oversight of Human Gene Transfer Research and Trans-NIH Pediatric Research, and provided a "public perspective" of clinical research issues in a number of national settings. Ms. Lappin has served as a member of the Advisory Committee for the National Institute of Arthritis, Musculoskeletal and Skin Disease, as a participant in the Institute of Medicine's public forum examining Clinical Research in the Public Interest, as a member of the IOM Committee addressing Changing Health Care Systems and Rheumatic Diseases, and as a member of an advisory committee at the Agency for Healthcare Research and Quality to examine future directions for the Center for Outcomes and Effectiveness Research. From 1996 to 1998, Ms. Lappin was the Chair of the Arthritis Foundation. Under her leadership, the Arthritis Foundation entered in a partnership with the Centers for Disease Control and Prevention to create the National Arthritis Action Plan, and into a collaborative alliance Robert Wood Johnson Family Interests to create the Alliance for Lupus Research. Today Ms. Lappin remains active as an Emeritus Trustee of the Arthritis Foundation, lectures as an adjunct faculty member in the Department of Medicine at the University of Colorado Health Sciences Center, and consults with academic, industry and non-profit clients in areas of science policy and collaborative partnerships.

Alan I. Leshner, PhD, American Association for the Advancement of Science (IOM)

Alan I. Leshner, PhD, is Chief Executive Officer of the American Association for the Advancement of Science (AAAS) and Executive Publisher of *Science* magazine. From 1994-2001, he was Director of the National Institute on Drug Abuse at NIH, and from 1988-1994 he was Deputy Director and Acting Director of the National Institute of Mental Health. Prior to that, he spent nine years at the National Science Foundation, where he held a variety of senior positions, focusing on basic research in the biological, behavioral and social sciences, and on science education. He began his career at Bucknell University, where he was Professor of Psychology. His research has focused on the biological bases of behavior, particularly the role of hormones in the control of behavior. Dr. Leshner is a member of the Institute of Medicine and a

fellow of AAAS and many other professional societies. He has received numerous awards from both professional and lay groups for his national leadership in science, mental illness and mental health, and substance abuse and addiction.

Gilbert S. Omenn, MD, PhD, University of Michigan (IOM)

Gilbert S. Omenn is Professor of Internal Medicine, Human Genetics, and Public Health at the University of Michigan. From 1997 to 2002 he was also UM Executive Vice President for Medical Affairs and Chief Executive Officer of the University of Michigan Health System. Previously he was professor of medicine and environmental health and Dean of the School of Public Health & Community Medicine at the University of Washington. He served as Associate Director of the White House Office of Science and Technology Policy and then the Office of Management and Budget in the Carter Administration, and chaired the Presidential/Congressional Commission on Risk Assessment and Risk Management from 1994-97. He has been a National Institutes of Health Research Career Development Awardee, a Howard Hughes Medical Institute Investigator, and founding director of the University of Washington Robert Wood Johnson Clinical Scholars Program. His research is focused on proteomics and cancer prevention, as well as health promotion for older adults, science-based risk analysis, and the ethical, legal, and public health policy aspects of genetics. Dr. Omenn holds an MD from Harvard and a PhD in genetics from the University of Washington.

Franklyn G. Prendergast, PhD, Mayo Cancer Center

Franklyn Prendergast is Director of the Mayo Clinic Cancer Center in Rochester, Minnesota, and Professor of Biochemistry and Molecular Biology. His research focus is in structural protein biology and bioimaging. He is a recipient of the E.E. Just award of the American Society of Experimental Biology. He is a member of the American Association for the Advancement of Science, the American Society for Biochemistry and Molecular Biology, and Sigma Xi. He earned his PhD in biochemistry from the University of Minnesota and his medical degree from the University of the West Indies.

Stephen J. Ryan, MD, University of Southern California (IOM)

Stephen Ryan is Professor of Ophthalmology and Dean, Keck School of Medicine of USC and Senior Vice President for Medical Care, University of Southern California. His research relates to macular degeneration, ocular trauma, retinal detachment, and other retinal diseases. He previously served as Chairman of the Department of Ophthalmology at USC and as a member of the National Advisory Eye Council for the NEI of the NIH. He is a member of the Institute of Medicine and currently serves as President of the National Alliance for Eye and Vision Research. He earned his MD from Johns Hopkins University.

Samuel C. Silverstein, MD, Columbia University (IOM)

Samuel C. Silverstein is John C. Dalton Professor of Physiology and Cellular Biophysics and Professor of Medicine at the Columbia University College of Physicians and Surgeons. His research focuses on structure and function of polymorphonuclear and mononuclear leukocytes and endothelial cells in innate immunity, in diseases associated with chronic inflammation such as atherosclerosis and Alzheimer's disease; and in host defense against infectious microorganisms including *Legionella pneumophila* and *M. tuberculosis*. He has served on the Councils of the American Society for Cell Biology (1988-92), and the National Institute of Allergy and

Infectious Diseases (1995-98); and as President of FASEB (1994-95). He is a Director of the Cancer Research Fund of the Damon Runyon Foundation and of Research!America; and is President of Funding First, the medical and health research policy program of the Mary Lasker Charitable Trust. Dr. Silverstein is a graduate of Dartmouth College with an AB in government, and of Albert Einstein College of Medicine, where he earned his MD. He is a member of The Institute of Medicine and of the American Academy of Arts and Sciences.

Harold C. Slavkin, DDS, (IOM)

Harold C. Slavkin is Dean of the School of Dentistry at USC. He previously served as director of the National Institute of Dental and Craniofacial Research, NIH. Under his direction, NIDCR spearheaded many advances and explored a broadening range of research topics, including oral cancer, the genetic causes of craniofacial defects, the link between oral and systemic diseases, biomimetics and tissue engineering. Slavkin is one of the world's leading authorities on craniofacial development and genetic birth defects. Slavkin was founding director of the School of Dentistry's Center for Craniofacial Molecular Biology and was the first holder of the school's George and Mary Lou Boone Chair in Craniofacial Molecular Biology. He earned his DDS from USC.

Judith L. Swain, MD, Stanford University (IOM)

Judith L. Swain is Chair, of the Department of Medicine, Stanford University. Her research focus is in molecular cardiology, angiogenesis, and she pioneered the use of transgenic animals to understand the genetic basis of cardiovascular development and disease. She is a member of the Institute of Medicine, and has served as President of the American Society of Clinical Investigation. She has been a member of two NIH Advisory Councils -- National Heart Lung and Blood Institute and the National Research Resources Council, and served as Director of the NIH US/Russia Cardiovascular Biology Program. She currently serves as a member of the Defense Science Research Council of the Defense Advanced Research Project Agency (DARPA). She completed her MD at University of California, San Diego.

Lydia Villa-Komaroff, PhD Whitehead Institute

Lydia Villa-Komaroff is Vice President for Research and Chief Operating Officer of the Whitehead Institute for Biomedical Research. Her research interests include molecular aspects of cell biology, academic administration, and biotechnology. Deeply committed to the recruitment and retention of minorities in science, Dr. Villa-Komaroff is a founding member and past officer of the Society for the Advancement of Chicanos and Native Americans in Science. She was Vice President for Research at Northwestern University and served as a member of the Advisory Committee for the Biology Directorate of the National Science Foundation and as a member of the NAS Committee on Assessing the System for Protecting Human Research Participants. She is currently on the Boards of the American Association for the Advancement of Science and the National Advisory Council of the National Institute for Neurological Diseases and Stroke. She earned her PhD in cell biology from the Massachusetts Institute of Technology.

Robert H. Waterman, Jr., The Waterman Group

Robert H. Waterman, Jr. is Founder and Chairman of the Waterman Group, Inc., a management research, writing and venture management firm. Probably best known as coauthor of *In Search of Excellence*, Waterman is also author of *The Renewal Factor*, *Adhocracy: The Power to Change*,

and *What America Does Right*. Between 1964 and 1985 Waterman was with McKinsey & Company, Inc., where he became a senior director working mainly in California, Australia, and Japan. Waterman currently is chairman of the board of the RLS (Restless Leg Syndrome) Foundation, serves on the NINDS Council, and is a member of the President's Council of the Academy of Sciences and the Board of the World Wildlife Fund. In the past Waterman has served on a variety of public company boards (McKesson, AES, Boise Cascade) and a variety of non-profit boards (San Francisco Symphony, US Ski Team, Center for Excellence in Non-Profit Management).

Myrl Weinberg, CAE, National Health Council

Myrl Weinberg is president of the National Health Council, an umbrella organization that has served as the place where "the health community meets" for 82 years. The Council's 117 members are national organizations that are committed to quality health care, and its core constituency of more than 50 of the leading voluntary health agencies represent approximately 100 million people with chronic diseases and/or disabilities. Ms. Weinberg has a long history of board and committee service, including serving as a member of the Institute of Medicine's Health Sciences Policy Board, Roche Genetics Science and Ethics Advisory Committee, NCQA Committee on Performance Measurement, and as chair of the American Medical Association's Ethical FORCE initiative. In addition, Ms. Weinberg serves as vice chair of the Governing Board of the International Alliance of Patients' Organizations. Ms. Weinberg also served on the Congressionally-mandated Institute of Medicine Committee created to assess how research priorities are established at the National Institutes of Health. Ms. Weinberg pursued advanced graduate study at Purdue University. She holds an MA in Special Education from George Peabody College and a BA in Psychology from the University of Arkansas.

Kenneth B. Wells, MD, University of California, San Francisco (IOM)

Kenneth B. Wells is Professor-in-Residence of Psychiatry and Biobehavioral Sciences at the UCLA Neuropsychiatric Institute (NPI), and a psychiatrist and health services and policy researcher. Dr. Wells directs the UCLA-NPI Health Services Research Center, which focuses on improving quality of care for psychiatric and neurologic disorders across the life span. He also directs training of psychiatrists in health services research, and is the Principal Investigator and Director of the NIMH-UCLA-NPI Faculty Scholars Program in mental health services research and Associate Director of the UCLA School of Medicine's Clinical Scholars Program, funded by the Robert Wood Johnson Foundation. He is a member of the Institute of Medicine. He holds an MD from the University of California, San Francisco and an MPH from UCLA.

Mary Woolley, MA, Research!America (IOM)

Mary Woolley is President of Research!America, a nonprofit public education and advocacy organization committed to making medical and health research a much higher national priority. She began her career in the then largest-ever NIH-supported clinical trial, the Multiple Risk Factor Intervention Trial. Following that, she served as CEO of the Medical Research Institute of San Francisco and as President of the Association of Independent Research Institutes. For her work on behalf of medical research, she has been awarded the Distinguished Contribution to Research Administration Award from the Society of Research Administrators, the Columbia University College of Physicians and Surgeons Dean's Award for Distinguished Service, the Federation of American Societies for Experimental Biology (FASEB) Special Award for Science

Advocacy, and the Friends of the National Institute for Nursing Research's Health Advocacy Award. She is a fellow of the AAAS and a member of the Institute of Medicine, and serves as a member of the IOM's Health Science Policy Board and the Clinical Research Roundtable. She earned a BS at Stanford University, an MA at San Francisco State University and studied advanced management at the University of California, Berkeley.

James B. Wyngaarden, MD, Duke University (NAS, IOM)

James B. Wyngaarden is Professor Emeritus, Duke University, and currently consults in biotechnology, advising on research agendas as well as strategic planning and organizational start-ups. He previously served as Director of the National Institutes of Health; Associate Director for Life Sciences in the Office of Science and Technology Policy, Executive Office of the President; Director, Human Genome Organization; and Vice Chancellor for Health Affairs at Duke University. He is a member of the National Academy of Sciences and the Institute of Medicine. He earned his MD from University of Michigan Medical School.

Tadataka Yamada, MD GlaxoSmithKline (IOM)

Tadataka Yamada is Chairman, Research and Development, Pharmaceuticals at GlaxoSmithKline. Previously, Dr. Yamada was President, SmithKline Beecham Healthcare Services, taking that post in February 1996. He joined SmithKline Beecham as a on-executive member of the Board of Directors in February 1994. He was formerly Chairman of the Department of Internal Medicine at the University of Michigan Medical School and Physician-in-Chief of the University of Michigan Medical Center. Dr Yamada is a Councillor of the Association of American Physicians, past President of the American Gastroenterological Association, and Master of the American College of Physicians. He has been a member of the Board of Directors of the American Board of Internal Medicine and a member at large of the National Board of Medical Examiners. He serves on the Board of Directors of diaDexus and is a Trustee of the Rockefeller Brothers Fund. Dr. Yamada is a graduate of Stanford University with a BA in history. He earned his MD from New York University School of Medicine.

Mr. DINGELL. What exactly, Dr. Zerhouni, does this privatization or outsourcing do that is not done by the 85 percent of your money that goes outside the walls of NIH to support work elsewhere?

Mr. ZERHOUNI. The idea is really competitive outsourcing. There are two words here. On the one hand it is responding—this initiative has been ongoing in the Government for years, I am told. On the one hand it is to try to assure taxpayers that we are doing the best job possible. On the other hand there is a sense that there are mission critical areas and non-mission critical. So OMB decides which jobs are commercial, for example, facilities, secretarial support, and which jobs are core to the mission. Then our employees determine what is the most efficient way we could render that service? That is then competed and the competition then determines and provides assurance that we have done the best job that we can.

In our case we have shown already with the grants management administrative functions that no one out there can provide the services well, these very specialized scientific support functions, as well as our own employees, and my recommendation has always been we should win these competitions if we can, and assure you that we are doing the most effective job possible.

Mr. DINGELL. Doctor, could you submit to us in writing exactly what this plan for outsourcing is, exactly what instructions you got from OMB so we can look and see? Would you do that for us, please?

Mr. ZERHOUNI. I certainly will.

Mr. DINGELL. I ask unanimous consent, Mr. Chairman, that be put in the record.

Mr. GREGG. Of course.

Mr. DINGELL. Doctor, just one more question. Were you consulted before this thing was put together and handed to you?

Mr. ZERHOUNI. No.

Mr. DINGELL. Was there any consultation with NIH before that happened?

Mr. ZERHOUNI. Yes.

Mr. DINGELL. There was?

Mr. ZERHOUNI. I understand that—and I should really defer to our management people, but the NIH consulted and discussed the implementation, the specifics of the implementation.

Mr. DINGELL. But not the idea that it was going to be done.

Mr. ZERHOUNI. Not the idea, no, sir.

Mr. DINGELL. Mr. Chairman, I think I have used my time. Thank you.

Mr. GREGG. Thank the Congressman.

In your roadmap, Dr. Zerhouni, do you need legislative changes to accomplish your roadmap relative to your authority or relative to the balance between the different institutes?

Mr. ZERHOUNI. Yes, I think we need to look at that. I am not sure exactly what form, but I think the report that Dr. Shapiro mentioned, addresses the two needs. Dr. Varmus also mentioned you need two components to this. You need a mechanism for planning, either clustering like institutes or the NIH Director doing it, and you need a funding mechanism that you explicitly support so that the NIH Director—institute directors are not put in the con-

flicted situation between deciding whether they invest for common good or for their specific missions.

Mr. GREGG. It would be helpful, maybe you should sit down with my staff and with Senator Kennedy's staff and with the staff from the House, both sides, and give us what you think you need, and we can maybe develop language that would accomplish the roadmap and reach a consensus so that it is not compromised, so it does not end up being divisive, but actually is constructive to the process, if you think you need that. We would offer that opportunity to you.

In the peer review process, does not the peer review process, as it is presently structured, inherently favor the silo approach in the sense that those folks looking at an issue are not likely going to look outside of the silo and look at a more interdisciplinary approach? I am not trying to undermine, I am just saying does it have some adjustments that might be needed?

Does the peer review process—I would be interested in all of your responses to this—does the peer review process adequately balance results to the population as a whole, health care results? What is the biggest risk? What is the best return to the dollar? What has the most impact? Where are we closest to getting something versus just the academics and the basic science?

Mr. ZERHOUNI. These are very important questions. These are core questions to the health of the Agency itself. In terms of peer review, actually my predecessor, Dr. Varmus, had undertaken the first review of the peer review sections in many, many years, and Dr. Ellie Ehrenfeld conducted a major change. What is important here is that the peer review sections are independent of the institutes. This is the beauty of the system. These are truly scientific panels, the membership of which rotates every 4 years, designed by the FACA rules to be very equilibrated in terms of representation across the country, different sources of scientists. From that standpoint that system had adaptive capabilities provided the Director provides the impetus for that.

The second question you are asking is I think the more fundamental one, and that is once we have looked at projects and decided that they are good, are we focusing on the priorities? That is what I think in my testimony I am referring to. We need to have better mechanisms to understand the portfolio in relation to science, public health and society, and manage it better. So those are my two comments.

Mr. GREGG. Dr. Varmus?

Mr. VARMUS. Two brief points. I am largely in agreement with Dr. Zerhouni said, but it is important to understand that there is a strong separation between program planning and review, so when Dr. Zerhouni sets up these imaginative new programs under his roadmap proposal, there would be a solicitation for grant applications, and then special study sections that are designated to review the applications that are returned in response to that solicitation, so there would be no conflict between making decisions about grants that would go to individual investigators in traditional institute programs and these trans-NIH programs. They would be separately reviewed.

The second issue you raise is what are the criteria by which individual reviewers review grants? It is important to understand here that although the NIH promulgates a set of broad criteria, which include innovation, significance for public health needs, feasibility, the track record of the investigator, the institutional context. Every individual reviewer is going to have their own view of what weight to give to those various criteria. When budgets are tight and success rates are low, there tends to be a bias toward feasibility and conservative funding, and when budgets increase more dramatically there is a willingness to take on more imaginative research to fund trans-NIH initiatives. It is important to remember that there is going to be a linkage between whether the NIH is constrained for funds in the immediate future, conditions that will promote institute directors to try to keep their own programs and investigators going without donation to the common pool, as opposed to a situation where NIH receives enough new money each year to ensure that there are a growth of programs and the expeditious pursuit of some of the new and dramatic plans that Dr. Zerhouni's roadmap outlines.

Mr. GREGG. But what you are both saying is you are sensitive to this and trying to resolve it, but it is an issue.

Senator Kennedy?

Mr. KENNEDY. Thank you very much, and thank our chairs for having this hearing.

All of us take an enormous sense of pride in the NIH, and to have three extraordinary individuals, Harold Shapiro from the Institute of Medicine, the present head of the NIH, Dr. Zerhouni, and the former Director, Dr. Varmus here, expressing much more agreement than differences is enormously important for the American people to hear. It is appropriate that we have this kind of hearing now at the dawn of the life sciences when the possibilities for discovery are breathtaking. The continued commitment, from Republicans and Democrats for in the funding of the NIH has been one of the most exciting things to happen in this city in terms of health care. So I thank all of you for your attention to this issue.

I want to quickly state for the record what we have seen with regards to the increases in the NIH budget over the past several years. During the doubling, the NIH received 14 and 16 percent increases. This year, that figure has dropped to 2.5 percent increase. The result of that has been, as you look at this, is the stifling of scientific innovation. The fact is that there is going to be actually a reduction in the number of non-biodefense grants. Many in the Congress say, well, look, we have invested enormously in the NIH, have we not overinvested? Are they not just swimming in resources? Here we see the result of the precipitous drop in funding. You cannot read these charts without being disappointed that we may be missing some kind of opportunity.

I would be interested—time is going to move along quickly—to hear from each of you your reaction to the pressure this line of funding will have on study-sections reviewing and selecting grant applications and comment on the quality of some of the applications that are not going to get funded? How much are we going to sort of lose out on it? Maybe just very quickly?

Mr. ZERHOUNI. Just very quickly, Senator. I think you are identifying the core administrative challenge for us, to go from acceleration to a rapid deceleration presents programmatic challenges that we are trying to address. That is No. 1.

No. 2, if the success rate drops significantly then I think Dr. Varmus' observation is correct, people will tend to be more conservative and take less risk in research.

Mr. KENNEDY. Dr. Varmus?

Mr. VARMUS. Senator Kennedy, I think we all appreciate the increase that NIH has received over the last several years with respect to its entire budget, and the consequence has been that the size of grants has been able to enlarge, to catch up to the pace that it should have maintained in intervening years, so grants are individually more expensive. We have attracted a lot more people into the field. The genome project and many other new innovations have created both remarkable new opportunities for doing biomedical science that means important things to the health of the American people and also costs more because of the kind of technology involved. To go from a series of 15 percent increases to a small percentage increase is going to have a very detrimental effect on our ability to continue that progress.

The Joint Steering Committee for Public Policy, representing a number of scientific societies which I chair, has a report which I would be happy to submit for the record, analyzing the impact of these anticipated changes on the ability of the biomedical research enterprise here to function adequately, and I would be happy to submit that for you.

Mr. KENNEDY. Dr. Shapiro?

Mr. SHAPIRO. Yes. This is a moment of extraordinary opportunity which I think this country does not want to miss. It is always difficult to make budget adjustments. We all understand this, but I do not think we want to pass by a moment of great opportunity here for the benefit of the citizens of this country and indeed around the world, in a time when we not only are continuing the normal activities at NIH, but as Dr. Zerhouni and others have mentioned before, because of the nature of the scientific developments that are taking place, to also sort of reshape some of it, to both reshape and adapt under these circumstances may cause us to lose an opportunity here.

Mr. KENNEDY. Just on the other subject that was brought up by Congressman Dingell about the privatization of jobs. I understand the Washington Post reported that the NIH spent \$7 million and over 100,000 staff hours, to study job functions and compete for the outsourcing of different jobs, and after it was all over, the NIH employees won the competition. Is that right?

Mr. ZERHOUNI. That is correct, Senator.

Mr. KENNEDY. So they have spent some \$7 million, and over 100,000 man-hours—I do not know how many of those grants could have been funded with that \$7 million.

I regret I missed your opening statement, Dr. Zerhouni. We have had a good opportunity to talk about the roadmap and I think all of us are impressed by what you are doing out there at the NIH and the thought that has gone into this roadmap. We want to have

a chance to study it and study it carefully and closely. We thank you.

Just one final point on political interference in scientific advisory committees. There are always the questions—and then my time is up, and I will ask each of you this—about political interference. We are talking about ideology overcoming science, whether it is from the left or the right. How extensive is it and how important is to be resolute and not let it interfere in the extraordinary work of the institute?

Mr. ZERHOUNI. I think it is very clear that science needs to advance in a way that is supported by the entire political spectrum, because as I said in my confirmation hearing, I do believe that disease knows no politics.

Mr. KENNEDY. Dr. Varmus?

Mr. VARMUS. I think it is very important that we reaffirm the principles that the leaders of the institutes and the advisers to the institutes be selected based on their qualifications as informed members of the scientific and medical communities.

There have been instances we know in the last couple of years, not common, but some, in which political questions have been raised and political considerations have influenced the choice of some advisers, and even a very small number of those examples sets off an alarm in the scientific community about the way in which the Government deals with the NIH. The NIH is a fragile flower in Government, and it is a remarkable creation of our Government, but it needs to be insulated from partisan politics, and all of us here agree with that.

Mr. KENNEDY. Dr. Shapiro, then my time is up.

Mr. SHAPIRO. I just would like to support what Dr. Zerhouni and Dr. Varmus have said, and indeed, one of the final recommendations on our report deals directly with this issue. For those of you that are interested and have the report, it is Recommendation 13 at page 91, but it is entirely consistent with what Dr. Varmus and Dr. Zerhouni just said.

Mr. BILIRAKIS. Thank you, Senator. Your time has expired.

Mr. Pitts to inquire for 5 minutes?

Mr. PITTS. Thank you, Mr. Chairman, and again, thank you for having this important hearing. Thank you, gentlemen, for your testimony.

I will submit my opening statement for the record, Mr. Chairman.

[The prepared statement of Hon. Joseph Pitts follows:]

PREPARED STATEMENT OF HON. JOE PITTS, A REPRESENTATIVE IN CONGRESS FROM
THE STATE OF PENNSYLVANIA

Mr. Chairmen, thank you for holding this important hearing. Per the Chairman's request, I will keep this opening statement brief.

I am eager to hear from our witnesses about how we can best accelerate the progress of medical research, for that truly is the purpose of the National Institute of Health.

According to its website, the NIH is the "steward of medical and behavioral research for the Nation," Congress trusts the NIH to use taxpayer money to fund studies and glean understanding from research in order to prevent illness and save lives.

As a steward of taxpayer resources, therefore, the NIH should be responsible in how it allocates that money to ensure that its research contributes positively to the life of our nation.

While I realize this hearing is primarily focused on the organizational structure of the NIH and program implementation there, I am concerned about several grants that have been funded recently. Hopefully, during the time of questioning, the witnesses will be able to address my concerns.

In the state of California, the NIH has funded a study of “commercial sex workers at massage parlors (Asian masseuses).” This is odd, given the fact that prostitution is illegal in California. Wouldn’t the money be better spent on a program trying to end this practice, finding these women the care they need and helping them find legitimate jobs?

The ones most disconcerting to me are a \$147,000 taxpayer-funded study that “will assess the subjective and genital arousal of 180 lesbian, bisexual, and heterosexual women as they watch erotic video clips” and a \$470,000 study which includes getting people drunk and showing them pornography.

The NIH also hopes that spending \$3 million of taxpayer money will help us gain insight into American Indian and Alaskan Native lesbian, gay, bisexual, transgendered, and two-spirited individuals.

Further, the NIH is spending \$276,000 to study the sexual habits of older men, \$107,000 to study “mediums, or individuals who regularly enter altered states of consciousness as part of religious ritual,” \$2.5 million on how to better promote the morning-after pill, \$26,000 to host a conference on sexual arousal, and \$1.2 million to study giant pandas in the Wolong Nature Reserve in China.

Mr. Chairman, I am not debating whether or not these issues should or should not be studied, but rather I am questioning the wisdom of using taxpayer resources to engage in research that has, at best, spurious benefits to our nation.

The NIH has the potential to engage in much needed worthwhile research. Congress has seen fit to provide the agency with the resources it needs to carry out its mission.

However, I question whether some of these studies are the best way to spend taxpayer money.

While the NIH can find money to pay women to watch pornography and study giant pandas in China, funding for breast cancer, AIDS, diabetes and Parkinson’s research continues to lag behind.

I understand the grants I have mentioned are only a few out of the some 44,000 applications that the NIH receives each year. As a nation seeking to combat terrorism, and dealing with budget deficits and a sluggish economy, we must make sure that the limited resources we have are being spent in the most effective way possible.

I yield back the balance of my time.

Mr. PITTS. Dr. Zerhouni, you indicated that the NIH is doing ground-breaking research, and you are to be commended for a great deal of much needed worthwhile research. I think Congress has seen fit to provide the Agency with the resources that it needs to carry out its mission, but in these days of tight budgets and increasing deficits, and as we have heard in the previous line of questioning, perhaps research that needs to be done that is not being done, perhaps we should look at some of the research that might not be as beneficial or provide as many benefits to our Nation as we think. I want to ask you a couple of questions. I am not raising these questions to debate whether or not these issues should or should not be studied, but rather, I am questioning the wisdom of using taxpayer resources to engage in research that I think at best has spurious benefits to our Nation.

We faced an amendment on the floor. I believe it was my colleague, Mr. Toomey, that offered the amendment to Labor-HHS appropriations bill, that would have prohibited funding for a number of grants, and one of them was to the Kinsey Institute. It was entitled, “Moot Arousal and Sexual Risk-Taking,” that in looking at this, it pays people to watch pornography, and another one pays some to drink alcohol prior to being shown pornography. Now, is this true? Why?

Mr. ZERHOUNI. I know you are very concerned about that, Congressman, and I know many of the members have expressed concern about these grants. I can tell you in that particular grant, we are not paying subjects, research subjects to drink alcohol. We are not paying them to watch sexually explicit material. We are paying them to participate in the research that was the point.

But I do take your point seriously. As I said in my opening statement, I think we owe it to ourselves to look at the balance between science, public health and society. To me, the most important issues was, No. 1, do we have a process here that has integrity in how these grants get funded, peer reviewed? I asked my institute directors. I said, "Inform me," because I heard about your concerns and I saw the Toomey amendment proceedings, and there is clearly a need for us to be transparent and open to make sure that you are comfortable, because it would be detrimental for all of us if a small portfolio of the Agency was opaque to taxpayers, so I wanted full transparency. I asked my directors, "Please review. The critique is not my area of expertise. Tell me how this was reviewed, how did it get to the point of being funded? Is this relevant research," as Dr. Varmus was saying? "Is it public health relevant," and so on.

The responses I have received from my experts is that at the end, when they reviewed all of these grants, there was scientific justification, there was definitely a public health connection. However, that being said, I think we need to address the fundamental question you are asking, and that is, are we putting the money in the right place, and that is a portfolio management analysis. As I said, this is a core issue that we will look into and study further.

Mr. PITTS. For the record, I am quoting the application here. "During the alcohol sessions, subjects are presented with an erotic film clip before they consume alcohol, and after they have reached two different blood alcohol levels they will be paid \$50 for their participation in the studies that do include the measurement of physiological responses." That is what it says.

Another question. What mechanisms do you have in place so that even if the peer review process finds these proposals credible, that we have some standard of science or common sense oversight before we write a check out from the taxpayers? I have a hard time answering my people in town meetings who ask me, "Are you paying people to get drunk, to watch pornography using taxpayer money?" They work hard all day. Can you give us a feeling of comfort here about these studies?

Mr. ZERHOUNI. I can definitely understand how one would be concerned if the research is presented that way and not look into the total context. But the key question you are asking is do we have a process that has integrity in it that represents the public's view? Our advisory councils are two-thirds scientific members and one-third public members. Each one of these proposals is in fact approved by a community-based institutional review board. I have to believe—it is not my area of research—I have to believe that these processes should work because they are stated in law. I want to review that. I want to make sure that we are doing everything that the law says we should do in terms of these processes. In addition

to that, I think we need to look at the total balance of the portfolio and understand exactly how we are responding to it.

Mr. PITTS. Thank you.

Mr. BILIRAKIS. The chair recognizes Mr. Brown, the gentleman from Ohio, to inquire?

Mr. BROWN. Thank you, Mr. Chairman.

I have a series of questions, Dr. Zerhouni, that I would like to submit in writing if you would answer those. Thank you for that.

I want to follow up on Mr. Dingell's comments a little bit about OMB and Senator Kennedy's about ideology over science. In response to a directive from OMB, NIH diverted \$233 million from research funding to develop and study anthrax vaccine. According to press accounts—and Mr. Waxman has raised this issue too—according to press accounts, NIH, to fund this project, reduced grants on TB, on AIDS and malaria, affecting more than 500 scientists, and you could certainly make the case affecting some 6 million people who die every year from those three diseases. Dr. Fauci of NIH was quoted as saying this was the first time in the 116-year history of NIH that any research institute has ever been ordered to carry out a major applied science program.

Would you share your thoughts with the committees on whether it is appropriate for OMB, a political arm of the White House, to direct NIH funding away from research, away from actual research grants in progress?

Mr. ZERHOUNI. I have looked into that issue. I do not think it is a political issue. It is a budgetary mechanism issue. When the budget of NIAID was urgently approved for an increase of \$1.6 billion, in that budget was \$250 million for procurement and development. The intent there was to have appropriated dollars to procure and develop anthrax vaccines as they became available. So NIAID worked on it, and between OMB and NIH, essentially the issue became: you have committed in the initial budget to purchase that. The Senate removed that \$250 million, allocated it to other areas. Basically the conflict that year was over \$233 that million was designated by OMB for one purpose and then another purpose appeared. I totally understand, and I am just as Dr. Fauci is, unwilling to see dollars for research go to dollars for procurement. That needs to be clarified. We worked on it. We clarified it. The base \$250 million is staying in the NIAID base and will be used for research on a going forward basis. I understand your point, but those are the facts, sir.

Mr. BROWN. They are the facts, but I think as Dr. Varmus pointed out, that politics/ideology should not trump science, and if Congress had come back and said: Spend this money on anthrax, and not that we do not want to do that perhaps, but it seems there is a trend here on the administration saying: Yes, we want to do more on HIV/AIDS, TB and malaria, then pulling back, whether it is saying in the budget request: Yes, we want to do it, but then pulling back and pulling another strong back that does not lead us in that direction. I am concerned about that ideology all too often trumping good sound science.

Let me shift for a moment on the National Institute for Diabetes and Digestive and Kidney Diseases has been chronically underfunded in comparison to other institutes. This is of particular con-

cern because many of these diseases disproportionately impact minority groups. You talked in response to Chairman Bilirakis, Chairman Gregg's questions about the roadmap. Can you assure us your roadmap will not leave minorities on the off ramp?

Mr. ZERHOUNI. I can assure you of that, absolutely. This is one of the core reasons we are organizing, for example, the community based clinical research enterprise, because we feel that is the only way we are going to address health disparities and minorities. If we are not present in their community, connected to a fully developed and federally supported system of clinical research, it would be hard for us to make progress.

Mr. BROWN. So what specifically are you doing with the National Institute for Diabetes and Digestive and Kidney Diseases?

Mr. ZERHOUNI. Again, I think your issue is related to rising diseases like diabetes and obesity. One of the things that we did not want the roadmap to be was to be generic to any particular diseases process because we thought if that was the case it should be handled by the disease specific institute. So Dr. Spiegel is leading a Trans-NIH obesity task force, and that is the way we are trying to address this issue, make the case, so that this obesity crisis can be managed.

Mr. BROWN. Are you coordinating with CDC on their anti-obesity campaigns?

Mr. ZERHOUNI. We are.

Mr. BROWN. How are you doing that?

Mr. ZERHOUNI. Basically, all of our obesity task force people have worked with FDA and CDC trying to find common ways—for example, in the diabetes area we have even coordinated the screening capabilities, trying to enhance the screening capabilities of CDC. I cannot give you the details of operations, but I know we intend and we are working with CDC. But the effort is early and we need to do more.

Mr. BROWN. I thank the chairman.

Mr. BILIRAKIS. Under agreement, the next round is for members of the Senate. Senator Clinton?

Ms. CLINTON. Thank you, Mr. Chairman. I welcome all of our House colleagues to the Senate, and our witnesses. I appreciate very much the opportunity to have this joint hearing. I think this is a very good example of the kind of cooperation that we actually need more of, and so I appreciate this effort here.

To the witnesses, I thank all of them for their years of work in their various capacities, and I am delighted to see my constituent and friend, Dr. Varmus, here today.

I wanted to ask about comparative effectiveness. I know that in the past the NIH has funded some studies such as evaluating the comparative effectiveness with respect to some of the high blood pressure and other issues. I know that last December the National Heart, Lung and Blood Institute published a study correcting the assumption that newer drugs such as the calcium channel blockers and the ACE inhibitors, which cost 30 to 40 times more than diuretics, which had been the long-term treatment for high blood pressure, that in fact the newer treatments were less effective than the old-fashioned diuretics.

Then in January of 2003 another NIH-sponsored study compared two glaucoma drugs and found that despite the fact that one of them, latanoprost was more popular; another, bimatoprost, was more effective. Now, this is the kind of information that patients and clinicians desperately need, and it is also important because oftentimes the new therapy is not more effective but much more expensive, so this has cost implications as well. Yet these types of comparative head-to-head studies are too few and far between.

Why has NIH not been able to provide more research in this area, which I think really falls within the definition of the work that should be done by the NIH? It is not cutting edge research, but it is extremely important to actual medical care. What would you recommend that we could do to improve comparative research? Dr. Zerhouni? Dr. Varmus?

Mr. ZERHOUNI. This is a very good question, because as you know, drugs are approved relative to a placebo, and when they come into practice they are not really compared to placebos, they are compared to other drugs. Doing clinical trials of this nature is extremely expensive. The entire budget of NIH would not suffice to address all the questions. It is very, very expensive, unless you have a infrastructure that is designed for that. That is actually one of the goals of the roadmap, to have an informatics infrastructure that links patients and understands what prescriptions have been prescribed so that we can detect trends very quickly.

Let me give you two examples. One is the Women's Health Initiative. I think if the country had had a system like this, we would have discovered much sooner and we would not have had to spend the hundreds of millions of dollars in the Women's Health Initiative, that the dogma, that long-term hormone therapy was good, was incorrect.

When we make selections—and you have mentioned NIH studies of comparative effectiveness—we have to look at the public health impact. In the case of high blood pressure it is such a public health issue, we had to invest. When you look at glaucoma, it is such a major rising cause of loss of vision, we had to invest. So again, the bar is we want to do research of that nature if we have the means and it does not imbalance the need for us to advance on a fundamental level, but we have to realize that we have limits, and our limit is set when we see that millions of people are affected, and our public health estimates indicate a need for that study.

The closing statement I would like to make for you is we decided to do the Women's Health Initiative against much opposition at the time, because as public health experts, if only 1,000 people take a drug and there's a 1 percent complication, it affects 10 people. But when 10 million people take the drug, then it is a million people. So for us, obviously, as a drug or as a pattern of practice affects more and more people, effectiveness studies become more important.

Ms. CLINTON. Dr. Varmus?

Mr. VARMUS. If I might just make a few additional comments? Obviously, I agree with what Dr. Zerhouni said. In many clinical trials of course there are comparisons between the standard of care and a new therapy. But there may be multiple standard therapies

and getting the comparisons of the sort you alluded to may not always be possible because of the high cost of doing clinical trials.

The NIH is sometimes in a better position than the pharmaceutical industry from a certain point of view, to do the kinds of advanced trials that you are alluding to because the drug industry has very little incentive to do studies of drugs that have already been approved, and therefore, this is a particularly attractive role for the NIH. Nevertheless, so-called Phase IV studies, efficacy studies of approved drugs, are expensive. They require large cohorts of patients. We have a difficulty in this country that not enough of our care is administered in the context of a clinical trial. In the case of adult cancer, for example, progress has not been as fast as you and I would have liked, because only about 3 percent of the adult cancer population is in a clinical trial, in contrast to what had happened in pediatric cancer. So it is important that we mobilize the resources of NIH and patient populations and community physicians, as the roadmap plan does to try to build an infrastructure that will allow the trials to occur with less expense because there are existing mechanisms for doing the trials, and in that way the roadmap plan could lead to more studies of the kind that you are suggesting.

Ms. CLINTON. Thank you.

Mr. BILIRAKIS. Thank you, Senator.

Mr. Flanagan, for 5 minutes?

Mr. FERGUSON. Ferguson, Flanagan, Irish role—

Mr. BILIRAKIS. Ferguson, Flanagan, I think I have made that mistake before.

Mr. FERGUSON. Thank you, Mr. Chairman. I want to thank our hosts in the Senate for having us here today. We appreciate it. I want to thank our witnesses for all of your good work. All of us and our loved ones have benefited in some way, and certainly our children and grandchildren will benefit in some way by the extraordinary work and the research of the NIH and we certainly appreciate all of your efforts on their behalf.

I want to lend very briefly my voice of support to the line of questioning that my colleague, Mr. Pitts, had before. It is a very real life concern when you have constituents who read in the newspaper or read in a publication about certain projects that are being funded by NIH and trying to justify that. I have a list of them and I will read a few of them without trying to be provocative. But the fact that we are funding projects which by talking about them in an open forum could be construed as provocative is problematic in itself, frankly. Study of porn reactions. This is a list of grants that have been made by NIH. Study of sexual habits of older men. Study to promote the morning-after pill. That is a quote, not to study, but a study to promote the morning-after pill. American Indian transgender research. A prostitute masseuse study. It is difficult to comprehend what medical benefit, what public health benefit could be derived. Perhaps there is some, but when you are weighing it against competing projects it is very difficult to see how that can be justified.

Dr. Zerhouni, if you would provide us, perhaps in writing. I know you said that you—I understand that these may not be areas of your expertise and you have talked to the folks in regard of the

Toomey language—if you could provide us just a written explanation for the medical benefit that is hoped to be derived from these studies, we would certainly appreciate it.

Just a quick comment. We looked at the chart before on the rates of increase of NIH funding. Just a quick question, Dr. Zerhouni. When we talked about doubling the funding for NIH over the course of years with 14 and 15 percent annual increases, was there ever any understanding on your part that those double digit extraordinary increases would continue annually in perpetuity?

Mr. ZERHOUNI. No, not at all. I mean there is no such thing as a perpetuity budget that I can imagine ever being given.

Mr. FERGUSON. So the fact that we have a 2.5 percent increase this year is perfectly reasonable?

Mr. ZERHOUNI. Like I said, I think that the macroeconomic environment we deal with always changes and decisions have to be made, obviously, that balance needs. There is no question though that going from a certain acceleration to a deceleration is challenging.

Mr. FERGUSON. Of course, clearly. But I do not think anyone at NIH would ever expect to see a 15 percent annual increase as far as the eye can see.

Mr. ZERHOUNI. I do not think anyone expects it. Budgets go year to year.

Mr. FERGUSON. Fair enough. I have a couple more questions, and my time will be short. Dr. Zerhouni, are you satisfied with the current relationship between the NIH, the academic community, the FDA and the private sector, in terms of taking the research that is done and funded through NIH, and getting that eventually to a product or a treatment that could actually help a patient?

Mr. ZERHOUNI. Not fully.

Mr. FERGUSON. Why?

Mr. ZERHOUNI. I think we need to make progress there. The pharmaceutical industry now has standards for investing related to market size. There are many other diseases which do not fall within that category. There are early steps, as I said, as in the roadmap, a presentation, the complexity that is not being addressed as well. We work very closely with FDA in terms of understanding adverse events, and we are building bridges to make it easier. But 13 years to go from a discovery to an application that is approved is too long.

Mr. FERGUSON. It is too long. What would be long enough? What goal would you have in your head to want to get that number to?

Mr. ZERHOUNI. Well, I think two things. One is we need to do more science to understand and predict what will work, what will not work. You know, out of 300 early candidate drugs, there is only 1 that eventually succeeds. That is such an unpredictability, it is very hard for anyone to invest with certainty. So science needs to improve the degree of predictability.

Then, obviously, we need to understand the safety issues better, and Commissioner McClellan is doing an outstanding job trying to link our two agencies so that we can make more predictable products that have a lesser burden of proof, if you will, for acceptability in the marketplace. There is no number there that I can give you,

by the way, for that, Congressman. Some products will take 10 years, it is unpredictable.

Mr. FERGUSON. Sure. Last question. As Dr. Shapiro certainly knows, New Jersey, my home State of New Jersey has more researchers and scientists per capita than any State in the Nation. We are very proud of that. I think it is one of the things that makes our Nation, certainly the health care of our Nation, as strong as it is.

My question is about the diversity, geographic and otherwise, the diversity of the grants that are made at NIH. Some people grumble that there has traditionally been a bias or a higher percentage of grants that go to maybe the more traditionally recognized academic institutions and other areas, like in California or Massachusetts, for instance. Are you satisfied with the diversity of the grants that are being made, particularly given the health care community in New Jersey and our extraordinary number of researchers and scientists?

Mr. ZERHOUNI. It is never perfect, as you know. Distribution of particular investments in science always follow the opportunities. But I see a good trend. I see improvements in that distribution related to economic development. For example, Arizona was not a State where there was any funding 20, 30 years ago. Now it is a major investment State for us. Washington State did not have much 35 years ago. So there is a correlation between numbers of researchers available, economic development, our ability to stimulate an infrastructure, and we are doing that. So the trend is toward the right direction. Is it perfect? No.

Mr. FERGUSON. Thank you again for all of your work, and appreciate your being here.

Mr. BILIRAKIS. The chair thanks the gentleman.

Mr. Green to inquire?

Mr. GREEN. Thank you, Mr. Chairman. Like my colleagues, I would like to thank our panels here this morning. First of all, Mr. Chairman, I will have my statement to put into the record.

[The prepared statement of Hon. Gene Green follows:]

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

Thank you, Mr. Chairman, for holding this joint hearing with the Senate Health, Education, Labor and Pensions Committee. It is a pleasure to join my colleagues here on the other side of the Capitol to discuss this very important issue.

The NIH is the crown jewel of the federal government's biomedical research endeavors. That the Congress upheld its commitment to double the NIH budget exemplifies the amount of trust and respect we have for the fine work done by this institution.

However, in the wake of that massive increase in funding, we have an obligation to study how those funds have been spent, whether there's ways we can improve the efficiency and function of the NIH, to identify major opportunities and gaps in biomedical research, and how we can assure that our goals for that doubling—better treatments and cures for a host of diseases—can be reached.

This hearing gives us an excellent opportunity to examine the recently released Roadmap that was announced by Dr. Zerhouni earlier this week.

Among the innovative initiatives in the Roadmap is the promotion of clinical research. Over the years clinical research is becoming more difficult to conduct.

The basic science discoveries demand clinical research; however, patients with serious disorders are more likely to be treated by community physicians than by academic centers.

The Roadmap would encourage the development of new partnerships among organized patient communities, community-based physicians and academic researchers, which would help in development of efficient treatments and prescriptions.

This plan also encourages the collaboration between different types of scientists, looking for scientists to share their findings and break that "silo mentality" which often isolates scientists from their peers.

The Roadmap not only encourages scientists to share their ideas, but will also reward scientists who engage in creative thinking and take on innovative approaches with \$500,000 grants. This could open the way for new discoveries in different areas, without the pressure of failure.

Looking to accelerate research and make it more available, the roadmap provides for the creation of biomedical computing centers and molecular libraries, which would provide endless amounts of tools and information for researchers. This amount of new technology, without doubt, will be beneficial in the development of new strategies and techniques.

NIH's Roadmap Plan is a very ambitious plan, however, if implemented it could open the door to a new kind of medical research in the 21st century; one that works towards common goals, one that is not afraid to take chances and one the works hand in hand with its patients.

I am interested in learning more about this issue, and look forward to questioning our panelists about this exciting issue.

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

Mr. GREEN. I would like to thank NIH for their success of researching disease and illnesses of our time, and the best of luck in the reorganization. I am glad it is the first time NIH is going to reorganize. I have been here 5 terms, and I think some Federal agency reorganized every term I have been here, so I am glad you are only doing it once and for the first time.

All of us have particular illnesses we have interest in, and of course the issues of today, the diabetes, stroke, cancer, things like that. But, Dr. Zerhouni, I would like to ask some questions about two particular ones because of constituents in our district.

Two years ago NCI researchers found that women with breast implants were twice as likely to die from brain cancer, three times as likely to die from lung diseases, and four times as likely to die from suicide compared to other plastic surgery patients. European studies have now found similar risk of suicide and lung disease for women with breast implants. What studies does NIH plan to conduct to examine these further? I think each of us probably have constituents in our district who have developed illnesses from breast implants. If you do not have an answer, we will be glad to submit or answer other questions on this.

Mr. ZERHOUNI. If you do not mind, I would like to submit for the record.

Mr. GREEN. I would appreciate a response. Also, two researchers at the National Institute of Environmental Health Sciences have conducted research indicating that women with silicone implants have undesirable immune responses that warrant further study. Again, what research does NIH plan to do to learn more about the impact of these immune problems? Those two researchers are Dr. O'Hanlon and Dr. Miller at the National Institute of Environmental Health Sciences.

Also, Dr. William Katzen of the Case Reserve, Western Reserve Medical School, has conducted research indicating that women with silicone gel breast implants have silicone in their lymph nodes. Of course, this means that the silicone can migrate throughout their bodies, and I would like to see what NIH plans to do to examine the health effects of these leaking silicone implants. And I have

some other questions on that in particular that I will be glad to submit, but I appreciate the information.

Another issue that we dealt with in our office is communicated on the issue of scoliosis research at NIH, and I appreciate the response we received, NIH outlining the research of ongoing conditions. I know that much of the research is being done of a preventative nature, which I agree is much better to deal with preventative, especially for adolescents. But one of the concerns I have is many women, especially our older women for who scoliosis was not diagnosed because screenings were not as prominent 40 or 50 years ago have no options for treatment for their pain. I would like to see if NIH would look at treatment avenues also for our aging population. Is NIH planning any studies on the potential treatments for older women? Again, I think begin with our aging population, that will be a problem.

Mr. ZERHOUNI. We will certainly follow up with you, sir.

Mr. GREEN. I am often shocked at how sometimes Congress severely limits the administrative budgets of some of our important programs. Social Security, Medicare, NIH are examples how extremely small operating budgets can inhibit the abilities of the agencies to do their work. Can you detail additional administrative resources that would help NIH to achieve some of the goals laid out in your roadmap? That one probably is the easy one. Those other ones are specific.

Mr. ZERHOUNI. That is right. Basically, the management budget of NIH went from about 4.2 percent to 3.2 percent in the doubling period, and obviously there is more absolute dollars, but relative to the size of the enterprise, it has not kept up with that. Actually, Dr. Shapiro could comment on that. It is certainly an issue because we will need to make investments to manage the portfolio better into more modern information systems.

Mr. SHAPIRO. If I could just say a word about that. That is a recommendation in our report, to increase funding for research management support because while it is always difficult to say you are going to increase money for management or administration, but the fact is that if NIH is going to manage its responsibilities properly, the Director does need more of an opportunity to really provide world-class management for a very difficult and increasingly complex organization. So we think this is an important thing for Congress to consider as it considers appropriations, authorizations for NIH.

Mr. VARMUS. Congress needs to remember that the NIH has had an increase in the number of grants that is very considerable, nearly 40 percent. Management of those individual grants largely in the institutes requires highly professional skilled scientific oversight, and I appreciate your remarks on this topic.

Mr. GREEN. Thank you, Mr. Chairman.

Mr. GREGG. I would just note, just to give everybody fair warning, that we are going to have to wrap the hearing up by 12:15 or 12:30. I understand there are about 9 people who still wish to question, which works out about right, but I do want to make that point, and I certainly appreciate our witnesses' courtesy in staying. The hearing was supposed to go till 12 o'clock. I appreciate our witnesses staying a little bit longer.

Mr. BILIRAKIS. No problem in your staying for an extra few minutes or so? Good. Mr. Shimkus to inquire?

Mr. SHIMKUS. Thank you, Mr. Chairman. It is great to be here, and I like many applaud the work that we are doing, and this restructuring, reorganization is good.

Transparency is a big word that we are using now in Washington for a lot, not just for Government agencies but for our corporate citizens. We do much better when everything is very transparent.

I was talking to my colleague, Mr. Greenwood, on the box that many of us were put on in an appropriation bill based upon the Toomey amendment. Many voted against it because they did not want to micro manage an agency, and I applaud them for making a decision. I voted for it because in this case I had to let ideology or politics, I had to let that intervene. I had to make a statement. So what my plea would be, let us be transparent.

And in the guise of maybe more management issues to bring help, I am also concerned about another issue within the management cycle. I think that the application for dollars should be vetted based upon the application. And I will provide the example. It is the same one Mr. Pitts did. Concern out there is that the NIH is actually directing, conducting, advising applicants to stay away from certain words that will cause concern based upon Members of Congress, of people that oppose certain types of spending. Has that gone on?

Mr. ZERHOUNI. No, this has not gone on from the standpoint of NIH. We never issued any instruction to anybody to modify what is it they think is scientifically justified to say or do. I actually heard that. There is no official or structured instructions to that effect.

Mr. SHIMKUS. Dr. Zerhouni, if you would then, for me and for the members that are concerned about this, do some research.

Mr. Chairman, I ask for unanimous consent to submit this side-by-side comparison of information placed on the NIH website, and it is on the same study Mr. Pitts mentioned. One dated June 13, 2003. The other one changed, posted, same application, same desire, same goals, with removals of some key buzz words that might cause people in a clearly transparent system to be confused by the application, and it is dated July 7, 2003.

Maybe if you could, and this will be submitted for the record, you can have it—

Mr. BILIRAKIS. Without objection.

[The comparison of Mr. Shimkus follows:]

Abstract (on NIH website 6/13/2003)
 Grant Number: 1R01HD043689-01A1
 PI Name: JANSSEN, ERICK
 PI Email: ejanssen@indiana.edu
 PI Title: PROFESSOR
 Project Title: **Mood Arousal and Sexual Risk Taking**

Abstract: DESCRIPTION (provided by applicant): Recommendations to study the role of mood and arousal in sexual decision making and risk taking have not yet been translated in much systematic research. This project focuses on the relationships between mood and arousal and investigates how these, separately and in interaction, influence sexual risk taking. The project will explore, in men and women, individual differences in these relationships, as well as underlying mechanisms. Mood is proposed to affect sexual risk taking in a direct manner, but also in interaction with sexual interest and arousal. Sexual interest and arousal themselves may be affected by positive and negative mood, but the degree and direction is proposed to vary from individual to individual, and to depend on a person's propensity for sexual excitation and inhibition. Negative mood (anxiety and depression) is hypothesized to lead to increased sexual risk taking, in particular in people whose sexual interest and arousability is not adversely affected by negative mood. In a series of laboratory studies, mood and sexual arousal will be induced and their individual and combined effects on sexual risk taking will be examined. A distinction will be made between positive and negative mood, sexual interest and arousal, and risk intent and behavior. A risk-taking paradigm is introduced that incorporates characteristics of established decision making tasks while increasing ecological validity for sexual behavior. An additional objective of the research program involves the validation of a self-report measure (assessing the effects of mood on sexual interest, response, and behavior) that could be used to identify and target relevant populations in future prevention and intervention programs.

Institution: INDIANA UNIVERSITY BLOOMINGTON
 P.O. Box 1847
 BLOOMINGTON, IN 47402
 Fiscal Year: 2003
 Department: KINSEY INST/RES/SEX/GEND/REPRO
 Project Start: 01-JUL-2003
 Project End: 30-APR-2005
 ICD: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
 IRG: ZRG1

Abstract (on NIH website 7/7/2003)
 Grant Number: 1R01HD043689-01A1
 PI Name: JANSSEN, ERICK
 PI Email: ejanssen@indiana.edu
 PI Title: PROFESSOR
 Project Title: **Mechanisms Influencing Sexual Risk Taking**

Abstract: DESCRIPTION (revised by applicant): Sexual risk taking contributes directly to high rates of sexually transmitted disease and the continued spread of HIV infection. Despite many years of research, the mechanisms that lead to risk taking behavior are still poorly understood. Specifically, prior research has largely assumed that sexual decision-making depends on rational thought processes, and has not adequately addressed the role that emotional state plays in influencing behavior. This project will conduct systematic research on the mechanisms underlying the interrelationships among various types of positive or negative emotional state and sexual risk taking. In a series of studies, the individual and combined effects of positive or negative emotional state and interest on sexual risk taking will be examined. Individual differences in these relationships will be studied in men and women. A risk-taking paradigm is introduced that incorporates characteristics of established decision-making tasks while increasing ecological validity for sexual behavior. An additional objective of the research program involves the validation of a self-report measure (assessing the effects of emotional state on constructs related to sexual behavior) that could be used to identify and target relevant populations in future prevention and intervention programs.

Institution: INDIANA UNIVERSITY BLOOMINGTON
 P.O. Box 1847
 BLOOMINGTON, IN 47402
 Fiscal Year: 2003
 Department: KINSEY INST/RES/SEX/GEND/REPRO
 Project Start: 01-JUL-2003
 Project End: 30-APR-2005
 ICD: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
 IRG: ZRG1

Taxpayer funding: FY03 \$237,038

Estimated 2-year cost \$470,000

Source:
<http://silk.nih.gov/public/cbz2zoz.@www.fy2003.indiana.txt>

http://crisp.cit.nih.gov/crisp/CRISP_1 JB.gst?doc=text&key=6094864&p_grant_num=1R01H043689-01A1&p_query=&ticket=3657692&p_audit_session_id=17251212&p_keywords=

Pitts

Mr. SHIMKUS. And then work with the staff and see if maybe there is something going on. Maybe there is not. Maybe it is not approved at certain levels. But the most challenging thing for us to be, if you need more people to manage the applications, to make sure they are doing the things that are helpful in the studies, versus some political correct ideology that we want to be all things to all people. I tell you that the folks in Southern Illinois, I continue to support funding for NIH. But stuff like this will cause me and my folks in Southern Illinois to say, do not fund anything. What are we doing here? And it is a small percentage. And that is the thing that drives us crazy. Let us clean up the act.

So that is the only line of questioning that I wanted to follow up on with Mr. Pitts. I do appreciate, again, the great work you are doing. I work with many of my colleagues on the Commerce Committee on extending stuff on research, and Chairman Bilirakis, Chairman Tauzin do a great job.

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

Mr. BILIRAKIS. I thank the gentleman. I want to make it clear. My intent is that as long as the witnesses are willing to stay, that we go through all the inquiry, so I do not mean to cut it off unless they have to leave, but we unfortunately will not be able to go through a second round which I had hoped we would be able to do. I would intend to include Ms. Tubbs Jones if she were to hang around.

But in any case, at this point, Ms. Capps to inquire?

Ms. CAPPS. Thank you, Mr. Chairman. I appreciate our Senators hospitality, and also the testimony of the three of you. This is a very important topic, and I appreciate the overall goal of the review that you are conducting.

Based on some past experience, I am mindful, Dr. Zerhouni, of the warning, if you will, or advice, the experienced advice from Dr. Varmus that we all strive to limit the role of politics—that is a fine thing for us to be talking about here—but in the management of the NIH it is dead serious that you be allowed to be scientists and carry out your work even with taxpayer monies because we trust your oversight.

Actually, this question should really be posed of your roadmap policies but it is very vulnerable, if I could say that, but it is also a little hard to tease out. We have had an example on the other side of a particular issue and for the purpose of using it as an example of how insidious this can be, let me ask you, Dr. Zerhouni, to talk to us about current Federal stem cell research policies, and perhaps frame it in your overview, your roadmap, if you wish to, but I want to know specifically because I have constituents who ask me every time this topic comes up, NIH, of which I am so proud, you know, what is happening with stem cell research? Are the restrictions interfering with our ability to capture the enormous potential here, and should these policies be reexamined?

Mr. ZERHOUNI. Again, let me state that prior to August 9, 2001 there was no funding at NIH for any embryonic stem cell research, so the fact is that we are not limited in the amount of funding we can direct to stem cell research, and we are aggressively pursuing the field. I have established a trans-NIH task force which is trans-

parent and involves members of the entire scientific community. We funded 88 supplemental grants. We are funding 25 new research grants. And we have worked very hard to make the lines that are eligible for funding available for wide distribution. The only limit we have is the decision the President made that derivations that occurred prior to August 9, 2001 are the only ones that the Federal Government can fund research on. Under that policy we are doing everything we can. There is no restriction on the amount of funding. If we have good proposals and they pass scientific muster, we will fund them.

Ms. CAPPS. What kind of funding do you have in this area? And then talk a little bit about the constraints that that decision, that Presidential decision placed on you.

Mr. ZERHOUNI. The funding, we started funding in 2002, September 30th, October 1, 2001, which is the fiscal year. In that year we committed about \$29 million to embryonic stem cells, new field, and we are increasing that. I do not have the 2003 numbers, but it is going at the right pace.

You are asking me what are the limitations. I can tell you from our analysis the most important limitation at this point is to stimulate more researchers and create more teams of researchers that are competent and have enough expertise to get into this field. This is a new field so we are funding training grants to enable the training of scientists in that area. The human factor is—I do not think cell lines right now, the number of cell lines available is the immediate obstacle. I think it is more human capital.

Ms. CAPPS. I want to get to Dr. Varmus too. But one follow-up question. What is the barrier in the human side of it that you just mentioned, that you want to get more researchers involved?

Mr. ZERHOUNI. Basically there are not enough people. This is a new field. This is something that just started and we need more people who understand how to culture these cells, understand their differentiation, their molecular pathways, how they become what they become. There is just not enough.

We had a symposium in July. In June we were pleased to see a large number of new entrants to the field. We had 600 people at the symposium at NIH. Two years ago there would be 40 people. So we are making progress, but if you ask me what is the No. 1 limiting factor, right now as a scientist I think it is having more people do more research in the field.

Ms. CAPPS. I will put this one to you, Dr. Varmus. But I will make the comment that in the public eye around this time of the President's decision, just reading the newspapers, you heard about researchers that were leaving this country because they felt a chilling effect. I am wondering if that has something to do with the difficulty in attracting new scientists. But, Dr. Varmus, this all came about under—the genome, the DNA—

Mr. BILIRAKIS. We are running out of time here. I am sorry.

Mr. VARMUS. I will respond very briefly. I believe that brain drain has been overemphasized. I agree with Dr. Zerhouni that we have built a cohort at the NIH of stem cell researchers. I would argue however that the ability to attract the best people into this field is going to be limited as long as there is the sense that the future of this field is not an open one. Those of us who run institu-

tions outside the NIH are seeking other kinds of funding other than Federal funding, to support our research that goes beyond the Federal restrictions. We do believe this is an extremely promising, and provocative, important field, and I for one would be happier if the Federal funds could be used for newly generated lines and lines generated by somatic cell nuclear transfer.

Ms. CAPPS. Thank you very much.

Mr. BILIRAKIS. Mr. Rogers to inquire?

Mr. ROGERS. Thank you, Mr. Chairman. Thank you, members, for being here, doctors, one and all.

I want to shift gears on you a little bit and talk about pain management. I know that the Pain Consortium with the National Institutes of Health has been deactivated or is not active, and was wondering, Dr. Zerhouni, if you can talk to me a little bit about what its status is today.

Mr. ZERHOUNI. Again, I am going to ask you to give me the opportunity to provide you more detailed answers on the record, but in terms of pain, one of the areas where the roadmap actually focused, and it is in the documents, is the sense that we need better tools to measure pain, better tools to measure the health outcomes in patients the way patients perceive it. So that is one area.

But in terms of the Pain Committee, I will submit that for the record.

Mr. ROGERS. Currently the only active pain research or attention that is being done is with the Dental Institute. Do you find that that is the right place for that activity?

Mr. ZERHOUNI. Root canals do hurt. Let me just review this and comment. I think the Neurology Institute is also involved, but let me, give me the opportunity to respond to you in writing.

Mr. ROGERS. I will take those in written form. One of the things that—and obviously, pain is very important. One in five Americans are suffering from chronic pain, and when you look at our education institutions, some of the leading physician training institutes and universities around America do not dedicate any time to train physicians on pain care management. It is a very real and significant issue. I have introduced a bill of recent to increase by \$60 million the money that we can spend at NIH for pain research, and I know that you are very active and passionate about going from the bench to the bedside in research, creating six regional facilities. What we found is overwhelmingly patients had nowhere to go. Doctors had very little understanding, for the most part, on how to treat chronic pain patients. You think this is the right direction to go?

Mr. ZERHOUNI. It is certainly a topic of concern. As I said, we think we need better tools to measure it. You cannot manage what you cannot measure in science, and we thought it was very important for us to develop much better behavioral measurement tools for this area so that we can make progress, and we will continue to do so.

The approach itself, I cannot comment. I am not really an expert in the field, but I will definitely look into it and provide you with responses. Your topic is very important.

Mr. ROGERS. Is there at any time going to be a national pain management meeting through NIH?

Mr. ZERHOUNI. To my knowledge there have been pain management meetings. I know that this is a topic of interest across the country at institutions as well. Coordinating the care around the pain is a difficult issue because as you mentioned we do not even know where it resides in terms of specialty or who owns the problem. So I think it is a fundamental question that I think we have not resolved and certainly want to work to help.

Mr. ROGERS. And you will include extramural leaders in that process as well?

Mr. ZERHOUNI. Always, always. We always do. NIH has almost a mantra to do nothing without side input from the extra-NIH community.

Mr. ROGERS. In your consortium, and you may have to respond in writing, but is there—who are the lead institutes that are participating?

Mr. ZERHOUNI. Again, I do not know who the lead institute is, but I will provide you with that information.

Mr. ROGERS. I appreciate it. And again, I voted for that amendment, or against the amendment on the floor because some of the research that was—I am switching gears here and the members previously discussed it—mainly because I wanted to make sure that you had the right and ability to make those decisions. Michigan State University actually was doing some research that did not sound well, but once you got beneath the surface, it made a lot of sense, on SARS research and other things. I too want to caution on some of these studies, and we have had a letter in to you for sometime and have received no response, from four Members of Congress. And I am going to resubmit that letter to you, and I would urge a quick response. We want to help you make good decisions over there, but you do need to understand some would argue this is politics from the right and some would argue that it has already seeped in from politics of the left. We do not want, again, to micro manage the NIH. I think the powerful things that you can accomplish are great if we get out of your way and let you do it, but I think you can understand, by the questions here today, why this is an important topic, and why we need some answers and how we can get to the right conclusion. I am a former FBI agent, and some of those sexual behaviors I think can be translated into rape cases, pedophile cases and other valuable research in law enforcement, but we do not know that. And by reading the applications, you cannot even come close to that conclusion. You can help us by being very clear and very transparent and allow us to make good decisions so we are not climbing in your knickers.

Mr. ZERHOUNI. I will do everything possible to make sure that the Agency does not become—that it remains the bipartisan supported agency that serves everyone, and I will do whatever I can do that.

Mr. BILIRAKIS. Mr. Allen to inquire?

Mr. ALLEN. Thank you, Mr. Chairman. Thank all of you for being here today. This is a very impressive panel and your proposals for NIH are most interesting.

Dr. Zerhouni, I wondered if you could back that visual display up one spot to the effect of portfolio management. I was struck by

that. That seemed to be a good way of looking at a lot of these different issues.

One issue, if you think about science, public health and society, and the interaction among them, one of the issues that we have been struggling with here in the Congress is how to make sure that not only are new and effective drugs developed but also that they are distributed, that people can actually get them who need them, and that is not directly your business. But I want to follow up on Senator Clinton's comments earlier about the comparative effectiveness and the cost effectiveness of different drugs, because I think that is a potential area for NIH to play a vital role. I am the sponsor of legislation in the House of Representatives which would authorize \$50 million to NIH for comparative effectiveness and cost effectiveness studies, plus \$25 million to the Agency for Health Research and Quality in Human Services.

What we are really trying to do is make more and better and more objective information available to patients, to clinicians, to State Medicaid agencies and frankly, to the private sector, or others that are purchasing large quantities of drugs. This legislation would emphasize effectiveness studies for classes of drugs that are particularly, classes which are purchased in large volumes for Medicare and Medicaid. But I thought when in response to—and I should say it does not involve a formulary. It is no effort to try to deny a drug to any individual who happens to need that particular drug, but if we are going to improve quality, if we are going to have effective evidence-based medicine, if we are going to contain costs, it seems to me we need independent research not just research done by the pharmaceutical industry itself.

In response, I think, Dr. Varmus, you made in response to Senator Clinton's question, you said, one of you said you thought you could do more in this field. A couple of questions. Would authorization from Congress explicitly help? And two, how would you envision going at particular classes of drugs in order to conduct such studies or to review such studies? You may be aware that Oregon has already started down this path and made some significant progress with 5 different classes.

Mr. ZERHOUNI. In terms of authorization, as you know the AHRQ, that agency has the mandate to look at that. NIH does trials to advance discovery, to advance knowledge that will then form the basis from which CDC will base its prevention and public health strategies. AHRQ would then address these questions. We do not tend to do research that is designed primarily to support decisionmaking for policymakers in the reimbursement area, but we are very committed. I can tell you that all of us at NIH we want our discoveries to be translated and we want our discoveries to be affordable and accessible and effective to all Americans.

The comment I was trying to make is to try to highlight for you a systemic issue which we agree with you is there and we are trying to address, and that is that with our current health care system, as fragmented as it is, with no uniformity of data standards, no real clinical information systems besides billing and getting a little bit of work flow done, you really cannot have a good view of what is happening on the ground in terms of usage of medication.

We do not even have electronic prescribing. I mean we cannot even tell who received what when in terms of effectiveness.

The problem with the current system is that if we just expanded the spectrum that we need to address, I can assure you that the budget of NIH will have to be quadrupled for us to do that. So we need a better system. I think any help we can get to get a more efficient information flow in terms of effectively, transmitting the clinical information. As you said, it needs to be available to the right person at the right time. That is the barrier, and I would like to really give it to Dr. Varmus. He has faced the same issues I am sure.

Mr. VARMUS. I definitely agree with what Dr. Zerhouni just said. I think it is important to keep in mind that improving our clinical research capabilities can help establish a network of investigators who can help pursue these questions, but I do think it is important to remember that the strength of the NIH has come from identifying important scientific issues and that NIH became an agency for vetting the comparative virtues of very similar drugs, for example, that it would actually not serve the country very well. It would be nice if there were ways to create incentives for drug companies to carry out some of these comparisons, but that may be difficult to envision.

Mr. ALLEN. Thank you. My time has expired.

Mr. Chairman, could I just ask that two articles focusing on the legislation that I have introduced be submitted for the record?

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

Mr. Waxman to inquire?

Mr. WAXMAN. Thank you very much, Mr. Chairman. Gentlemen, I appreciate your testimony. I have always supported NIH since I first was elected to Congress in 1974 and I want to make sure that the NIH's scientific mission is protected from political interference. I have a sense that there is more and more political interference. You cannot help but have that sense by just attending this hearing and hear the kinds of questions that are being asked of you, Dr. Zerhouni, about some grant application and some summary of a grant application. What has been raised is a question of political correctness. I do not want your decisions on research to be based on somebody else's view of political correctness. I think it ought to be based on the validity of the scientific research.

In order to grant any of those projects, you have to have a scientific merit review system, and I think the one you have had is the best that has been developed. If Congress is going to come in and micromanage and make these decisions, I think that is very dangerous.

I thought Mr. Shimkus put it well when he said he voted for the Toomey amendment because he thought he ought to let his ideology and political views dictate his vote, even though he did not like the idea of micromanaging NIH. If we follow that dictate, we are politicians. We have to face the voters. We do not want people voting on whether they think the title of an application before NIH sounds like it is a good idea.

There is also a theme in the areas where there is an objection. It seems to be a theme based on sex and sexual research. It seems to me that sexuality and sexual relationships are a very important

part of the lives of most adults and leads to all sorts of problems like with respect to the fact that Representative Rogers, who is an FBI agent, made the point that he wants this research—and has seen the benefit when he looks below what he is being told by some right-wing group that wants to discredit this kind of research.

I am also, by the way, quite concerned about the limitations on the embryonic stem cell research. I do not see that any different than what is being pushed here at this hearing, and that is to have a chilling effect on research. Maybe it is not bad yet, but if you are having trouble, Dr. Zerhouni, in reaching the human capital to do this research, I think it is because researchers do not want to be in a situation where they are going to be gagged, where there is not going to be funding for it, that the rug may be pulled out from under them because a bunch of Congressmen or even a President may decide that because of some right-wing or left-wing pressure group that the research is not going to be acceptable even though it can lead to cures.

Dr. Zerhouni, I want to raise a specific issue with you, and that is the Commission Corps of the U.S. Public Health Service, which employs 6,000 scientists and clinicians across dozens of Federal agencies including NIH. In July Secretary Thompson proposed major changes to the corps including new mandatory physical fitness standards, weight limits and other requirements. There is widespread concern those changes are going to drive talented senior scientists out of public service. Two weeks ago Representative Van Hollen and I released a letter from FDA Commissioner Mark McClellan in which he objected to many key elements of the proposal to restructure the Corps.

I would be curious to know if you have seen that, Dr. McClellan's letter, if you agree with his concerns, and whether you have written a letter yourself to express similar concerns?

Mr. ZERHOUNI. First of all let me say that the notion of transforming the Corps is something that we need to consider. How it is done is really the issue. And to be very direct in my responses to you, I think as you are trying to transform a Corps that contains officers who have been there 20 years, 25 years, and then officers that have been there 2 years, and then impose a new requirement of deployment, it does present challenges. I have heard my Commission Corps officers come to me, come to Dr. Wyatt, who is my assistant for these issues, and express concerns in terms of their ability to stay in the Corps and their—

Mr. WAXMAN. Have you passed on their concerns to Secretary—

Mr. ZERHOUNI. I did.

Mr. WAXMAN. You did. Would you be willing to share with us any correspondence you sent to him?

Mr. ZERHOUNI. I will have to check with the Department, but if it is available, I will be happy to share it with you.

Mr. WAXMAN. I am pleased that you have expressed concern because I know many people in the Corps feel this is an interference in the Corps itself and the job that it was set up to do.

Mr. ZERHOUNI. Again, Congressman, I think the Secretary wants to accomplish a deployable Corps, which has some public health

merit, and we need to look into. The issue is not the what. The issue is how you get there.

Mr. WAXMAN. There is a widespread concern in the scientific community about political manipulation of NIH study panels and advisory committees, and I wanted to ask you specifically whether you believe it was appropriate for a potential appointee to the advisory committee to the National Institute on Drug Abuse to be asked whether he voted for President Bush, or whether it was right for a nominee to the Muscular Dystrophy Research Coordinating Committee to be asked her views on the President's stem cell policy, or whether you think it is appropriate for political officials at HHS to have any role in interviewing potential scientific appointees?

Mr. ZERHOUNI. I became Director after this incident, but I can tell, I do not think there is any role for that sort of vetting for scientific advisory positions. My position is very clear. I have made it clear—and I am supported in that regard by Dr. Jack Marberger and the Secretary himself, and I have made sure since I took over that there is—if I hear of anything like this, obviously my position is very clear, is that scientific advisory positions should be based on competency, demonstrated competency.

Mr. WAXMAN. Mr. Chairman, I just want to conclude by saying that all of these issues that I have raised—and I have not asked questions about them because of the limited amount of time to express my own views—I think that they represent political considerations that are interfering with NIH's mission, and if they are allowed to continue, NIH risks losing its reputation for scientific independence and excellence. We are going to lose good people, and we are going to lose out as a society on what those researchers could give to all of us and the future of this country.

Mr. BILIRAKIS. I thank the gentleman. I suppose a better, more improved transparency would probably maybe give us the—

Mr. WAXMAN. Well, if transparency means we are going to have things out there that are just going to be used to attack—

Mr. BILIRAKIS. No. I am talking about letters of consent inquiring to find out why certain research is taking place. If there had been maybe responses, it would have delayed, if you will, what has taken place. In any case, I appreciate the gentleman yielding back.

Ms. DeGette to inquire?

Ms. DEGETTE. Thank you, Mr. Chairman. I would like to add my thanks to the panel for coming today.

As the Co-Chair of the Diabetes Caucus in the House, I share Ms. Capps' and Mr. Waxman's concern about stem cell funding, and I would like to ask the panel some follow-up questions about that. Dr. Varmus, you were talking at the end of Ms. Capps' time about the researchers feeling chilled from making applications for NIH funding. I do not want to put words in your mouth, but I talked to a lot of researchers myself, and what they have told me is they are reluctant to file applications for research grants to the NIH because researchers at essence are not political and they do not want to get involved in a big political mess, and they also do not want to have to comply with a lot of the restrictions that the President's Executive Order, they feel, has put on their research. I wonder if you can comment on that.

Mr. VARMUS. Well, I do not think that investigators should feel shy about applying for research for which Federal funds are available. Indeed, as Dr. Zerhouni's comments reflect, there are over 50 investigators who have received funding and they are working effectively with cell lines that are available for funding.

But as I pointed out, I am concerned that the narrow scope of research that is allowable is making young investigators who are choosing a field of investigation wary of entering a field in which the future is uncertain. There are limitations unless one has access to funds other than Federal funding, which does not happen in every institution. So I associate myself with part of your remarks, but I think that there is an area, there could have been none. Those of us who have been watching this very closely for a long time were relieved that the door was at least partially open and some NIH-supported work in this area can be conducted.

Ms. DEGETTE. I know all three of you are supporters of stem cell research. Dr. Zerhouni, I want to commend you for the recent announcement this week about the three small grants for embryonic stem cell research. But I think we can all agree that embryonic stem cell research is in the early stages. Dr. Zerhouni, I believe you testified to that effect. I guess one concern I would have is with the tremendous potential of this research what is going to happen if, as I understand it, it looks like we maybe have 11 cell lines right now that are workable, and at some point it is going to become pretty clear that these cell lines are limiting to the research, they are either too old or they are not diverse enough. What is your thinking what we are going to do at that point? And this could happen quite rapidly.

Mr. ZERHOUNI. We have 12 cell lines widely available. It is hard to predict. As you know, science goes by with unpredictable steps. At this point there is no clinical trial that is being proposed by any investigator. There is too much to be done to understand better these cells and how they behave, how they get differentiated, how do we prevent their multiplication? So I cannot predict—

Ms. DEGETTE. But this research is proceeding apace, both in a limited way through the NIH, but also in a very dramatic abroad in other countries and by private organizations, is it not?

Mr. ZERHOUNI. We have checked on that. I actually had a discussion with my colleague, Dr. Radda, in England 2 weeks ago, and asked him how many lines they have developed for research, and at this point they have not developed any, even though they have less restrictive—

Ms. DEGETTE. But in fact, they are establishing a stem cell bank in Britain right now, are they not?

Mr. ZERHOUNI. They are establishing a stem cell bank. There is no cell available from that bank at this point. They are working on the legislation that will do it. So the characterization to say that we are falling behind in drastic terms I do not think is factually correct.

Ms. DEGETTE. That was not my question.

Mr. ZERHOUNI. Sorry.

Ms. DEGETTE. My question was: as we move forward with this research, if the NIH researchers determine that the existing cell lines, 11 or 12, whatever you want to say, are insufficient, what

then will happen? Because it seems to me, just like Mr. Waxman, this limitation that has been made is a political limitation, not a scientific limitation.

Mr. ZERHOUNI. That is correct. I think the decision is based on moral and ethical considerations of the President and we are basically under that policy, applying the policy to its largest extent possible. I do not know what may happen months from now and the discoveries that will be made, but I am looking forward to seeing those discoveries.

Ms. DEGETTE. Dr. Varmus?

Mr. VARMUS. I think in that event we will become increasingly dependent upon institutions like the Howard Hughes Medical Institute, our own institution, and several others around the country that are investing their non-Federal resources in this area of research.

Ms. DEGETTE. So the Federal Government will lose its leadership edge in that case.

Mr. VARMUS. The Federal Government, as you know, is the major source of academic funding, and I personally regret the idea that we will be having one segment of academic research conducted with non-Federal funds.

Ms. DEGETTE. Thank you.

Thank you, Mr. Chairman.

Mr. BILIRAKIS. Ms. Tubbs-Jones is not a member of this committee, but she asked if she might sit in, and she has been very patient, one of the first people in the room. And we appreciate your interest and you are now recognized for 5 minutes.

Ms. TUBBS JONES. Mr. Chairman, thank you very, very much for the opportunity to be a part of this hearing this morning. Good morning to all the physicians, doctors.

I am Stephanie Tubbs Jones. I represent the 11th Congressional District of Ohio, and I serve on the Ways and Means Committee. I have introduced a piece of legislation called the Uterine Fibroid Research and Education Act. It is also being sponsored in the Senate by Senator Barbara Mikulski.

First of all I want to thank the chairman for giving me this opportunity to be here, and I want to thank his staff for supporting me. I also want to thank John Ford from the Energy and Commerce Committee staff. He has been a real rich guy helping me out, and I appreciate it, and my staff as well, Anthony and Sheshrina.

I am concerned about uterine fibroid research. Of the \$27 billion that you have in your budget, only \$5 million is being spent on uterine fibroid research. I have had the pleasure of meeting with Dr. Estelle Perette of the NICHD, Dr. Barbara Davies of the National—all these acronyms get me, but NIEHS; Dr. Vivian Penn of the Office of Research on Women's Health. They have told me some of the findings on uterine fibroids. What I have learned is that 20 to 25 percent of women of reproductive age have uterine fibroids and we have not figured out what causes uterine fibroids, and that 3 to 9 times—excuse me, let me say that again. That 3 to 9 times this condition occurs in African-American women. It is the highest cause of hysterectomy among both white women and African-American women. I would just encourage you, as you are

looking at that issue, that you please pay attention to uterine fibroids.

I would also say to you that it is so important that we look at health disparities. I associate myself with the comments of all of my colleagues who have spoken today, but as an African-American woman, it is so important that we focus in on health disparities. On Saturday of last week I had the opportunity to do a presentation with Dr. Wernie Reed of Cleveland State University. I had the Chairman of the National Institute of Cancer Research, and we did a piece on the Urban Cancer Project, which is a research piece funded by the NIH, looking at clinical research and why African-Americans tend not to participate in clinical research. And if we are going to do research in the area of disease affecting African Americans we have got to figure out how we bring them back into the fold.

Finally, I will say, and then I am going to let you respond however you choose, that all politics ain't so bad, and the reason I say that is because I come here to Congress as a result of political stands that I take. Some of the research that has been done specific to African-Americans and minorities came as a result of the political push of the body politic to bring it to the top of the table. So I do not want you to be swayed by the issues of political life, but also I do not want you to be immune to the importance of the body politic saying to you, this is an issue that is important.

Please, gentlemen, feel free to respond to any of the things I have said, but I ask you to pay close attention to the research that we do in the area as it affects minorities and African-Americans in particular.

Mr. ZERHOUNI. I am going to ask my predecessor.

Mr. VARMUS. Let me just comment briefly about your comment about the political activism that led to increased interest in health disparities. I agree entirely with your point, but I would respond by saying, as someone who has been a strong supporter of research on health disparities, that there are facts, public health facts that represent the phases of the argument that have influenced the increased expenditure at NIH and indeed institutions like my own in New York to make greater investments in this area. It is clear that in a variety of areas, not just uterine fibroids, but cancer, heart disease, infectious illnesses and others, that people of lower economic status, people in the African-American and Hispanic-American communities do have higher rates of morbidity and mortality and we need to understand why that occurs. There are many possible explanations. This requires study.

I work very closely with Harold Friedman, who has been a major proponent of the need to look in poor communities, and so I agree entirely. But that is the body politic bringing facts and figures to us, and it is an important role you play. Thank you.

Mr. SHAPIRO. If I could just say a word. I know Dr. Zerhouni will want to answer. I think that scientists do not have a monopoly on understanding what the most important health concerns are. They are just one constituency which understands evolving health concerns. Other constituencies, as you pointed out, are yourself and your constituencies and so on, and it is entirely appropriate, in my judgment, that the health concerns of the public be a major factor

considering what we should do. Only scientists can know what areas are open for investigation and we have to rely on that, but bringing these concerns forward is not only essential, it is a responsibility of you and your constituencies to help inform the Nation of what the real health concerns are.

Mr. ZERHOUNI. I agree first of all about uterine fibroids. We are quite aware of the need for research there. I know there are efforts in that direction. NIEHS has a very interesting program in that regard. The causes of uterine fibroid developments are not well known. We need to understand that better.

As I said in my statement, and I mentioned the evolving challenges that we are facing, health disparities remains a challenge. I think in many ways when you mention the body politic, I think it is reflected in the slide that is up there in the tryptic, and I put society at the bottom because it is the base upon which we work. So we are completely aware of that, provided that the debate is open, that the transparency that we are asking for is there, and that there is reasoned discussion of what it is that drives the need for investments.

In the case of health disparities, I totally agree with you, there is a problem. The minority populations do not participate in trials, and NIH is trying to do what it can to change that. We have had one of the most successful heart studies called the Jackson Heart Study in Mississippi. We funded a national primary care center at Morehouse, which is connecting 136 community based organizations to be able to have that partnership. I think what happens is unless you have a partnership and a community of research, it is very hard to do the research. One of the tryptic of our roadmap is to try to build that new culture of having patients at the center of the research enterprise.

Ms. TUBBS JONES. Thank you.

Mr. BILIRAKIS. I thank the gentlelady.

I want to thank Dr. Zerhouni for his flexibility, for his willingness to—we know about protocol and whatnot—but your willingness. If we had not allowed or suggested or asked your permission to go ahead and move the second panel in with you, we would just now be starting with the second panel.

Mr. ZERHOUNI. I have to tell you that everything they said was music to my ears.

Mr. BILIRAKIS. Also of course, thanks to Senator Gregg, his staff, all the Senate staff. They have been great hosts in allowing us to use this room.

Again, I would repeat, we would like to have the authority to be able to submit questions to you and receive response from you in a timely fashion, but again, there are things which apparently we must do in order to give the Director the authority to accomplish the many things that we are talking about, so let us know what that is. Give us some suggestions so that we can sort of help you to help all of us.

Thank you very much, gentlemen, for being here today and for so much good that you have done for all of us.

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

Mr. VARMUS. Thank you.

Mr. SHAPIRO. Thank you.

Mr. BILIRAKIS. This hearing is adjourned.
 [Whereupon, at 12:28 p.m., the joint hearing was adjourned.]
 [Additional material submitted for the record follows:]

PREPARED STATEMENT OF HON. PATRICK J. TOOMEY, A REPRESENTATIVE IN
 CONGRESS FROM THE STATE OF PENNSYLVANIA

As Members of Congress, we are faced each day with visits to our offices by constituents impacted by the circumstances of life-threatening illness affecting themselves, their family members, and, often times most tragically, their children. All of these constituents understand the stakes involved in finding cures for debilitating disease; without treatment their loved one will literally face a battle for life.

All Members want to help. And we have helped already—over the past five years Congress has doubled the funding for the National Institute of Health.

Our work has been a just, and overdue endeavor. However, our duties should extend beyond appropriations. Too often we relinquish our obligation to ensure responsible utilization of taxpayer dollars.

On July 10, 2003, I offered an amendment to the Departments of Labor, Health and Human Services, and Education Appropriations Act of 2004. My amendment was about simply doing just a little bit more for those families struggling with incurable illness. As any of these families will attest, every little bit counts.

While the majority of the projects and grants directed by the NIH are productive and efficient, several seem lacking in merit.

My amendment sought to reprogram grant money that the NIH has decided not to spend on researching life-threatening illnesses. This amendment would have prevented the NIH from funding four specific grants in Fiscal Year 2004 that are currently receiving funding.

It is important to note that my amendment would not have reduced total appropriations to the NIH; again, it simply prevents the agency from funding a few specific projects.

Four of the specified grants were:

Grant Number RO3HDO39206: "Study on Sexual Habits of Older Men." This study seeks to determine whether older men experience a decline in sexual behavior and if that decline is associated with sexual dissatisfaction, *"especially with behaviors (such as masturbation) that may be substituted for more rigorous activities."*

Grant Number R01DA01386: "Study on San Francisco's Asian Prostitutes/Masseuses." An excerpt from the grant abstract *"The proposed study will describe drug use and HIV-related behaviors among Asian female commercial sex workers at massage parlors."*

Grant Number R01MH065871: Study on American Indian Transgender Research. This study aims to get a general understanding of the *"American Indian and Alaskan Native lesbian, gay, bisexual, transgendered, and two-spirited individuals... who are a drastically understudied and underserved group."*

Grant Number RO1HD043689: "Mood Arousal and Sexual Risk Taking." An excerpt from the grant abstract: "In a series of laboratory studies, mood and sexual arousal will be induced and their individual and combined effects on sexual risk taking will be examined."

I am not making this up. I could not make this up. These descriptions are taken directly from the NIH website and written by the researcher themselves. These grants are a ridiculous waste of taxpayers money and go to prove that if you propose something crazy enough, our Government just might fund it.

Of greater insult, I recently learned that this last grant given to the Kinsey Institute on "Mood Arousal," which is ongoing and slated to receive a total of \$470,000, involves supplying participants with varying quantities of alcoholic beverages and then having them watch sexually explicit videos. In other words, the NIH has approved a grant to pay people to get drunk and watch pornography. Your constituents and all taxpayers will be shocked to learn that their money is going to grants like these.

The combined value of these grants is roughly \$1.5 million for FY 2004, a small fraction of the total NIH budget. But these funds can represent a real contribution to the study of life-threatening diseases.

If these grants did not raise an eyebrow with the peer-review groups who approved these grants, then I submit that something is wrong with our peer-review process. I submit there exists a disconnect between the grant making authorities at the NIH and the taxpayer.

NIH spokesmen have publicly claimed that these grants research infertility and will lead to the development of abstinence curricula. However, the researchers

themselves claim no such thing. My amendment does not subvert the process of peer-review, the process in these instances and perhaps others clearly has subverted itself.

Moreover, it is within the clear purview of Congress, under the Constitution, to be the ultimate peer-review body. It should not be our goal to undermine the peer-review process of individual agency, but rather to uphold our responsibility to oversee all expenditures of taxpayer dollars. When money is going to study the sexual habits of older men or transgendered Native Americans versus trying to solve life-threatening diseases, Congress must step in.

If there is support for researching these areas, then perhaps it should be funded independently, but not with taxpayer dollars. Studying the effects of pornography on people in different states of inebriation is not a priority of most Americans and should not get the benefit of taxpayer-funded research.

The National Institute of Health should have higher priorities. Grants like these diminish the good reputation that the NIH enjoys.

PREPARED STATEMENT OF JEFFREY C. MARTIN, CHAIRMAN OF THE BOARD,
PARKINSON'S ACTION NETWORK

I thank the House Committee on Energy and Commerce for inviting this statement on behalf of people with Parkinson's disease and the entire Parkinson's community. The topic of the Committee's hearing, Managing Biomedical Research to Prevent and Cure Disease in the 21st Century: Matching NIH Policy with Science, is of vital interest to people suffering from chronic diseases.

There is much to praise about the National Institutes of Health (NIH). It is a very popular domestic program with the public. NIH has powered this country's remarkable success in basic biomedical research, such as new discoveries involving genetics, proteins, and cells. The current leadership of the NIH, moreover, recognizes that the public expects more than basic science from the tax dollars it provides to the NIH. The public wishes to earn a public health return on its public investment. This does not mean that the public health benefit must be immediate, but the research funded with public dollars should make sense as part of a plan to help either in the long-run or the short-run to understand, prevent, treat, or cure disease.

This is where the grantmaking processes of the NIH warrant careful scrutiny and potential overhaul. The current system envisions science occurring primarily through a principal investigator in a laboratory at an academic health center supported by a four year grant and assorted postdoctoral students and equipment. But that paradigm, though quite useful regarding much of basic science, is ill-suited to the translation of basic science discoveries into actual treatments or therapies for people. Those gaps are not filled so much by hypothesis-driven research at individual labs, but by pulling together experts and resources to solve particular problems in ways not typically done by academic researchers.

These efforts, for example, may involve screening potential drugs against molecular libraries, systematically exploring the effects in various animal models, and then developing appropriate clinical trials.

While NIH has a new emphasis on translational research under Director Zerhouni, the resources necessary to truly yield the payoff we are seeking have not yet been committed. For example, in the Parkinson's area, the first step in demonstrating a serious commitment to translational research would be to increase the staffing at NIH that is devoted to understanding and managing the existing portfolio of Parkinson's research. Currently, only part-time of one Program Director is dedicated to this. Unless you know how the currently funded NIH research is actually progressing and how it fits into the wider portfolio of Parkinson's research generally, one cannot intelligently try to fill the gaps to develop new therapies.

Moreover, NIH should upgrade the position of Program Director by giving them real authority to pursue translational opportunities within a certain budget, while tying future funding of those projects to outcome measures.

Once the gaps are identified, finding the money to fill those gaps runs into several obstacles. First, because most of the money appropriated by Congress each year is part of NIH's "commitment base" and dedicated to prior year grants, it is difficult to turn this large ship very quickly. Second, while there is, theoretically, the possibility of terminating unproductive grants or grants of peripheral importance to public health, it is rarely done. Third, the peer review processes at NIH are largely populated by academic bench researchers who tend to value basic science over the often more expensive translational and clinical research necessary to develop new treatments. Fourth, the review processes that an institute may employ, such as advisory councils, are once again populated largely by academic scientists who feel it is im-

portant to “maintain the pay line” in order to encourage bright students to devote their research careers to the particular field in question—which once again, diminishes the availability of resources for initiatives to target particular therapeutic or translational opportunities.

The upshot of all this is that the more that one learns about NIH processes, the more one becomes convinced that some serious change is needed if the public confidence in the NIH to produce cures and treatments is going to be realized. Such a change involves staffing, peer review processes, and a fundamental culture change in academic medicine. But if we do not undertake to effect this difficult change, I fear that the public’s confidence in NIH will be eroded, and the implicit social contract whereby we fund science with public dollars in order to produce a public benefit when possible, will be shredded.

Medical research, of course, is important not only to people with chronic diseases and their families, but to everyone. We should not view the NIH dollars as committed to academic research for its own sake, but we should also be careful not to overmanage or overregulate scientists. NIH needs to be sophisticated enough to identify the key gaps and ask the important questions and then call on the creativity of the scientific community to supply the best answers. We should provide the resources to do this through increased appropriations, and if necessary, by reducing the commitment base through a serious review process regarding the productivity of existing multiyear grants. I urge the Congress to stay involved in this as the public’s representative. This matter is too important to be left to the scientists alone. While this Congress has been appropriately reluctant to legislate dollars for diseases in an earmarked fashion, it should not be reluctant to ensure that the public dollars are being spent for public health purposes in an effective way.

In addition to new processes of grantmaking and additional staff and resources, the NIH needs to exercise leadership and require grantees to share their data in a very prompt way with the NIH program directors, who can then use the information to redirect resources. The current system is much too glacial in pace because data is released only after publication, and publication is usually more than a year after discovery. Finally, NIH should also undertake appropriate development of public/private partnerships with both industry and the nonprofit community in order to leverage federal funds and maximize the effectiveness of the research dollars it spends.

Earlier this week, Director Zerhouni announced the outlines of his Roadmap initiative. Some of the ideas are similar to these suggestions. But we have four questions we would pose. What resources are being committed? What human talent will lead these areas and what is their staff? Should not the Roadmap—which was part of the Administration’s proposed FY04 budget for NIH—take into account the report language addressed to the NIH by Congress? And finally, is it all outcome oriented and directly connected to improving human health in the long or short run?

In closing, let me say that NIH grantmaking might seem like a dry, bureaucratic topic and in some ways it is. But active oversight of this dry topic by this Congress may mean the difference for the development of cures and improved treatments for millions of Americans, and also may determine whether the rising cost of disease and disability as the Baby Boom generation ages takes the steam out of our economy. Thus I submit it is pretty interesting. I thank the Committees and look forward to working with the Committees and their staffs on this vitally important topic.

PREPARED STATEMENT OF THE AMERICAN CANCER SOCIETY

On behalf of our millions of volunteers and supporters, the American Cancer Society is pleased to submit this statement for the hearing record.

When Congress and President Nixon declared war against cancer in 1971, cancer was largely a death sentence. Three decades later, our national research investment has reaped remarkable returns. Today, early detection can defeat some of the common cancers, such as cancer of the cervix, breast, colon and prostate, which represent more than half of all cancers. We now have strategies that can help prevent many cancers from occurring. And development of therapeutic agents such as Gleevec and Herceptin has shown that specific molecules in cancer cells can be effectively targeted when treating the disease.

Thanks to these advances, cancer survivorship has now become part of our vernacular. Indeed, nine million Americans alive today have a history of cancer—this is twice the number of survivors compared to 30 years ago.

Despite this progress, cancer remains the number two killer in the United States. This year, 1.3 million Americans will be diagnosed with cancer and approximately

556,500 are expected to die—more than 1,500 people a day. In addition to lives lost, the NIH estimates overall costs for cancer at \$171.6 billion in 2002, including \$60.9 billion in direct health expenditures.

Without quick action, changing population demographics will make the situation worse. Cancer can strike at any age, but it is a disease that disproportionately affects the elderly. Nearly 60 percent of new cancer diagnoses and 70 percent of all cancer-related deaths occur in the 65 and older population. Indeed, cancer is the leading cause of death for Americans aged 60-79. As the Baby Boomers reach retirement age, we will see the number of Americans over age 65 double in the next 30 years, translating to a dramatic increase in the number of new cancer cases. Moreover, medically underserved populations continue to bear a disproportionate cancer burden and research is required to address this health disparities gap.

The American Cancer Society applauds the Senate Health, Education, Labor and Pensions Committee and the House Energy and Commerce Committee for holding this hearing to examine whether the National Institutes of Health (NIH) is prepared and organized to advance the fight against diseases like cancer in the 21st century.

The following testimony highlights the importance of NIH research to the war against cancer and urges Congress to protect provisions of the National Cancer Act that provide the National Cancer Institute (NCI) with the necessary tools to continue the fight.

INVESTING IN CANCER RESEARCH SAVES LIVES

A strong Federal commitment to biomedical research and public health programs represents the nation's best defense against cancer and provides hope of survival to the over 1.3 million Americans who will be diagnosed with cancer this year.

We are grateful to Congress and the Administration for the extraordinary leadership shown in doubling the NIH budget over the past five years. Research conducted at the NIH, including NCI and the National Center on Minority Health and Health Disparities (NCMHD) holds the key to taking our progress against cancer to the next level.

We have learned that cancer is complex, representing more than 100 different diseases. We are at a critical point in time during which we must not only maintain our current momentum, but also push forward with new research to bring the next breakthroughs to cancer patients. The development of molecularly-targeted drugs, such as Gleevec, that attack only cancer cells while leaving healthy tissue alone is one example of the remarkable advances the public investment in NIH has generated. Other major advances include:

- Promising results from research that may lead to a vaccine targeting pancreatic cancer, which remains one of the deadliest cancers. Currently, approximately 95 percent of those diagnosed die within 15 months.
- As a result of a host of new drugs for the treatment of childhood leukemia, the cure rate has reached 80 percent.
- A national investment of \$56 million in testicular cancer research has enabled a 91% cure rate and a savings of \$166 million annually.
- Development of tools to detect cancers earlier, when they are more localized and therefore more successfully treated. For example,
 - Colon cancer screening tests have led to a 90 percent five-year survival rate for colon cancers when they are caught in their earliest, localized stages and 64 percent when the cancer has spread only to adjacent organs or lymph nodes. Once the cancer has spread to other parts of the body, the five-year survival rate drops to just eight percent.
 - The development of a simple and inexpensive blood test to help detect prostate cancer at an early stage. In the past five years, annual prostate cancer deaths have been reduced by 28%.
 - Progress in early detection and treatment of breast cancer has resulted in decreasing mortality rates, with more than 90% of breast cancers now diagnosed at localized or regional stages. This translates to a five-year survival rate of 97% for localized breast cancer and 79% for regional breast cancers.

Perhaps most significant, cancer mortality rates have declined by 57 percent since the early 1970s as a direct result of our national cancer research investment. This year's *Annual Report to the Nation on the Status of Cancer, 1975-2000*, shows that death rates from the four leading cancers—lung, breast, prostate and colorectal—declined nationally and in most states during the 1990s. Despite these promising trends, our work is far from over. Research is required to develop early detection and treatment tools for rarer forms of cancer that remain deadly. More work also needs to be done on the most common cancers. For example, few treatments are currently available to those with advanced lung cancer. In addition to breakthroughs

in the area of cancer, federally funded research at the NIH has provided a lifeline to numerous patients suffering from a range of diseases.

The American Cancer Society urges Congress to maintain its strong commitment to funding biomedical research. Last year, NIH leadership testified that current scientific opportunities lend themselves to an increase in the range of 8-10 percent. For Fiscal Year 2004, the American Cancer Society has recommended an 8.5 percent increase for NIH.

PROTECTING THE NATIONAL CANCER ACT IS CRITICAL TO THE WAR AGAINST CANCER

At the request of Congress, the Institute of Medicine (IOM) recently released a report—*Enhancing the Vitality of the National Institutes of Health: Organizational Change to Meet New Challenges*—regarding the structure and operation of the NIH. Of the many recommendations included in the report, the American Cancer Society would like to call attention to a specific recommendation regarding the National Cancer Institute (NCI).

The IOM report encourages Congress to re-examine several of the provisions of the National Cancer Act of 1971—the driving force behind the recent progress made in the fight against cancer. Of particular concern is the recommendation that Congress reconsider a provision of the National Cancer Act that provides the Director of the National Cancer Institute with authority to prepare and submit an annual cancer research budget directly to the President of the United States.

The NCI budget outlines promising areas of research that—if pursued—offer the best hope for enhancing and expanding cancer prevention and early detection, developing better cancer treatments, improving quality of life for people living with cancer, addressing survivorship issues and reducing health disparities in cancer with the ultimate goal of eliminating them. The budget is developed in a public process and reflects the best thinking of cancer researchers, patients, clinicians and other constituency groups.

The 92nd Congress showed extraordinary vision and leadership in establishing the structure and charge of the National Cancer Institute and recognizing that research could go from a good bet to a sure bet. President Nixon agreed:

... it is important that this program be identified as one of our highest priorities, and that its potential for relieving human suffering not be compromised by the familiar dangers of bureaucracy and redtape. For this reason, I am asking the Congress to give the Cancer-Cure Program independent budgetary status and to make its Director responsible directly to the President. This effort needs the full weight and support of the Presidency to see to it that it moves toward its goal as expeditiously as possible. (Statement by President Nixon on the National Cancer Act, May 11, 1971)

After three decades of progress, it would be shortsighted for Congress to strip the NCI of its ability to develop a public, strategic research plan and budget that reflects the advice of thought leaders in the cancer community.

The NCI budget represents our national battle plan against cancer. It provides the blueprint for future progress, clearly outlining extraordinary research opportunities and providing a detailed budget showing how taxpayer dollars will be used. In fact, the IOM report recognized the value of these aspects of the NCI budget:

... the requirement that the NCI prepare a bypass budget every year has some positive aspects in that the institute must undertake an annual strategic planning process. This useful exercise should not be dropped if NCI changes its administrative status as recommended above. Rather, all ICs [Institutes and Centers] should be required to develop an annual strategic plan, if they are not already doing so. (IOM Report, Page 89)

The American Cancer Society also urges Congress to protect the other provisions of the National Cancer Act of 1971, including:

- Broad authority of the Director of the National Cancer Institute, a Presidential appointee, to implement the nation's cancer research agenda.
- Establishment of a National Cancer Board, whose 18 scientific and lay members advise the President on major initiatives in the war against cancer.
- Creation of the President's Cancer Panel, a three-member panel of experts, including a consumer, who independently appraise the progress of the national cancer program and submit an annual report to the President.

The National Cancer Act is a critical component in America's war against cancer. The reasons for its enactment over 30 years ago remain true today, and the American Cancer Society urges Congress to protect this vital legislation. Since its enactment, cancer survival rates have increased from 25 percent in the 1970s to more than 60 percent today, and the quality of life for cancer patients has dramatically

improved. With its current structure and charge, NCI has a proven track record of success. The fight against cancer has come too far to turn back the clock.

The American Cancer Society is dedicated to eliminating cancer as a major health problem by saving lives, diminishing suffering and preventing cancer through research, education, advocacy and service. Founded in 1913 and with national headquarters in Atlanta, the Society has 15 regional Divisions and local offices in 3,400 communities, involving millions of volunteers across the United States. For more information anytime, call toll free 1-800-ACS-2345 or visit www.cancer.org.

PREPARED STATEMENT OF THE NATIONAL ACADEMY OF SCIENCE

THE NATIONAL ACADEMY OF SCIENCES CHALLENGES THE "SPECIAL STATUS" OF THE NATIONAL CANCER INSTITUTE

On October 2, a recent National Academy of Sciences (NAS) study on the National Institutes of Health (NIH) will be the subject of bicameral hearings by the House Energy and Commerce Committee, and the Senate Health, Education, Labor and Pensions Committee.

The NAS study, requested by Congress, stressed the need to re-examine the "special status granted the National Cancer Institute (NCI) by the 1971 National Cancer Act." The Act authorized the President to appoint the director of NCI and control its budget, thus bypassing the authority of the overall director of all other 26 National Institutes of Health (NIH) and Centers. As a result of this anomaly, NCI's current \$4.6 billion budget, 17% of the NIH, is beyond control of NIH's director.

The NAS expressed further concerns that NCI's "special status" could cause "an unnecessary rift between (its) goals and mission, and the leadership of NIH." As seriously, NCI's independence has led to its virtual isolation from the public health and general scientific communities.

Beyond the immediate scope of the NAS study, NCI's "special status" has resulted in generally unrecognized problems, which are largely responsible for failure of the National Cancer Program. These include:

- Contrary to NCI's misleading claims and assurances, overall cancer incidence rates, and those of a wide range of non-smoking cancers, have escalated over recent decades, while overall mortality rates have remained high and unchanged. (FACT SHEET I)
- The leadership of NCI, and its major Centers, is marred by pervasive conflicts of interest, and a revolving door with industry, particularly the cancer drug industry. (FACT SHEET II)
- NCI policies are fixated on damage control—screening, diagnosis, and chemoprevention ("secondary prevention"), treatment and related research—with minimal priorities for prevention. (FACT SHEET III)
- Contrary to the 1971 Act's requirements, the NCI has failed to inform the public of a wide range of avoidable causes of cancer. This denial of the public's right to know has even extended to the suppression of such information. (FACT SHEET IV)
- Since 1998, and in close collaboration with the American Cancer Society (ACS), the National Cancer Program is being surreptitiously privatized. (FACT SHEET V)

FACT SHEET I

EXAGGERATED CLAIMS OF PROGRESS IN THE WAR AGAINST CANCER

For over the last two decades, the NCI has made a series of highly publicized and misleading claims of major advances in the "War Against Cancer." These include:

- NCI's 1984 announcement, in its "Cancer Prevention Awareness Program," that cancer mortality would be halved by 2000.
- The same assurance in NCI's 1986 "Cancer Control Objectives" report.
- The 1998 NCI and American Cancer Society (ACS) "Report Card" announcing a recent reversal of an almost 20-year trend of increasing cancer incidence and deaths.
- The February 2003 incredulous "pledge" by NCI director Andrew von Eschenbach, former ACS President-elect, to "eliminate the suffering and death from cancer by 2015."

In a September, 2003 "Annual Report to the Nation on the Status of Cancer, 1975-2000," the NCI, ACS, and the Centers for Disease Control and Prevention claimed that "considerable progress has been made in reducing the burden of can-

cer.” However, this claim is inconsistent with NCI’s own data, as detailed in its SEER Cancer Statistics Review, 1975-2000:

- From 1975-2000, overall cancer incidence rates have increased by 18%; rates for Blacks have increased by 20%.
- From 1975-2000, there has been a dramatic increase in the incidence rates of a wide range of non-smoking cancers. These include: non-Hodgkin’s lymphoma (71%); thyroid (54%); testes (54%); breast cancer (29%); acute myeloid leukemia (15%); and brain (14%). These increases have more than offset the decline in lung cancer rates due to decreased smoking in men.
- From 1975-2000, childhood cancer incidence rates have increased as follows: acute lymphocytic leukemia (59%); brain (48%); kidney (43%); and bone (20%).
- From 1996-2000, the period which the Report emphasizes in its claim of “considerable progress,” there have been major increases in the incidence rates of the following cancers: thyroid (16%); acute myeloid leukemia (11%); childhood brain (10%); and testes (10%).
- From 1975-2000, overall cancer mortality rates have remained high and unchanged, 199/100,000; rates for Blacks have increased by 6%.
- From 1975-2000, mortality rates from prostate cancer, one of the major cancer killers, have decreased by only 1%.
- From 1975-2000, mortality rates have increased by 46% for non-Hodgkin’s lymphoma, and 10% for brain cancer.

These increasing incidence and static overall mortality rates are in striking contrast to the 30-fold escalation of NCI’s budget, from \$220 million in 1971 to the current \$4.6 billion.

FACT SHEET II

CONFLICTS OF INTEREST AND A REVOLVING DOOR WITH INDUSTRY

Benno C. Schmidt, the first chairman of President Nixon’s NCI three-member Executive Cancer Panel, was an investment banker and senior drug company executive, with close ties to oil, steel, and chemical industries. He was followed in the 1980’s by Armand Hammer, the late oil magnate, and Chairman of Occidental Petroleum, one of the nation’s largest manufacturers of industrial chemicals, with major responsibility for the Love Canal disaster. Schmidt and Hammer showed no interest in cancer prevention. Instead, they focused on the highly profitable development and marketing of cancer drugs.

The late Dr. Frank Rauscher, appointed NCI director by President Nixon in 1971 to spearhead his “War on Cancer,” resigned in 1976 to become Senior Vice President of the American Cancer Society (ACS). In 1988, he moved on to become Executive Director of the Thermal Insulation Manufacturers Association, which promotes the use of carcinogenic fiberglass, and fights against its regulation.

A 1993 analysis of conflicts of interest by board members of NCI’s Memorial Sloan-Kettering Comprehensive Cancer Center revealed extensive ties to cancer drug companies, and oil, steel, fiberglass, and tobacco industries, apart from \$4 million institutional holdings in drug companies.

Dr. Samuel Broder, NCI director from 1989 to 1995, frankly admitted the reality in a 1998 *Washington Post* interview. “The NCI has become what amounts to a government pharmaceutical company.” Taxpayers have funded R & D, and expensive clinical trials for over two-thirds of cancer drugs on the market. These drugs are then given, with exclusive rights, to the industry, which sells them at inflated prices. Broder resigned from the NCI to become Chief Scientific Officer of Ivax, and later Chief Medical Officer of Celera Genomics, both are major manufacturers of cancer drugs.

Dr. Vincent DeVita, NCI director from 1980 to 1988, and Dr. John Mendelsohn, President of NCI’s University of Texas MD Anderson Comprehensive Cancer Center, were both consultants and board members of ImClone Systems, Inc., which had been seeking FDA approval of its targeted cancer drug, Erbitux. Neither DeVita nor Mendelsohn disclosed these interests in media interviews promoting targeted cancer drugs.

In October 2002, DeVita published an article, “The War on Cancer,” in *The Cancer Journal*, of which he is co-editor, claiming major progress in cancer drug treatment. However, he failed to disclose his commercial interests in targeted drugs, and in his CancerSource.com web site. This is contrary to the Journal’s disclaimer: “No benefits in any form have been or will be received” by any authors. The Journal has failed to respond to a request to publish evidence of this conflict.

FACT SHEET III

NCI'S IMBALANCED PRIORITIES

The research policies and priorities of the NCI remain dominated by professional mindsets fixated on damage control—screening, diagnosis, chemoprevention, treatment—and treatment-related research. High priority for screening persists in spite of long-standing challenges as to its questionable effectiveness for cancers such as prostate, lung, pre-menopausal breast, and childhood neuroblastoma. Minimal emphasis, and even indifference, remains directed to the prevention of a wide range of avoidable causes of cancer, other than lifestyle factors, smoking, inactivity, and fatty diet, without consideration of carcinogenic contaminants.

In sharp contrast to predominant expenditures on treatment, NCI's prevention budget has been and remains minimal. A published, and unchallenged, analysis of its 1992 budget revealed that less than 2.5% of a \$2 billion budget, in contrast to a claimed 20%, was allocated to research on avoidable carcinogens in air, water, food, the home, and the workplace.

In May 1998 exchanges between Congressman David Obey (D-WI) and former NCI Director Klausner, he claimed that 20 percent of NCI's \$2.5 billion budget was allocated to research on environmental causes of cancer. Following Obey's request for further information, Klausner failed to respond, other than increasing his 20 percent estimate to 40 percent.

NCI's limited comprehension of prevention is revealed in the "Highlights" of its 2001 *Cancer Facts*. The opening sentence states: "Cancer prevention is a major component and current priority—to reduce suffering and death from cancer." This was followed by the claim that 12 percent of NCI's \$3.75 billion budget is allocated to prevention. However, this was defined in exclusionary terms of tobacco and faulty diet, without any reference to environmental and occupational carcinogens.

Not surprisingly, in February 2003 Congressman John Conyers (D-MI), Ranking Member of the House Judiciary Committee, warned that so much cancer carnage is preventable. "Preventable that is, if the NCI gets off the dime and does its job."

In view of NCI's exaggerated and inconsistent claims for its prevention budget, Congresswoman Jan Schakowsky (D-IL), in February, 2003 requested the General Accounting Office (GAO) to investigate NCI's "fight against cancer." Specifically, she requested the following budgetary information:

"1. Funding for Research on Prevention: For programs whose primary objective is focused on prevention, rather than research in which prevention is incidental to other primary objectives.

"2. Funding for Outreach: Providing the public, and also Congress and regulatory agencies, with a scientifically documented comprehensive registry of avoidable causes of cancer, and avoidable exposures to carcinogens in: air, water, the workplace, and consumer products (food, cosmetics and toiletries, and household products); prescription drugs; and diagnostic radiation."

GAO's response is pending.

FACT SHEET IV

FAILURE TO INFORM THE PUBLIC OF AVOIDABLE RISKS OF CANCER

With the exception of smoking and faulty diet, the NCI has failed to inform the public of a wide range of avoidable causes of a wide range of cancers, particularly from involuntary and unknowing exposures to chemical and radioactive industrial carcinogens. These fall into three major categories: (1) environmental contaminants in air, water, soil, the workplace, and food; (2) carcinogenic ingredients in consumer products, particularly pesticides; (3) carcinogenic prescription drugs and high-dose diagnostic medical radiation, particularly pediatric CAT scans.

As critically, NCI has failed to inform Congress and regulatory agencies of such avoidable exposures to industrial and other carcinogens, incriminated in standard rodent tests and in epidemiological studies; such information could have enabled the development of corrective legislative and regulatory action. This silence has also encouraged petrochemical and other industries to continue manufacturing carcinogenic products, and corporate polluters to continue polluting unchallenged.

NCI's silence on cancer prevention is in flagrant violation of the 1971 National Cancer Act's specific charge "to disseminate cancer information to the public." This silence is in further violation of the 1988 Amendments to the National Cancer Program (Title 42, Sec. 285A), which call for "an expanded and intensified research program for the prevention of cancer caused by occupational or environmental exposure to carcinogens."

In May 1998, Congressman David Obey addressed the following question to NCI director Dr. Richard Klausner. "Should NCI develop a registry of avoidable carcinogens and make this information widely available to the public?" Dr. Klausner responded, "Such information is already available from NCI's Cancer Information Service." However, there is no basis whatsoever to support this claim.

NCI's silence on avoidable causes of cancer has even extended to suppression or denial of such information, as illustrated by the following examples.

In 1983, the Department of Health and Human Services directed NCI to investigate the risks of thyroid cancer from I-131 radioactive fallout following atom bomb tests in Nevada in the late 1950's and early 1960's. NCI released its report in 1997, based on data which had been available for over 14 years, predicting up to 210,000 thyroid cancers from radioactive fallout. These cancers, whose incidence has almost doubled since 1973, could have been readily prevented had the NCI warned the public in time, and advised them to take thyroid medication. At a September 1999 hearing by the Senate Subcommittee of the Committee on Government Affairs, former Senator John Glenn (D-OH) charged that the NCI investigation was "plagued by lack of public participation and openness." Senator Tom Harkin (D-IA) charged that NCI's conduct was a "travesty."

As serious is NCI's frank suppression of information. At a 1996 San Francisco "Town Hall Meeting" on breast cancer, chaired by Congresswoman Nancy Pelosi (D-CA), former NCI director Richard Klausner insisted that "low level diagnostic radiation does not demonstrate an increased risk." However, this was contrary to NCI's long-term studies on patients with spinal curvature (scoliosis), which showed that such radiation was responsible for 70 percent excess breast cancer mortality.

FACT SHEET V

PRIVATIZATION OF THE NATIONAL CANCER PROGRAM

In 1998, ACS created and funded the National Dialogue on Cancer (NDC), co-chaired by former President George Bush, and Barbara Bush. Included were a wide range of cancer survivor groups, some 100 representatives of the cancer drug industry, and Shandwick International PR, whose major clients include R.J. Reynolds Tobacco Holdings.

Without informing NDC's participants, and behind closed doors, ACS then spun off a small Legislative Committee. Its explicit objective was to advise Congress on the need to replace the 1971 National Cancer Act with a new National Cancer Control Act, which would shift major control of cancer policy from the NCI to the ACS. The proposed Act would also increase NCI funding from this year's \$4.6 billion to \$14 billion by 2007. The ACS was assisted by Shandwick in drafting the new Act, besides managing the NDC.

However, with the February 2002 appointment of ACS President-Elect von Eschenbach as NCI director, the National Cancer Program has been effectively privatized. As a condition of his appointment, von Eschenbach obtained President Bush's agreement to continue as Vice-Chairman of NDC's Board of Directors, a position he has held since 1998 as a key founder of the Dialogue.

Subsequent to von Eschenbach's appointment, NDC was spun off into a non-profit organization. NDC then hired Edelman, another tobacco PR firm, following a pledge that it would sever its relations with the industry. Edelman still represents the Brown & Williamson Tobacco Company, and The Altria Group, the parent company of Philip Morris, the nation's biggest cigarette maker; Edelman also represents Kraft and other fast food and beverage companies now targeted by anti-obesity litigation. Edelman is also a Board member of the Centers for Disease Control and Prevention Foundation, which fosters relations between the Centers, ACS, and the NCI. Edelman has thus become firmly embedded in national cancer policy making.

In July 2003, it was discovered that Edelman had reneged on its pledge, and was continuing to fight tobacco control programs from its overseas offices. Attempting damage control, Edelman claimed that this was just an oversight. Once more, it agreed to terminate tobacco support programs, and to donate this income to charity.

As disturbing is the growing secretive collaboration between the NCI and the ACS-NDC complex, as revealed in the August 2003 *Cancer Letter*. The latest example is the planned privatization of cancer drug clinical trials, and the creation of a massive tumor tissue bank. This would cost between \$500 million and \$1.2 billion to operate, apart from construction costs in the billions. This initiative would be privatized, ripe with conflicts of interest, exempt from the provisions of the Federal Advisory Committee Act and the Freedom of Information Act, and free from federal technology transfer regulations.

Samuel S. Epstein, M.D., professor emeritus Environmental & Occupational Medicine, University of Illinois at Chicago School of Public Health; Chairman, Cancer Prevention Coalition.

Nicholas A. Ashford, Ph.D., J.D., Professor of Technology and Policy, Massachusetts Institute of Technology.

Quentin D. Young, M.D., Chairman of the Health & Medicine Policy Research Group; past President of the American Public Health Association.

For supportive documentation, see the Cancer Prevention Coalition's February 2003 report, "The Stop Cancer Before It Starts Campaign," endorsed by some 100 leading experts in cancer prevention and public policy, and representatives of consumer and environmental groups. See www.preventcancer.com.

FOLLOW-UP QUESTIONS AND RESPONSES SUBMITTED FOR THE RECORD OF DR. HAROLD VARMUS

QUESTIONS SUBMITTED BY CHAIRMAN W.J. "BILLY" TAUZIN

Question 1. With direct control of only 2 percent of the total NIH budget, in your opinion, does the NIH Director really control the research agenda of the agency?

Response. No. The Director has some influence over programs and budget and can provide leadership, but his/her authority should be increased by enlarging the Director's budget and staff. It would be a mistake, however, to cede most of the authority for program development to the Director; most of it should continue to reside in the Institutes and Centers. The Director should have greater authorities for developing novel, trans-Institute programs.

Question 2. In a recent article you admitted, "By the time I was through being director, I was becoming increasingly jealous that the institute directors were really running the scientific programs." (Washington Fax, September 18, 2003). In your testimony, your top recommendation is to expand the authority of the NIH Director. How will this improve the operation of what you have referred to as a "highly balkanized scientific enterprise?"

Response. It will allow the Director to achieve greater coordination among the Institutes and Centers and to initiate novel, trans-IC research programs—for example, like those described in Dr. Zerhouni's Road Map.

Question 3. The Public Health Service Act already provides the NIH Director with the authority to consolidate or expand institutes and centers at the NIH. In your personal opinion, why do you believe this authority has never been fully utilized?

Response. I would need to reread the Act to understand these authorities fully; I doubt whether an NIH Director could truly consolidate (as opposed to increase collaboration among) Institutes and Centers. Certainly strong pressure from Members of Congress and disease-based advocacy groups would (appropriately) restrain such major actions by the NIH Director without full evaluation by the legislative and executive branches.

Question 4. You have advocated in the past for what some term "drastic" consolidation of the institutes and centers at NIH. Of course, another could term this effort "efficient management and operation" of the most important public health agency. I notice that "cancer" remains one of the disease areas you highlight. Why?

Response. Cancer is highlighted because it is a large group of diseases that affects half of our citizens over their lifetimes; furthermore, about 20% of the NIH budget resides in the NCI, so it seems convenient to leave the NCI intact when attempting a reorganization that creates about five Institutes of roughly equal size. As my testimony makes clear, I do not support special privileges for the NCI (as are currently conferred by the National Cancer Act of 1971).

Question 5. Your written testimony discusses the concept of "clusters" of institute and center research collaboration. What are the emerging scientific opportunities that would benefit from this form of structured research?

Response. Many of these are based on use of sequences for the human and other genomes; on new technologies (for imaging, gene expression, analysis of mutants, and chemistry) that apply to many scientific problems; on clinical research and training programs; and on computational methods that are increasingly used in all areas of science. Many of these opportunities are described in the new NIH Road Map.

QUESTIONS SUBMITTED BY SENATOR DEWINE

Question 1. The reorganization of NIH—both in the Secretary's Roadmap and the NAS study—focuses on the restructuring and reshaping of centers and programs. Please explain how this reorganization will benefit specific areas of research—such as pediatric research? I would appreciate learning of specific examples.

Response. It would improve coordination among Institutes and Centers with common interests, allowing them to pool resources to carry out expensive programs that might otherwise be difficult for any single IC to undertake. For example, research requiring clinical studies (in pediatrics or many other fields) would become more feasible as illustrated in the NIH Road Map.

Question 2. The Pediatric Research Initiative, which my colleagues and I plan to reauthorize next year, is currently housed in the Office of the Director of NIH. Is this the best place for the initiative or is it better suited in another NIH institute?

Response. Because pediatric disease is addressed by virtually every IC, the initiative is best housed in the OD/NIH. However, the OD needs greater authority, funds, and scientific expertise to best administer the initiative. Individual components of the initiative should ultimately be assigned to individual ICs or clusters of ICs for long term support.

Question 3. Increasing pediatric research is a priority of mine. I think the practice of pediatric research should be elevated and encouraged among young doctors and physician researchers. What can be done to enhance the quality and quantity of pediatric research?

Response. The most important avenue is the training of pediatricians in clinical and laboratory research through K08 and K23, K24, and K30 awards.

Question 4. How will the re-organization facilitate furthering translational and basic research into diseases with a genetic basis that have become increasingly important in pediatric care and in determining predictors of diseases with onset in childhood that become major health issues in adults?

Response. The reorganization I have proposed (IC clustering and enhanced authorities for the NIH Director) will make the goals of the NIH Road Map easier to achieve; these include expansion of clinical research and training, as well as computational infrastructure that is essential for genome-based and genetic research and for long-term clinical research (e.g. to identify pediatric findings as harbingers of adult disease).

Question 5. How does the re-organization address the increasing need for complex and state-of-the-art core services that empower and facilitate individual research programs?

Response. The reorganization I have proposed (IC clustering and enhanced authorities for the NIH Director) will make the goals of the NIH Road Map more achievable, and these goals include improved infrastructure, technical tools, and training.

Question 6. The practical benefit of pediatric research is vital to the lives of many American children. How will the NIH reorganization ensure that new discoveries and updates to pediatric research findings will be more quickly disseminated to the field?

Response. The reorganization itself will not ensure greater dissemination of findings. For this, the NIH needs to be committed to expanding its digital public library of scientific reports (e.g. PubMedCentral at the NLM) and to encouraging open access publications.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

The Honorable W. J. "Billy" Tauzin
United States House of Representatives
Washington, DC 20515

Dear Representative Tauzin:

I am responding to your October 2, 2003, letter to Dr. Elias Zerhouni, Director of the National Institutes of Health (NIH), following up on the Joint Senate Health, Education Labor and Pensions and House Energy and Commerce Committees oversight hearing. Enclosed are responses to the questions you forwarded from members of both committees. We look forward to working with both committees during their review of the NIH.

I have also provided copies to Representative John Dingell and Senators Judd Gregg and Edward Kennedy.

Sincerely,

Marc Smolonsky
Associate Director for
Legislative Policy and Analysis

Enclosures

Responses**Representative Tauzin****What in your opinion is the most important thing that Congress can do to help you manage the nation's public biomedical resources in order to maximize the payoff in terms of improved public health?**

Since the initial passage of the Public Health Service Act in 1944, Congress has exercised wise stewardship of legislative authorizations and investments of resources that have made NIH the premiere biomedical research organization in the world today. The health of the Nation is better than ever before, and NIH enters the new world of scientific opportunities in a position of strength that will allow the scientific research community to build on the new foundation of discoveries in genomics, proteomics and molecular pathways. Of course, continuing support of resources will be necessary to maximize the payoff you ask about. Also, maintaining the independence and integrity of the peer review system will be vital to ensuring a productive future for NIH. In short, Congress should take a scientific approach to NIH: identify priorities and match them against opportunities, a formula that has served the Nation well.

With direct control of only 2 percent of the total NIH budget, does the NIH Director really control the research agenda of the agency?

The Director of NIH should not control the research agenda of the 27 Institutes and Centers comprising NIH. But the Director should be able to manage the portfolio of NIH research and help implement trans-NIH research priorities that transcend the abilities of any one Institute or Center. Currently, the NIH Director lacks the authority to effectively manage the research portfolio by shifting or compiling resources in ways that best serve the scientific enterprise. Thought should be given to legislative mechanisms that will enable the Director to respond to new priorities and manage NIH research in the most efficient and effective manner.

With 27 institutes and centers each controlled by its own director and advisory councils, with research budgets separately determined by the individual institute or center and earmarked by Congress, how is overall NIH priority setting conducted?

Priority setting at the NIH occurs at multiple levels, involving many decisions and decision-makers. Each Institute and Center (IC) addresses public health needs; attempts to capitalize on promising scientific opportunities, including funding the most meritorious research proposals; attempts to maintain a diversified portfolio of projects to assure progress in multiple areas; and balances support of current research with investments in training of new investigators and in research equipment and facilities. To set research priorities, each IC seeks the best information and judgment from hundreds of people with diverse experience and expertise, including scientists, advisory committees, public health and health services experts and IC staff,

including the directors.

Though each IC determines how it will deploy its talent and funds, the NIH Director plays an active role in shaping the agency's activities and outlook. The Director is responsible for providing leadership to the ICs and for continually identifying needs and opportunities, especially for efforts that involve multiple ICs. The Director keeps apprized of each Institute's priorities and accomplishments through regular senior staff meetings, discussions with extramural and intramural scientists and briefing sessions with IC directors. Similar to the priority setting process at the IC level, the NIH Director also seeks advice from individuals and advisory bodies, such as the Advisory Committee to the Director, NIH, and the NIH Council of Public Representatives.

NIH sets priorities based on our collective assessment of how best to reduce the burden associated with specific diseases and determining how best to capitalize on scientific opportunities. Research and the NIH priority setting process are inherently dynamic. They develop and adjust to new opportunities. The distribution of funding for any year is but a snapshot of an evolving process. The relationship between scientific opportunities, burden of illness, and disease-specific funding is multifaceted and not always straightforward or linear.

Once an emerging problem is identified, the amount of disease-specific funding is largely determined by the state of the science. If previous basic research or related disease-specific research suggest promising hypotheses to explore, more disease-specific research, development and clinical evaluation may be proposed and, ultimately, funded. The relatively rapid advance of research on HIV/AIDS was built on extensive knowledge of retroviruses and the immune system, and is a striking example of capitalizing on findings from previous research.

If more gaps in knowledge than opportunities are identified, the most productive next step may be to initiate more basic research until new opportunities are developed. Hence we must continually evaluate what is known, what is not known, and what we need to know to solve the problem before us – identifying knowledge gaps and proposing solutions.

The amount of NIH funding identified with a particular disease incompletely indicates the attention paid to that condition. Disease-specific funding fails to reflect the likely benefits of basic research or research coded to other conditions. New scientific opportunities often flow from NIH-sponsored research on broad scientific themes (such as genome projects, development of instrumentation, training in clinical research, or developments in basic science). Historically, support of these themes yielded insights and capacity to stimulate research to address specific diseases.

Assessing the burden associated with a specific disease is also complex. Burden includes more than a count of the number of deaths during a single year. NIH must also consider the incidence, severity, and economic costs of a disease as it judges the burden of a specific disorder, or we would never study, chronic, non-life threatening conditions such as blindness, deafness, or arthritis. For priority setting, the major contribution of measures of burden is to identify trends,

rather than to rank different conditions. Is there an emerging problem? Will it grow in the future? Has there been any progress in preventing a disease or managing a condition?

ICs frequently collaborate on or jointly fund projects of mutual interest, and as such, many other diseases under study at the NIH require the input of more than one IC. The NIH Director, has a unique overview of the range of endeavors across the entire NIH, and serves to influence all the Institutes to focus on matters of importance to them all and to the nation's health. In addition, program offices in the Office of the Director are also responsible for enhancing some of the cross-Institute coordination of research on disease prevention, rare diseases, women's health, AIDS, and behavioral and social sciences. The priority setting process at NIH, both at the level of the NIH Director and the ICs, functions cooperatively in an effort to fulfill NIH's mission to improve human health through research. Additional information on NIH priority setting can be found in the NIH report "Setting Research Priorities at the National Institutes of Health," <http://www.nih.gov/about/researchpriorities.htm>.

The NIH Roadmap represents a new mode of trans-NIH collaboration, and it involved the continued participation of each IC in an effort to reshape the biomedical research agenda. The NIH Roadmap focuses on efforts that the NIH as a whole must address to make the biggest impact on the progress of medical research. Further information about the NIH Roadmap can be found at: <http://nihroadmap.nih.gov>. In addition to exemplifying a trans-NIH planning and implementation process, NIH Roadmap initiatives will be unique in how they will be funded. All ICs will contribute, proportionate to their budgets, funds toward a pool of resources that will support NIH Roadmap initiatives. This will ensure that a steady multi-year and flexible stream of funding is available and also establishes a corporate process for decision-making about trans-NIH priorities. This approach should enable rapid responses to emerging opportunities that do not clearly fit within the mission of a single or small group of ICs.

In your opinion, has science outpaced the current organizational structure of the NIH?

The current organizational structure of the NIH enables the agency to address the complex challenges facing fundamental basic science as well as clinical research. NIH's success in meeting its mission—to uncover new knowledge that leads to improved health of everyone—is a reflection, in part, of its organizational flexibility to catalyze research effectively. The import of keeping pace with science encourages the NIH to continue seeking ways to improve upon its innovative research strategies.

In FY 2003, the NIH developed a series of far-reaching initiatives known collectively as the NIH Roadmap. The NIH Roadmap is designed to deepen our understanding of biology, stimulate interdisciplinary research teams, and reshape clinical research to accelerate medical discovery and improve people's health. It provides a framework of the priorities that the agency as a whole must address in order to optimize its entire research portfolio. The NIH Roadmap identifies the most compelling opportunities in three main areas: new pathways to discovery, research teams of the future, and re-engineering the clinical research enterprise.

One of the challenges in crafting these trans-NIH initiatives was the need for enhanced authorities of the NIH Director—in planning and in resource re-allocation. While there is presently some flexibility in both of these arenas, a clearer mandate for the NIH Director would enable him/her to more rapidly effect changes to the research portfolio to meet emerging scientific needs now and in the future.

The NIH is the largest public health agency within the Department of HHS. Since you became Director of the agency, what steps have you taken to improve working relationships between the NIH and the Food and Drug Administration and the Centers for Disease Control and Prevention?

Long-standing and successful collaborations exist between the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) agency staff and programs. NIH has established close working relations with the directors of both agencies, has visited their agencies and maintains routine communication with each of them. We have discussed our respective missions and the future directions for each agency.

Initial steps in building upon our working relationships have included a review of the existing collaborative activities between NIH and each of these agencies, and designating a NIH liaison to each agency. Activity goals for the liaisons include keeping the directors informed of collaborations; facilitating communication between the agencies; managing the interface, and synergizing collaborations.

The CDC-NIH liaisons were designated in July, 2003. The liaisons hold weekly discussions to review issues of relevance to both agencies. They have facilitated that partnering of staff and programs and are clarifying extramural research policies and practices shared between the agencies. NIH staff members are participating in the working groups for CDC's Futures Initiative and sharing the NIH Roadmap process and outcomes. Recently, Dr. Julie Gerberding, Director of CDC, presented a seminar at NIH to describe CDC's Future's Initiative and her staff members are scheduled to present the status of this initiative to the NIH Prevention Coordinators Committee. Through these and other efforts we are interested in proactively identifying additional areas for collaboration among the agencies and creating a seamless interface, while maintaining the complementary boundaries of each agency. We believe some degree of duplication is appropriate and that coordination would limit unnecessary overlap.

The FDA-NIH staff will also be scheduling regular meetings to discuss a wide range of issues of mutual interest. Agency liaisons will formalize and build upon a wide variety of working relationships that have already been established. For example, discussions are beginning on the harmonization of clinical research regulatory policies and processes, an issue that has been crystalized through the NIH Roadmap process as one of the most important elements of the effort to re-engineer the clinical research enterprise. Both agencies have made a commitment to work together and with other relevant HHS components and Federal departments to try to achieve greater consistency in the rules governing clinical research and, in the process, also enhance the safety of research participants. We have started discussions on the establishment of common

reporting requirements for adverse events, one specific area where we think progress can and should be made. The agencies have already achieved greater harmony in the reporting requirements for gene transfer research, and we intend to look at other areas where greater commonalities in reporting may be achieved. We are also working to advance the use of information technology in clinical research, another major goal of the NIH Roadmap. Discussions are underway to establish common medical vocabularies to facilitate the oversight of clinical trials and advance the analysis of clinical trial data. We have teamed up to develop a national database to enhance analysis and scientific understanding of gene transfer research, an initiative that the Secretary recognized with a 2003 Secretary's Award for Distinguished Service as an outstanding example of interagency collaboration.

Both agencies are also committed to doing our utmost to speed the translation of scientific discoveries to practical applications. We each have distinct but complementary roles to play in this process and the more seamless we can make the process, the faster we will be able to bring beneficial products to the American people. This has also been the goal of our teamwork in the implementation of the Best Pharmaceuticals for Children Act (BPCA).

Following passage of BPCA in 2002, I delegated authority for carrying out much of the NIH responsibilities for implementing the new law to the National Institute of Child Health and Human Development (NICHD). Working closely together, Dr. Mark McClellan, Director of the FDA, and Dr. Duane Alexander, Director of NICHD, have synchronized the two organizations for the common purpose of carrying out the BPCA, despite substantial differences in organizational mission and goals. The two agencies have developed a joint strategic plan for building a collaborative science base and accomplished the following:

- Developed two listings of drugs to be tested in pediatric populations, published in the *Federal Register* in January and August, 2003, with a third list to be published in early 2004;
- Planned and developed a Request for Proposals for the Data Coordinating Center for the clinical trials of pediatric drugs, reviewed the responses, and awarded the contract;
- Collaborated on 12 drug indication Written Requests (a request from the FDA to the company asking them to conduct pediatric drug tests for a currently marketed drug) to be sent to pharmaceutical companies asking them to conduct pediatric drug testing and seek new labeling for their formulations;
- Transformed the three Written Requests turned down by industry into Requests for Contracts and published; two of those drugs will begin clinical trials by early 2004;
- Began to work with the Foundation for the NIH to develop an approach for testing the one on-patent drug that has been referred to the Foundation.

The third theme of your Roadmap, "Re-engineering Clinical Research," will require extensive collaboration with the Food and Drug Administration. At an Energy and Commerce hearing in July, we heard testimony from both the FDA and the National Cancer Institute regarding new interagency agreement to help speed the approval process and post market surveillance of new therapies. At the time, the two agencies were still in

the process of working out the details. Often, in legislative language we either require an agency to "consult" or "coordinate" with another. Are there any legislative barriers that you have noticed during your tenure at NIH that makes this task more difficult with the Food and Drug Administration?

There are no legal barriers to consultation with the FDA, a sister agency within HHS, that have prevented NIH from collaborating with the agency.

This summer, you announced the formation of an NIH Steering Committee – with a rotating membership of ten directors derived from and representing the 27 NIH Institutes and Centers – to give "crisp strategic direction" to the agency and streamline its decision making processes. (The three largest institutes of NIH will have permanent seats National Cancer Institute, National Heart, Lung, and Blood Institute, and the National Institute of Allergy and Infectious Diseases). How many times has the steering committee met and how does it appear to be working this far?

The Steering Committee appears to be working quite well. As with any governance model, it is likely that some fine-tuning will be necessary as we gain more experience but am very pleased with its operation to date. The Steering Committee's purview includes oversight of corporate non-scientific governance issues and, in this regard, it exercises stewardship over corporate resources, provides policy oversight to assure that NIH's mission is being achieved, and assure that mechanisms are in place so that NIH is operating within established standards. In order to streamline decision-making, the Committee is comprised of 10 Institute Directors. As you note, the three largest Institutes have permanent membership, with the remaining members being selected for time-limited terms. The setting of scientific priorities cannot be delegated to a smaller group, however, and will continue to be the purview of the "Committee of the Whole", i.e., all of the Institute and Center Directors.

The Committee meets regularly every two weeks and we have had 6 meetings to date. Examples of issues that have been addressed include assessing the scope of the NIH effort in basic behavioral and social science research and training; providing corporate resource allocations; implementing administrative streamlining initiatives; and defining the organizational structure for implementing and coordinating the Roadmap Initiative. At the present time, we are finalizing the formation of several working groups organized around our major corporate functions - Management and Budget (including Human Resources), Intramural Activities, Extramural Activities, Facilities, and Information Technology. The membership of these Working Groups will be sufficiently representative but small enough to be manageable and will be co-chaired by a member of the Steering Committee and the senior member of my immediate staff for that function. Each Working Group will provide policy oversight and provide recommendations to the Steering Committee for governance issues within its purview. I am confident that this structure, which links these Working Groups with the Steering Committee, will provide the corporate governance and streamlined decision-making that is required of NIH as it operates in today's complex research environment.

Does the Director of NIH provide for the most part the direction in cross-institute research collaboration? Or are co-funded research initiatives between Institutes and Centers at NIH primarily driven by the institute directors themselves?

In the past, the NIH Director has identified areas of research emphasis, but relied on the good will and judgement of the Institute and Center Directors to fund new priorities. The NIH Roadmap signals a major change in how research that crosses Institute and Center boundaries will work in the future. The NIH Director will provide leadership in identifying research priorities and funding them.

The majority of NIH research dollars are doled out to the university community to support investigator driven research. It is my understanding that the Center for Scientific Review assigns each grant application to the institute or center it deems most appropriate to fund the grant. Does this not mean, that by definition, the organizational structure of NIH can predetermine that certain areas of research will always be funded? And how does this process adequately take into account the burden of disease when awarding grants?

Since each of the NIH Institutes and Centers (ICs) receives its separate appropriation, each is required to manage that budget and determine priorities in funding. In practice, no IC, nor any scientific area supported within an IC, will be able to support all the applications assigned to it. While success rates may differ slightly across ICs and for programs within ICs, the success rates remain relatively similar within NIH, at approximately 30%. In allocating resources from year to year, an IC will assure that its diverse portfolio is managed equitably. Through constant monitoring of the burdens of the various diseases and conditions relevant to the IC's mission, advancements in health and research here and abroad, and judicious use of advice from our outside community of stakeholders, ICs anticipate what research needs to be conducted. Overall, the distribution of funding within each IC primarily takes into account, and balances between, the prospects for reducing the burden of disease and the relative promise of different fields of investigation.

The NIH has recently come under fire for some grant awards, that although they may have "scientific merit," they do not easily stand up to what some Members of Congress perceive NIH's primary mission to be: helping to find cures for disease. How do we ensure that NIH prioritizes its grant funding so that life-threatening and debilitating disease research is given greater consideration?

See [Enclosure 2](#) for response.

Dr. Lindberg, Director of the National Library of Medicine recently testified before the Energy and Commerce Committee about NIH initiatives to share information with the public, medical, and research communities. In your opinion, what additional steps need to be taken to expand access to the information and knowledge generated through NIH projects?

One of the major objectives of the overall NIH communications plan is to increase public awareness that the NIH is a credible, reliable source of health and medical information. As Dr. Lindberg testified, the National Library of Medicine (NLM) provides access to the world's largest collection of biomedical literature, a growing array of high quality electronic health information resources for the public developed by NIH ICs, and molecular biology data ranging from DNA sequences to protein structures. One of the strategies for expanding access to these resources involves fostering more collaboration with other stakeholders. For example, a pilot project with the state of North Carolina, called "MedlinePlus Go Local" provides MedlinePlus users with access to local, county, and state health resources in North Carolina, while simultaneously linking North Carolina users with authoritative health information from the NIH. In another prototype, NLM is working with the College of American Physicians to provide materials to health care practitioners so that they can give their patients "information prescriptions," connecting them to get high quality online information on their conditions and diseases. Targeting special populations is another method for reaching underserved communities with critical information from the NIH. The recently released NIHSeniorHealth.gov not only contains information from across NIH of special interest to seniors, but also is presented in a format that is especially usable by senior citizens.

Of particular importance to the research and medical community is the work being done to link molecular biology data with the associated literature in the field. NIH's National Center for Biotechnology Information (NCBI), is committed to ensuring that the outpouring of data from molecular biology laboratories around the world is turned to life-enhancing purposes. Scientists and health professionals can now move seamlessly among databases containing sequence data, citations to the journal literature, and the actual articles themselves, either by connecting to the publisher's website or retrieving them from PubMed Central, the digital archive of life sciences literature maintained by NCBI. PubMed Central now provides free access to over 100,000 articles from over 130 journals. Providing this digital archive of the electronic versions of biomedical journal literature is a major contribution to ensuring expanded access to knowledge generated by NIH-funded research.

Do you think the NIH should play a greater role in facilitating NIH-funded researchers to share their data with other researchers in order to advance the research more expeditiously?

NIH is firmly committed to the sharing of research data resulting from NIH-funded activities and believes that data sharing is essential for translating research results into knowledge, products, and procedures to improve human health. A standard term and condition for all NIH grant awards is to make available to the public the results and accomplishments of the activities it funds. Moreover, certain costs associated with communicating with the public and press about accomplishments under grant-supported projects, such as public relations and publication costs, are allowable charges to NIH grants. Within the last year NIH has taken additional steps to ensure that NIH-funded investigators share their data with other researchers. As of the October 1, 2003, receipt date, all researchers seeking NIH funding of \$500,000 or more in direct costs in any single year are expected to include a plan for data sharing in their application or state why

data sharing is not possible.

NIH's recently announced Roadmap Initiative reinforces the importance of data sharing in the context of re-engineering the clinical research enterprise. NIH is proposing that a standardized data system, the National Electronic Clinical Trials and Research Network (NECTAR) be developed that will facilitate the sharing of data and other clinical resources to advance the discovery process. By adopting common data standards and ensuring interoperability among systems NIH will significantly improve the flow of information within the clinical research enterprise and speed the translation of research results to the bedside.

The promise of genomics research transcends all of the Institutes and Centers at the NIH. Notably, this is one of the themes of in your Roadmap, "New Pathways to Discovery." However, the funding allocations do not seem to directly coincide with this potential. With less than two percent of the overall NIH budget, the National Human Genome Research Institute does not appear to be "leading" the NIH as we move forward with genomics research. With all of the separate silos at NIH, from an outside viewpoint this appears very problematic. What is your insider's view?

While some outside NIH have had concerns about a lack of coordination amounting to the potential for "silos" at NIH, this is not currently an issue in terms of genomic research. Perhaps the most impressive testimony to the effective leadership of the National Human Genome Research Institute (NHGRI) within the NIH regarding genomics research is that genomics has now become a pervasive tool of inquiry at the agency. We are proud and excited that today virtually every Institute and Center (IC) at the NIH is invested in genomics research and that this area of research involves an extensive degree of coordination and collaboration between the ICs.

The Human Genome Project (HGP) was completed on April 14, 2003, marking the dawn of the genomic era. As you know, this success would not have been possible without an outstanding partnership between Federal agencies, international organizations, and the private sector. The success of the HGP partnership was cited in a recent PricewaterhouseCoopers report, "Managing Big Science: A Case Study of the Human Genome Project," which noted: "A major implication for the future lies with the partnership model of R&D that HGP's organization revealed. As a result of the HGP partnership, the first chapter of the human genome revolution is coming to a successful end, and next steps are underway." With the completion of the human sequence and all of the original goals of the HGP, the NHGRI led the development for the NIH of "A Vision for the Future of Genomics Research," published in the journal *Nature* in April 2003. This bold new vision, the outcome of almost two years of intense discussions with more than 600 scientists and members of the public, is structured around three major areas of focus: Genomics to Biology, Genomics to Health, and Genomics to Society. Many other NIH senior staff participated in the process, and this vision stresses the necessity of collaboration across scientific disciplines to meet the grand challenges it presents.

The NIH Roadmap for Medical Research is a prime example of how the NIH is building on the track record of the HGP to translate basic biomedical research findings into new tools to assist in

biomedical research discoveries. As an example, the NHGRI will take a lead role, in coordination with several other institutes, in developing a "small molecule," or chemical genomics resource. This initiative will offer public sector researchers access to high throughput screens for small organic molecules that can serve as chemical probes to study cellular pathways in depth. It will provide new ways to explore the functions of major cellular components in health and disease. In addition, this resource should speed the development of new drugs and agents to treat both common and rare diseases, by providing early stage compounds for private sector licensing that encompass a broad range of novel targets and activities.

Three key technological advances drive the NIH's foray into chemical genomics. First, the successful completion of the HGP has provided an enormous cache of biological information and identified a wealth of potential new targets for small molecules. Second, developments in combinatorial chemistry have given academic researchers potential access to compounds previously available only to researchers in private sector pharmaceutical and biotechnology companies. Third, advances in robotic technology and informatics now allow investigators to screen hundreds of thousands of compounds in a single day, orders of magnitude more than was possible only a decade ago.

For this effort to provide maximal benefits, the library of small molecules must contain a sufficient number of compounds to screen for a large number of new activities and applications. To build such a library, a network of six national centers will establish a common collection of approximately 500,000 chemically diverse small molecules, of both known and unknown activities. Over time, this collection will be expanded and modified to provide a working set of compounds that will target larger domains of "biological space," the total set of biomolecular surface domains that are capable of interacting with a small molecule. Investigators who have developed assays suitable for high throughput screening will apply to the screening centers. After peer review, suitable assays will be screened against the 500,000 compounds, with the "hits" subjected to a first pass of medicinal chemistry optimization to generate useful compounds. We anticipate that this new resource will be of interest to many NIH funded scientists.

Thus, while the NHGRI may have less than two percent of the overall NIH budget, it plays an important leadership role in many crosscutting NIH initiatives. The NHGRI is known for developing broad public-private partnerships that leverage the resources of many NIH institutes and private companies to provide needed research tools to the entire research community. The advent of the NIH RoadMap places the NHGRI in an even more central leadership position, with the opportunity to play a vital role in the future of biomedical research that will ultimately transform medicine and the health of the American people.

Many researchers perceive the National Institutes of Health to be primarily focused on "hypothesis" based research. The Human Genome Project could however be classified as an anomaly to this general rule. By that, I am referring to the fact that the Human Genome Project did not propose to specifically answer a direct scientific question, but

rather was established to create a tool through which we will be able to ask more questions. Given the potential of genomics research, this seems every bit as important as the traditional hypothesis based research. What are some of the impediments in place at the NIH that restrict research opportunities in this area?

While it is true that most of the research at NIH is "hypothesis" driven, over the past decade the NIH has demonstrated increasing willingness to support the development of large scale research tools that will assist a broad array of researchers. The human genome sequence is the most obvious example of this type of non-hypothesis driven project, often referred to as "discovery research."

A special committee of the U.S. National Academy of Sciences (NAS) first articulated the main goals of the Human Genome Project (HGP) in 1988. As of April 14, 2003, the principal goals laid out by that committee had all been achieved, more than two years ahead of schedule and under budget, including the essential completion of a high-quality version of the human sequence. Other goals included the creation of physical and genetic maps of the human genome, which provided a necessary lower resolution view of the genome and were of major value to research in their own right. The HGP also accomplished the mapping and sequencing of five model organisms, including the mouse. This information has greatly expanded our ability to interpret the human genome, rather like the Rosetta stone allowed the decryption of ancient languages. The NAS study also recommended that, "access to all sequence and materials generated by these publicly funded projects should and even must be made freely available [to all]." The NIH has adhered to that standard throughout the 13 years of the project and continues to do so.

The HGP would not have occurred without the visionary leadership and determination of the Congress. At the outset, many in the scientific community had not completely embraced the model of discovery research, nor did they think that the HGP could be completed in a timely fashion or for an affordable cost. But key members of Congress felt that it was essential that the United States government play a leading role in this project, and they correctly predicted that the project could be completed without diverting resources from other important science. The Congress' recent doubling of the NIH budget allowed a dramatic increase in the pace of the HGP.

Discovery research continues to grow at NIH, with the major barrier being limited resources. As an example, NIH is now planning the development of a new chemical genomics resource. This initiative will enable a small molecule approach that will offer public sector researchers access to high throughput screens for small organic molecules that can be used as chemical probes to study cellular pathways in greater depth. This resource will provide new ways to explore the functions of major cellular components in health and disease. In addition, this initiative should speed the development of new drugs and agents to detect and treat both common and rare diseases by providing early stage compounds that encompass a broad range of novel targets and activities. This chemical genomics approach will be yet another discovery tool provided to the biomedical research community by the NIH for use in efforts to understand, and ultimately treat, disease more effectively.

Another non-hypothesis driven project that the NHGRI has led, and that a number of NIH institutes have supported, is the International Haplotype Map (HapMap). With completion of the HGP, a critical new priority is to study the role that genetic variation plays in health and disease. There are at least 10 million DNA sites where people commonly differ in their DNA sequences, and some of these variations affect individuals' risk for disease or their response to drugs. To study genetic variation across the genome more effectively, a team of international partners has launched the International HapMap project.

The NIH leads a six-country collaborative effort to develop the HapMap, a catalog of common regions of linkage disequilibrium (haplotype blocks) and the single nucleotide polymorphisms (SNPs) that tag them. The goal of the International HapMap Project is to determine the common patterns of DNA sequence variation in the human genome and to make this information freely available in the public domain. The international consortium is developing a map of these patterns across the genome by determining the genotypes of one million or more sequence variants in DNA samples from populations with ancestry from parts of Africa, Asia, and Europe. When complete, the HapMap will enable the discovery of sequence variants that affect common disease, the development of diagnostic tools, and the ability to choose targets for therapeutic intervention.

These are but a few examples of the many non-hypothesis driven research projects that NIH is supporting. While several institutes have such efforts underway, the NHGRI will continue to play a leadership role for this type of large-scale discovery research, which does not exemplify hypothesis driven research, but rather enables it.

The recently unveiled NIH RoadMap includes several additional initiatives that fall squarely in this category, including the chemical genomics project described above, a new effort to identify cellular pathways and networks, an initiative on structural biology, and a focus on nanomedicine. These efforts often involve large scale production components, which present new challenges for resource identification and effective management. But the success of the HGP has provided a strong sense of momentum for discovery research, and previous resistance in the scientific community has greatly diminished.

The Small Business Administration (SBA) provides start-up funding to small businesses in a variety of ways. One program is the Small Business Innovation Research program (SBIR). Under the SBIR program, a specific percentage of all federal R&D grant monies are reserved for small business applicants through the NIH, in addition to other Federal Agencies. Are you aware that after nearly 20 years, and without notice, the SBA has reinterpreted the way the SBIR program is administered through the NIH resulting in the exclusion of biotech companies with 51% venture capital backing from participating in the SBIR program?

NIH and other SBIR-participating agencies are obligated to follow the program regulations and guidance outlined in the Small Business Administration (SBA) SBIR Policy Directive and clarified by the SBA.

As a result of having received many questions from SBIR applicants concerning eligibility, in October 2002, the Small Business Administration (SBA) provided to all 10 SBIR-participating agencies clarification of the statutory requirements for a small business concern to receive SBIR awards. In particular, the clarification highlighted the requirement that a small business concern be at least 51% owned and controlled by one or more individuals who are citizens of, or permanent resident aliens in, the United States; and not have more than 500 employees, including its affiliates. The clarification addressed eligibility as it pertained to wholly-owned subsidiaries.

In July 2003, the SBA submitted a proposed Rule Change to OMB that would permit an SBIR firm to be owned and controlled by another small business concern, including venture capital (VC)- backed small businesses, provided that the parent company is still 51% owned and controlled by individual(s) and has less than 500 aggregate employees. However, VCs that are owned by pension plans, pension funds or corporate investors are ineligible to own and control a small business participating in the SBIR program. The SBA's Office of Hearing and Appeals has ruled that these types of VCs are "institutional investors" and not "individuals."

VC companies unquestionably play a vital role in the world of small technology companies. They are sought-after and appreciated partners in commercializing innovations under Phase III of the SBIR program.

Representative Dingell

Is there a problem with the operations of National Institutes of Health (NIH) that the outsourcing program there is intended to address? If so, please be specific in describing the problem. If not, then why is the outsourcing program moving forward?

Outsourcing is a required program directed by the OMB Circular A-76.

Whatever the intended purpose of outsourcing is, were any alternatives considered and, if so, why were they not tried?

In addition to outsourcing, NIH is improving operations and gaining efficiencies through internal reorganization initiatives.

Does the outsourcing program take into account the individual or collective performance of the personnel involved? Why would you want to out source individuals or units that are outstanding performers?

NIH has considered a variety of factors in choosing which programs to study under OMB Circular A-76 to include current performance indicators as well as cost.

It is my view that NIH consists and a large number of enormously talented and dedicated individuals, who work very hard to improve public health. Outsourcing is understandably very upsetting to many of them. Can you assess for me the impact on morale of the outsourcing program?

We understand many people are concerned and we address these concerns as best we can through continuous communication. The NIH Director has held several Town Hall meetings with all employees.

NIH is a highly selective organization that attracts top notch personnel. As a matter of maintaining the caliber of people and the quality of their work, do you think you will do better with outsourcing?

The principle behind competition is to get the best value for the taxpayers while meeting the requirements of the job. Indeed NIH has top notch personnel as demonstrated by the results of the two large studies that were conducted in FY2003, where the in-house most efficient organization won the competition.

Have the definitions of "commercial" and "inherently governmental" activity as these terms are used in OMB Circular A-76 changed during this administration? If so, how and why?

The revision to the Circular in 2003 provides new classification rules for FAIR Act inventories.

Agencies must submit inventories in electronic format for both commercial and inherently governmental activities, and publish these inventories for public review and protest. The definition for an inherently governmental activity was also further clarified.

How long will it take for NIH to complete the job of determining which jobs are "commercial" and which are "inherently governmental"?

NIH is currently reviewing the initial inventory designations using the refined definitions. The next inventory which is due to DHHS in Jun 2004 should reflect any adjustments made.

How frequently will the process of putting jobs up for competition occur? Will there be an annual rite of passage for personnel who are doing an outstanding job?

A-76 studies will be ongoing for the foreseeable future. Once an activity has been reviewed, it will be re-reviewed in three to five years, depending on the initial review and terms from the winning service provider.

With respect to the areas of grant review (pre-award) and grant administration (post-award), which jobs, if any, will be outsourced?

In the recently completed competitive sourcing study of extramural administrative support services, NIH's in-house team won the ability to perform both pre and post-award administrative support with federal employees.

Does NIH have a numerical or other goal for the amount of outsourcing it hopes to accomplish? If so, what is that goal and how was it established?

The DHHS has a plan to study 100 percent of non-exempt commercial competitive positions over 10 years.

Is outsourcing mandatory or discretionary with you? In other words, are you free to limit or eliminate the NIH outsourcing program if you determine that doing so is in the best interest of the organization and the public it serves?

This is a government-wide program. The goal of the new A-76 guidelines is to make competitive sourcing an ongoing aspect of our business operations.

What method do you have in place to keep the Congress informed of activities taking place at NIH pursuant to the outsourcing program? I request a comprehensive status report on the NIH's outsourcing program that provides a list of jobs that have been determined to be "inherently governmental" jobs that are "commercial." Please provide a list of the jobs for which these determinations have not yet been made and an estimate of when the categorization of these jobs will take place. Please update the list on a quarterly basis. With respect to those jobs that you have determined to be "commercial" have they been

put up for competition and, if so, what was the result?

OMB Circular A-76 requires publishing an annual inventory that includes jobs that have been determined to be both commercial and inherently governmental. The 2002 DHHS/NIH Inventory is posted on the OMB website as well as the NIH A-76 website: <http://a-76.nih.gov/>. The 2003 inventory is currently pending OMB approval. In FY2002, NIH conducted 36 small studies and won 34 of them keeping 171 positions in-house; NIH also directly converted 302 positions to contract. In FY2003, NIH conducted 2 large studies and won both of them keeping approximately 1000 positions in-house.

Can you estimate the total cost to NIH of the outsourcing program? Please provide details used to make the estimate. Is the cost of the outsourcing program listed anywhere in the NIH or Department of Health and Human Service budget justifications for this or any fiscal year?

We estimated the cost in FY2003 to be \$3.5 million for contractor advisory and assistance service, and \$3.5 million for NIH staff services. These costs were absorbed within the FY2003 budget approved by Congress.

Have stakeholders of NIH (patients, grantees, the general public, etc.) been involved with your outsourcing program? If so, how? If not, why not?

At this point we have not involved them in any of these outside organizations. We have received numerous e-mails and letters and have considered these points in our decision making.

Representative Brown

The National Academy of Science (NAS) committee's report recommended interdisciplinary research and support for trans-NIH research across Institutes, Centers, and Divisions as part of the NIH Roadmap for the Future of Biomedical Research. NIH has been endeavoring to make such efforts by bringing together interdisciplinary research as can be seen in the trans-NIH Working Group to Develop a Strategic Research Agenda on Health Disparities. In 2001 the Institute of Medicine (IOM) issued a report, "Exploring the Biological Basis of Human Health: Does Sex Matter?" which recommended the need for a focus on fundamental biological sex differences and the significant impact understanding these differences will have on the prevention, diagnosis, and treatment of disease in men and women.

In light of the IOM report, will the NIH establish a working group addressing research on sex differences throughout the NIH similar to the trans-NIH Working Group on health disparities?

The NIH already has a working group to address research on sex differences, and has gone beyond just a working group to issue a Request for Applications (RFA) from which there are already funded Specialized Centers of Research (SCORs) on Sex and Gender Factors, as well as Interdisciplinary Centers of Research on Women's Health and Sex and Gender Factors. NIH is pleased that trans-NIH collaboration has already advanced to implement new research centers, support the career development of researchers in this area, and to expand research on this topic.

Specifically, the mechanism to address sex and gender issues exists through the Office of Research on Women's Health (ORWH) in the Office of the Director, which convenes a trans-NIH Coordinating Committee on Research on Women's Health (CCRWH), composed of the Directors, or their designees, of the national research institutes and chaired by the Director of the ORWH. In FY 1999, the ORWH initiated a program that has funded 12 Centers to Build Interdisciplinary Research Careers in Women's Health, with a focus on sex and gender factors, and was expanded to fund 12 additional Centers in FY 2001. In FY 2002, this trans-NIH collaboration headed by the ORWH developed and funded eleven Specialized Centers of Research (SCORs) on Sex and Gender Factors (SCORs) that have a specific focus on sex and gender factors from basic research to clinical interdisciplinary research and applications to advance scientific discoveries out of the laboratory into the clinical setting. In fact, the IOM report, "Exploring the Biological Basis of Human Health: Does Sex Matter?," was one of the documents utilized in preparing the RFA that resulted in these new centers of research on sex and gender.

In FY2003 the ORWH also began another trans-NIH working group, The NIH Intramural Program on Research on Women's Health that serves similarly to the CCRWH as the focal point for NIH intramural research addressing sex and gender comparisons within the Intramural Research Programs (IRP) at the NIH. This is the first effort of this type, and is already bringing benefits of networking among scientists to further the attention to sex and gender issues across the NIH intramural research community.

Representative Waxman**What are Dr. Zerhouni's concerns about the transformation plan for the Commissioned Corps? Please include a copy of the letter from Dr. Zerhouni to Sec. Thompson on the Commissioned Corps.**

I am concerned about the new requirement under the transformation plan for full deployment capability of all commissioned officers by 2005 because of the negative effect this may have on the pursuit of research at NIH. I am also concerned about pay parity in the Corps, as well as the NIH's inability to rehire officers into the Civil Service without a break in service after they retire from the Corps with between 20 to 30 years.

What is the status of implementation of the Autoimmune Diseases Research Plan? Please describe the progress the agency is making toward reaching its goals.

The NIH Autoimmune Diseases Coordinating Committee (ADCC) Research Plan was submitted to Congress in December 2002, in accordance with the requirements under Title XIX of Public Law 106-310, the Children's Health Act. The ADCC Research Plan is a comprehensive, long-term agenda for autoimmune diseases research in epidemiology and burden of disease; etiology and pathogenesis; diagnosis, treatment, and prevention; and training, education, and information dissemination. The ADCC Research Plan highlights new programs and research areas in which future progress will benefit all autoimmune diseases and facilitate the translation of new knowledge into more effective treatments and prevention strategies.

Since submitting its report to Congress last year, the NIH ADCC has initiated a comprehensive inventory of initiatives and activities in autoimmune diseases research and associated components of the plan that are addressed by these efforts. This inventory will identify research supported by the many NIH Institutes and Centers who support research on autoimmune diseases, including the National Institute of Allergy and Infectious Diseases, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Eye Institute, the National Institute of Neurological Disorders and Stroke, and the National Heart, Lung, and Blood Institute, to name just a few. In addition, it is anticipated that this process will be extended to ADCC members outside the NIH, including the Centers for Disease Control and Prevention, the Food and Drug Administration, the Health Resources and Services Administration, and the Department of Veterans Affairs as well as private organizations. The inventory will identify areas of the plan that are being addressed and those areas that may need additional effort. When this inventory is completed, the NIH ADCC will be able to provide a more detailed report on the status of the ADCC Research Plan.

The Institute of Medicine (IOM) recommended interdisciplinary research and support for trans-NIH research across Institutes, Centers and Divisions. Two years ago, the IOM released "Exploring the Biological Basis of Human Health: Does Sex Matter?" The report recommended that research focus on the fundamental differences between male and female

biology. It indicated that an understanding of these differences could have a significant impact on the prevention, diagnosis, and treatment of disease in men and women. Will the trans-NIH initiatives described in the roadmap address the need identified by the IOM committee for targeted, interdisciplinary, hypothesis-driven research on sex differences? Would a Working Group on Sex Differences contribute to this effort?

The NIH already has a working group to address research on sex differences, and has gone beyond just a working group to issue a RFA from which there are already funded Specialized Centers of Research (SCORs) on Sex and Gender Factors, as well as Interdisciplinary Centers of Research on Women's Health and Sex and Gender Factors. NIH is pleased that trans-NIH collaboration has already advanced to implement new research centers, support the career development of researchers in this area, and to expand research on this topic.

Specifically, the mechanism to address sex and gender issues exists through the Office of Research on Women's Health (ORWH) in the Office of the Director, which convenes a trans-NIH Coordinating Committee on Research on Women's Health (CCRWH), composed of the Directors, or their designees, of the national research institutes and chaired by the Director of the ORWH. In FY 1999, the ORWH initiated a program that has funded 12 Centers to Build Interdisciplinary Research Careers in Women's Health, with a focus on sex and gender factors, and was expanded to fund 12 additional Centers in FY 2001. In FY 2002, this trans-NIH collaboration headed by the ORWH developed and funded eleven Specialized Centers of Research (SCORs) on Sex and Gender Factors (SCORs) that have a specific focus on sex and gender factors from basic research to clinical interdisciplinary research and applications to advance scientific discoveries out of the laboratory into the clinical setting. In fact, the IOM report, "Exploring the Biological Basis of Human Health: Does Sex Matter?", was one of the documents utilized in preparing the Request for Applications (RFA) that resulted in these new centers of research on sex and gender.

In FY2003 the ORWH also began another trans-NIH working group, The NIH Intramural Program on Research on Women's Health that serves similarly to the CCRWH as the focal point for NIH intramural research addressing sex and gender comparisons within the Intramural Research Programs (IRP) at the NIH. This is the first effort of this type, and is already bringing benefits of networking among scientists to further the attention to sex and gender issues across the NIH intramural research community.

The components of the NIH Roadmap are part of a well-thought out national portfolio of research to meet the health demands of the 21st century; these initiatives are not disease-specific, nor do they focus on gender-specific areas of research. The purpose of the NIH Roadmap is to deepen our understanding of biology, stimulate interdisciplinary research teams, and reshape clinical research to accelerate medical discovery and improve people's health. The NIH Roadmap provides a framework of the priorities that the agency as a whole must address in order to optimize its entire research portfolio. It presents a vision for a more efficient and productive system of medical research. It identifies the most compelling opportunities in three main areas: new pathways to discovery, research teams of the future, and re-engineering the clinical research

enterprise.

There were several questions raised at the hearing about research conducted by NIH on various sexuality-related topics. Can you explain how sexuality-related research fits into NIH's mission?

See Enclosure 2 for response.

Human sexuality is a natural biological/behavioral function. How many of the ICs support sexuality-related research and to what extent?

The missions of several Institutes of NIH lead to their support of sex-related research. Approximately half of the NIH Institutes currently support sexuality-related research. The type of research supported ranges from basic research on the development and physiology of sexual functioning to research on public health outreach to prevent potentially adverse outcomes of sexual behavior such as sexually transmitted diseases (STDs).

More specifically, examples of areas receiving NIH support include:

- Normal psychosexual development
- Biological factors contributing to psychosexual differentiation and management regimens when differentiation is disrupted
- Animal studies examining brain mechanisms with the aim of reducing the adverse effects associated primarily of medication-induced sexual dysfunction
- Sexual functioning and quality of life among cancer survivors
- Sex hormone changes associated with weight-loss
- Preventing sexual abuse, especially among vulnerable populations, e.g. children and the elderly
- Clinical trials of interventions designed to delay initiation of sexual behavior among young men and women
- Decision-making regarding child-bearing and contraceptive use
- The health and medical consequences that can result from the interaction between drugs and sexual behavior, including the acquisition and transmission of infectious pathogens such as HIV/AIDS and STDs.

Representative Stearns

Given the current heated controversy and misinformation being disseminated regarding silicone breast implants, what initiatives does NIH have planned to provide comprehensive information to consumers and medical professionals and enable patients to make informed choices?

The National Institutes of Health (NIH) is making available to the medical and public communities information related to NIH funded research on silicone implants. A summary of NIH research has been posted at <http://www4.od.nih.gov/orwh/implants.pdf>, and will continue to be updated as new information occurs. Hard copies of this information are also available when requested, and have been widely distributed.

In addition, Institutes and Centers (ICs) are also individually making their research results available. For example, the National Cancer Institute (NCI) of the NIH develops materials for the press, medical and scientific communities, and consumers based upon specific research papers on silicone breast implants in order to provide the resulting scientific information that patients and their physicians can utilize to make informed decisions. This information is available both in hard copy as well as from the web, and is distributed pro-actively as needed and requested, including to other federal agencies.

Examples of such web sites include:

<http://www.cancer.gov/newscenter/siliconefactsheet>

<http://www.cancer.gov/newscenter/silicone-mortality>

<http://www.cancer.gov/newscenter/silicone-othercancers>

<http://www.cancer.gov/newscenter/siliconebreast>

<http://www.cancer.gov/newscenter/siliconeqa>

Representative DeGette

Do you think that current law and regulations are adequately protecting human subjects?

Federal regulations for the protection of human subjects in research conducted or supported by the Department of Health and Human Services (HHS) include those issued by HHS and the Food and Drug Administration (FDA). The HHS regulations [45 CFR part 46] apply to research involving human subjects conducted by the HHS or funded in whole or in part by the HHS. The FDA regulations [21 CFR parts 50 and 56] apply to research involving products regulated by the FDA. Federal support is not necessary for the FDA regulations to be applicable. When research involving products regulated by the FDA is funded, supported or conducted by FDA and/or HHS, both the HHS and FDA regulations apply.

While existing human subjects protections are adequate, enhancements could be made that would further augment an institution's understanding of and compliance with the regulations. It has also been suggested that the current HHS regulations be extended to apply to all human subjects who participate in research, including those that are not covered under current regulations. Another enhancement would be to harmonize existing regulations

In addition, the NIH has taken several steps to help ensure the protection of human subjects in NIH-funded studies. For example, in order to inform and optimize protections for human participation in research, the NIH implemented a requirement for submission of clinical trial monitoring plans, funded short-term training on ethical issues in research, particularly those involving human participants, and supports research addressing the ethical challenges of involving human participants in research.

I am concerned that unclear and unregulated adverse event reporting has hidden the number of deaths due to clinical research. We know of at least three deaths in the past few years, but there may be more. What do you think should be done about this?

We share your concern with the unclear definition and reporting requirements for adverse events. To the extent that such confusion detracts from human subject protection, we are committed to bringing clarity to this issue. An important part of the NIH Roadmap focuses on harmonization of regulatory requirements and removing barriers in human subject research. We have engaged other Federal agencies, e.g, FDA and the Office for Human Research Protections (OHRP), in this endeavor that will require the partnership of all the stakeholders in order to be successful.

What assurances do you think the public needs to repair confidence in clinical research ethics?

The public needs to have assurances that there is a system of protection for human subject research where the first and foremost principle is to do no harm. We must enhance public trust in the clinical research enterprise and it is for this very reason that we have included public trust as an important component of the NIH Roadmap. We recognize that this is complex since the

system of protections has multiple components including the researchers, Institutional Review Boards (IRBs), Data Safety and Monitoring Boards (DSMBs), the regulatory entities, FDA and OHRP, as well as the sponsors, NIH. Each of these components has important roles and responsibilities that must be well integrated. The goal is to strive toward transparency and providing participants with information to make informed decisions about participation.

What kind of guidance does NIH give on Conflicts of Interest?

As the major sponsor of biomedical research, the NIH has sought to work in partnership with research institutions and university groups to harmonize approaches to financial conflict of interests (COI) issues, and to address these in a way that does not hinder scientific innovation and discovery. A notice was published in the NIH Guide on June 5, 2000, on "Financial Conflicts of Interest and Research Objectivity: Issues for Investigators and Institutional Review Boards" that outlines the concerns and shared strategies used by IRAS to consider investigators' COOS. This was followed by a forum held at the NIH Natchez Building on August 15 and 16, 2000, to discuss sharing of information on the conduct of clinical trials between IRAS and compliance offices that deal with institutional policies and procedures on investigators' COOS.

The NIH held a meeting on September 30, 2002, that invited wide-ranging discussion from diverse viewpoints to inform Federal officials involved in developing, implementing, and monitoring policies to disclose, assess, and manage conflicts of interest. The meeting underscored the need for a proper balance between federal regulation and self-regulation, with the primary onus on research institutions to develop guidelines and mechanisms to ensure and enhance research integrity. The research community understands that serious action on their part in demonstrating compliance can help to mitigate increasing public pressure for government regulation.

In March 2003, DHHS published draft guidance on financial conflict of interests at the following site: <http://ohrp.osophs.dhhs.gov/humansubjects/finreltn/newdraft.htm>. The NIH participated in the development of this draft guidance and plans to participate in the development of final guidance based on public comments.

You have stated in your "Roadmap" documents that making better use of citizen volunteers, or research subjects, is an integral part of accelerating the pace of medical discoveries. How does NIH plan to achieve this goal?

The promise of 21st century medicine brings both opportunities and challenges to making further progress in understanding, preventing, treating, and potentially curing human diseases. One such opportunity and challenge involves engaging a workforce that is well trained and appropriately qualified, and in which the public can place full confidence. As part of its Roadmap initiative, the NIH is planning to develop a program called the National Clinical Research Associates, to engage in clinical research physicians on the front lines.

The National Clinical Research Associates would encompass a cadre of up to 50,000 community-based practitioners. Trained and certified in clinical research, these providers would

participate in conducting community-based studies, assist in patient recruitment, administer experimental treatments, and be the first to integrate new research findings into routine healthcare delivery. Specific training programs, including incentives to attract and retain clinicians, would be developed to encourage community-based health care providers to learn about clinical research and ethical research practices, and to provide them with the necessary skill sets and tools to generate high quality data.

Several preliminary studies are needed to realize the vision of the Associates. These include a study that will examine the feasibility of involving community practitioners in clinical research and explore possible mechanisms for such involvement. Building on the results of this study, recommendations on ways to reduce barriers to building a model workforce for conducting clinical research are expected to evolve. Based on the results of the feasibility and pilot studies, NIH intends to create regional Centers that will train Associates in an integrated approach in "real-world" settings.

Other efforts will focus on the establishment of national core competencies and best practices needed to conduct high-quality clinical research and to translate research into clinical practice. These efforts will apply to researchers working in community or academic settings. Competencies would include relevant board certification, knowledge of conflict-of-interest regulations and documentation of training in protecting participants in clinical trials. Best practices for research teams might include methods for managing study data, as well as developing cost and staffing estimates. It is expected that all of these efforts will improve patient recruitment, participation and trust in clinical trials.

What kinds of research will you be funding with these "Innovator Awards" for high-risk research?

This new type of award is designed to encourage investigators to embark upon unexplored avenues of research that may carry a significant risk of failure, but also possess the potential for ground-breaking discoveries. The awards are not directed toward a particular area of research; rather, they will be made to investigators whose imagination and creativity permit them to see new ways to approach and perhaps solve fundamental problems in biomedicine. It is anticipated that 10 such awards will be made in 2004, and that the program will be monitored carefully and evaluated, and grown slowly in the coming several years.

What steps do you intend to take to protect subjects in this research?

Protecting individuals who volunteer to participate in research is of great importance to the NIH. Both intramural and extramural investigators follow the Department of Health and Human Services (HHS) and FDA regulations, where applicable. These protections include protocol review and approval by an IRB before the research begins, the informed consent of the individual, and ongoing research oversight by the IRB. The NIH also requires institutions receiving NIH funds to train key personnel involved in human subjects research.

For example, IRAS are required to assess whether risks to subjects are minimized and reasonable with respect to any benefits that may result from the research. The informed consent process must address, among other things, research risks, and, where a probability of heightened risk exists, whether compensation or medical treatments will be made available if injury occurs.

Federal laws and regulations for the protection of human subjects in research also require IRAS to monitor and oversee the research while it is being conducted. IRAS are responsible for assuring that risks are minimized to the extent possible. If, for example, an IRB identifies a risk that needs to be managed, it may require the investigator to incorporate into the research activity safeguards to reduce the probability of harm or limit its severity or duration. It is expected that the level of monitoring will be commensurate with the risks and the size and complexity of the clinical trial. NIH requires that oversight and monitoring under Phase III clinical trials should be in the form of Data Safety and Monitoring Boards. A DSMB also may be appropriate for Phase I and II clinical trials if the studies have multiple clinical sites, are blinded (masked), or employ particularly high-risk or vulnerable populations. The DSMB monitoring function is above and beyond that traditionally provided by IRAS; however, the IRB must be cognizant of the procedures used by DSMBs, and the DSMBs must provide periodic reports to investigators for transmittal to the local IRB.

Are the schools currently protecting human subjects adequately?

NIH is one of the few Federal agencies that require reporting of investigators' financial conflicts of interest as a condition of grant award. The Federal regulations governing grants, which were promulgated in 1995, are found in 42 CFR Part 50 Subpart F, "Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought," and establish standards to ensure there is no reasonable expectation that the design, conduct, or reporting of research funded under PHS grants or cooperative agreements will be biased by any conflicting financial interest of an investigator; this requirement is a term and condition of all NIH grant awards. A recently issued draft GAO report found that every institution in its sample of 171 reported that they have financial conflict of interest policies in place that are consistent with Federal requirements. GAO's finding is reflective of NIH's 2002 study that found that its 300 top funded grantees all had financial conflict of interest policies. GAO also found that the majority of institutions in its sample have financial conflict of interest policies that apply to all Federally funded research, not just research funded by NIH. These two studies give NIH reasonable assurance that its grant recipients are managing, reducing, or eliminating identified conflicts of interests of their investigators in accordance with Federal requirements.

In the initial review of research applications involving human subjects, reviewers are required to evaluate the adequacy of the protection of research subjects. If concerns are raised in this regard, these must be addressed to the satisfaction of the NIH prior to awards. NIH requires oversight and monitoring of all human intervention studies to ensure the safety of participants and the validity and integrity of the data. Before funds are awarded by NIH for competing applications involving human subjects, investigators must provide a description of education completed in the protection of human subjects for each individual identified as "key personnel" in the proposed

research. Key personnel include all individuals responsible for the design or conduct of the study. This requirement was implemented to strengthen the Federal commitment to and oversight of the protection of human research participants.

Has your office collaborated with the Universities and Medical Centers about the need to better protect human subjects?

The Office of Extramural Research, NIH, initiated a series of proactive compliance site visits in FY 2000 to assess institutional understanding of Federal policies and regulations, to minimize or eliminate noncompliance, and to nurture a productive partnership between the NIH and its grantee institutions. The major topics for these visits include financial conflict of interests, monitoring and oversight of clinical trials, roles and responsibilities of investigators, etc. The success of the initial site visits resulted in continuance of the initiative in FY2001 and FY2002.

The site visits were not designed to address specific problems. They are not viewed as investigations or audits. Rather, they are conducted in a proactive mode, intended to facilitate dialogue regarding NIH policies in a non-crisis, non-adversarial manner. Through this educational outreach effort, we hope to enhance administrative oversight of sponsored research. We encourage representatives of the grantee institutions to join NIH as both partners and stewards in the conduct of biomedical research. NIH completed more than 30 site visits since FY 2000.

This Office also conducts annual regional seminars involving universities and medical centers to provide technical assistance and updates on policies and regulations. A recurring topic for these seminars is human subject research. These are useful forums in which to educate investigators and institutional officials on the need to protect human subjects in research.

I understand that academic medical centers value their independence, but what do you think needs to be changed on a national level to improve how clinical research is conducted?

Major changes are needed on a national level to improve the efficiency and effectiveness of clinical research in order to take advantage of new knowledge and technologies in biology and genetics and to translate these findings into new drugs, drug combinations, and diagnostic and prognostic tests.

The nation's need for a strong, clinical research enterprise cannot be emphasized strongly enough. More effective approaches are needed to speed inquiry from bench to bedside, in order to translate basic discoveries into treatments – and just as critically, systematic methods are needed to more efficiently move clinical insights from bedside to bench, in the effort to better guide discovery and enhance understanding of the origins of disease.

To more quickly translate the benefits of research to the public, the NIH is rethinking the technical and human infrastructure requirements for a more effective clinical research enterprise.

This is being accomplished, in part, through the "NIH Roadmap," which is a coordinated plan to guide NIH research into the coming decade and beyond. The Roadmap objectives are to accelerate the pace of discoveries in the life sciences, to speed the translation from laboratory to practical applications, and to develop novel approaches to treatment and prevention that are orders of magnitude more effective than current approaches. After an extensive national consultation process to identify the major roadblocks and propose potential solutions, the NIH is engaged in a broad-based re-engineering effort, including partnerships with sister agencies, academic health centers, community-based professionals, industry, and patient groups. The goal is to establish a systematic and standardized national clinical research infrastructure which includes: 1) national facilities to aid bench-to-bedside research, 2) integrated clinical research networks, 3) standardized interoperable information systems, and 4) a systematically trained workforce.

Could you explain why the National Cancer Institute provided zero dollars of funding for stem cell research in FY03?

In FY 2002, the National Cancer Institute (NCI) spent \$95,076,000 on stem cell research. This includes research on adult stem cells in both humans and animals, as well as human umbilical cord blood and animal embryonic stem cells. In FY 2003, NCI estimates they will spend \$95,500,000 on stem cell research.

I believe that Dr. Zerhouni said during the hearing that the British stem cell bank currently has no viable stem cell lines, but I have heard from other sources that they have at least one. Could you clarify that point?

As of October 23, a spokesperson for the Medical Research Council in Britain reported that "there are no stem cell lines in the UK Stem Cell Bank, but several applications to deposit stem cell lines in the bank are currently under consideration by the Stem Cell Steering Committee. The identity of the applicants needs to remain confidential until a decision has been made. The Steering Committee meets at the end of November and may be able to provide you (The NIH Stem Cell Task Force) with more information in December."

Representative Engel

I am aware of growing concern about the level of research funding for Charcot-Marie-Tooth Disorders (CMTD). Given the number of people affected by CMTD I believe the National Institutes of Health (NIH) could be doing more to find treatments or a cure. The FY 2004 funding level of \$4,866,000 is simply inadequate, and CMTD research should be at least doubled. What is NIH considering allocating for CMTD research in 2005 and into the future? Do you feel that the NIH could be doing more to fight CMTD?

Charcot-Marie Tooth disease (CMTD), also known as hereditary motor and sensory neuropathy, comprises a group of disorders that affect peripheral nerves. Typical features include foot and lower leg weakness, weakness and atrophy in the hands, and resulting difficulty with fine motor skills. Mutations in genes that produce proteins involved in the structure and function of either

the peripheral nerve axon or the myelin sheath have been implicated in a number of forms of CMTD. An understanding of the genetic basis of these disorders may facilitate the development of effective therapies for CMTD.

The National Institute of Neurological Disorders and Stroke (NINDS) supports the majority of research at NIH on CMTD, including research that led to the discovery of the genetic mutations underlying certain forms of CMTD. The NINDS has significantly increased its support of CMTD research in recent years. From FY 2001 to FY 2002, NINDS funding for CMTD increased from \$2,953,000 to \$4,422,000, and it is encouraging to note that NINDS funded two new projects on CMTD in FY 2003. The funding level you cite for FY 2004 (\$4,866,000) is an estimate only. The amount of money NIH spends on CMTD research for FY 2005 and beyond will depend on the nature and quality of grant applications received in this area, and the outcome of the peer review process. The NIH is committed to funding the highest quality research on a wide range of neurological disorders, and will continue to fund CMTD applications of the highest merit, and respond to scientific opportunities for significant advances in this area.

More broadly, NIH also funds research on other forms of neuropathy, including other peripheral neuropathies. Much of this research may be relevant to understanding and treating CMTD.

Will the NIH utilize increased funding to participate with the North American Collaborating Center (NACC) with regard to the international classification of functioning, disability and health (ICF) to create a national registry of Charcot-Marie-Tooth patients utilizing the ICD-10 diagnosis, which will, considerably, enhance information retrievable from clinical records and assist patients in their efforts to obtain disability compensation?

The North American Collaborating Center (NACC) is located at the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC) in the U.S. Department of Health and Human Services. The NACC coordinates activities related to the International Classification of Diseases and Health Problems (ICD) and the International Classification of Functioning, Disability, and Health (ICF). The International Classification of Diseases (ICD) is designed to be used in the collection, classification, and presentation of mortality statistics. The tenth revision (ICD-10) does not list a unique code for Charcot-Marie-Tooth disorder (CMTD); CMTD is classified under the heading "Hereditary Motor and Sensory Neuropathy." The International Classification of Functioning, Disability, and Health (ICF) was developed to try to classify the consequences of disease. The NIH was represented at the October 9, 2003, meeting of the Interagency Subcommittee on Medical Rehabilitation of the Interagency Committee on Disability Research, where the ICF was discussed. At this meeting, it was concluded that the classification system, in its current form, is not appropriate to be used for clinical measurements, that the ICF is not ready for clinical use, and that it should be used in research settings only on a limited basis. Based on this conclusion, NIH would not expect to fund any research using the ICF. The NIH is, however, looking at ways to address issues surrounding quality of life and disability measures. Recent NIH activities, including a workshop entitled "Physical Disabilities Through the Lifespan," held on July 21-22, 2003, raised a number of issues related to longitudinal research on individuals with disabilities, which NIH plans to explore further.

Representative Gordon

Various documents have reported that NIH is deficient in funding for bladder, liver and digestive disease. For example, the NIDDK Bladder Research Progress Review document reported that bladder research is "deficient both in total and in proportionate funding when compared to other organs and major disease areas that affect the human condition...." These concerns have been raised in a bi-partisan way in floor statements, appropriations reports, and even in current legislation.

Do you share these concerns? If so, are you willing to work with Congress to address these deficiencies, including efforts to enhance the leadership and research portfolio at these Institutes if necessary?

These interactions often help spur NIH efforts to invigorate, inviting earmarks. Research on bladder, liver, and digestive diseases is led by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), with research efforts also pursued by many other NIH components.

We agree that the Bladder Research Progress Review Group provided important scientific recommendations. This strategic planning process guided recent decisions to renew large-scale clinical trials networks for the urologic disorders, interstitial cystitis (IC) and chronic prostatitis; to launch initiatives to enhance basic research on IC and the bladder; and to plan for a new clinical initiative for the pediatric urologic disease, vesicoureteral reflux. The guidance gained from this planning effort--which was initiated by the NIDDK in recognition of the need to strengthen the NIH urology research portfolio--is continuing to assist the NIH in expanding our activity in bladder disease research.

Significantly strengthening NIH support of liver disease research is the newly-established NIDDK Liver Disease Research Branch. This branch will focus and accelerate basic and clinical research in liver disease, and provide leadership for research coordination with other Federal agencies, including the Centers for Disease Control and Prevention (CDC) and the Veterans Affairs Administration. With leadership from the branch, the newly-formed Liver Disease Subcommittee of the statutory Digestive Diseases Interagency Coordinating Committee (DDICC) is preparing a strategic Action Plan for Liver Disease Research, which we anticipate will enhance liver disease research across the NIH. These enhancements to basic and clinical liver disease research are building upon a number of ongoing activities, including NIH-supported clinical trials on prevention and treatment of hepatitis C in adults and children, a consortium to study the cause(s) and optimal treatment of biliary atresia, a clinical network to study non-alcoholic steatohepatitis (NASH), a multi-center collaborative database on adult living donor liver transplantation, and a hepatotoxicity network to study drug-induced liver damage, as well as an important new initiative supporting both basic and clinical research on the pathogenesis, natural history, therapy, and prevention of hepatitis C.

Digestive diseases research will benefit from a new NIH-supported genetics consortium for

inflammatory bowel disease (IBD) and a planned NIH Consensus Development Conference to assess the state-of-the science and develop recommendations for future research directions in celiac disease. The NIH is continuing its support for Digestive Diseases Research Centers focused on specific diseases, including IBD, whose return on this investment are important insights into the fundamental biology and immunobiology of the intestine that are crucial to understanding causes and developing treatments for many of these diseases. The NIH also coordinates and encourages government-wide research in digestive diseases through the activities of the Digestive Diseases Interagency Coordinating Committee. The Committee recently highlighted new research opportunities in IBD, including those outlined by the strategic research plan of the Crohn's and Colitis Foundation of America. This plan will assist the NIH in developing future initiatives in IBD research.

These are just a few highlights of the steps the NIH is taking to move research forward on bladder, liver, and digestive diseases. The NIH will continue to work with the Congress to further strengthen these and other parts of the national biomedical research enterprise.

Do you think there needs to be an NIH restructuring to address such under-represented "orphan" conditions?

NIH restructuring is not needed to address bladder, liver and digestive diseases, given the proactive steps NIDDK and the NIH, including the Office of Rare Diseases, are already undertaking. Specifically, regarding bladder research, the NIDDK has recruited a distinguished urologist within its Division of Kidney, Urologic, and Hematologic Diseases to serve as a Senior Advisor to the NIDDK Director. This individual has already played a key role in strategic planning efforts, not only for bladder diseases, but also other urologic disorders. Moreover, the Institute is being guided by the strategic plan developed by an external group of expert advisors, the Bladder Progress Review Group, to help propel its program development, with several new initiatives already launched.

In the area of liver research, the NIDDK has created a new Liver Diseases Research Branch within its Division of Digestive Diseases and Nutrition; has appointed a new Branch Chief following a national search; and is currently recruiting for an additional liver disease program officer to complement staff assigned to this new Branch. The Liver Disease Branch Chief is currently leading a liver disease strategic planning process under the auspices of the statutory Digestive Diseases Interagency Coordinating Committee. Multiple NIH institutes and centers with an interest in liver diseases are participating actively in this planning process led by NIDDK.

Also within the area of liver disease research, the NIDDK, with co-funding from the NIH Office of Rare Diseases, is supporting the Biliary Atresia Research Consortium, which is a consortium of nine pediatric liver disease centers and a central data coordinating center. The central aims of the Consortium are to develop and test hypotheses on the cause of biliary atresia and to help define the best means of diagnosis and management of this disease.

For research on digestive diseases other than liver disease, the Director of the NIDDK's Division of Digestive Diseases and Nutrition works closely with the Institute's Director in planning research initiatives in conjunction with constituency groups such as the American Gastroenterological Association, the Crohn's and Colitis Foundation of America, and the International Foundation for Functional Gastrointestinal Disorders. The Division Director also chairs the Digestive Diseases Interagency Coordinating Committee, which has representatives from other NIH institutes and centers, and which has undertaken significant trans-NIH initiatives in digestive diseases such as celiac disease and functional gastrointestinal disorders. Following completion of the liver diseases strategic plan noted previously, the Division Director is expected to lead a planning process addressing non-liver digestive diseases. In addition, in FY 2003, the NIH Office of Rare Diseases, the NIDDK, and other NIH components cosponsored an initiative for a Rare Diseases Clinical Research Network, as well as a scientific conference on the conduct of clinical trials in Crohn's Disease. Also, the Office of Rare Diseases is in the process of convening a trans-NIH rare diseases working group which should provide an additional means of collaboration in rare/orphan diseases research regarding bladder, liver, and digestive diseases.

Thus, there are excellent strategic planning and coordination mechanisms in place to promote vigorous research on the bladder, and on the liver and other digestive diseases, and no restructuring is required.

How do you plan on involving/integrating those Institutes such as NIDDK not represented on the Advisory panel to provide input and have their issues and concerns raised regarding intra-agency efforts?

Each and every NIH Institute and Center (IC) has been involved in planning and implementation of the NIH Roadmap. IC leadership and staff participated in the consultation process referenced in your question. There was no Advisory panel that provided input regarding intra-agency input to the NIH Roadmap. The NIH Roadmap has been discussed with a wide range of constituencies—scientific, health care professionals, and the general public—through presentations and discussions at meetings, including the IC National Advisory Councils and Boards, the NIH Council of Public Representatives, and the Advisory Committee to the Director, NIH.

How have you involved the patient and health community in developing your road map? How will you include the patient communities in future planning, especially in intra-institute and intra-agency funding? How will you ensure that basic research is translated to clinical use to improve the care and treatment of patients?

The NIH has and continues to seek input from a wide range of constituencies—health care professionals, the general public, policymakers, and scientists—through meetings of the IC National Advisory Councils and Boards (that include representatives of the public and health

care professionals), the NIH Council of Public Representatives, and the Advisory Committee to the Director, NIH.

The NIH Roadmap presents a vision for a more efficient and productive system of medical research to improve human health. For example, efforts to re-engineer the clinical research enterprise are intended to promote better integration of existing clinical research networks, encourage the development of technologies to improve the assessment of clinical outcomes, harmonize regulatory processes, and enhance training for clinical researchers. A major goal is to more fully involve and empower the public in the research process.

Through the NIH Roadmap, we hope to remove some of the biggest roadblocks that are keeping research findings from reaching the public as swiftly as possible. These efforts include basic biological research, such as determining protein structure, to activities that will ultimately affect the front lines of clinical research and care, e.g., regional translational research centers and development of technologies that improve assessment of clinical outcomes.

Representative Solis

We all know that the National Institutes of Health (NIH) is the nation's leading research and technology institute responsible for a majority of the medical discoveries in this country. The benefit of this research extends to those suffering from a variety of illnesses, including diabetes, HIV/AIDS, asthma and others. When we look closely at these diseases, however, we see that minorities are disproportionately affected. I know that the NIH has created a National Center to promote minority health and address racial and ethnic health disparities. As the NIH structure is being re-organized, I hope that we will remember the importance of this center to the health of millions of Americans.

I would like to ask if you could give your opinion about the effectiveness of this center, and if you have any thoughts about any structural changes you would make to enhance this center? Do you believe this center is able to contribute to and utilize the research from all the other NIH institutes and centers? Also, how does this center disseminate its research and information to the public?

The National Center for Minority Health and Health Disparities (NCMHD) was established by *The Minority Health and Health Disparities Research and Education Act of 2000* (Public Law 106-525) to promote the health of minorities and other underserved populations and to lead the National Institutes of Health (NIH) in its effort to reduce and ultimately eliminate health disparities. To accomplish these goals, the NCMHD (1) conducts and supports basic, clinical, social sciences, and behavioral research; (2) promotes research infrastructure and training; (3) fosters emerging programs; (4) disseminates information to underserved populations; and (5) reaches out to minority and other health disparity communities.

The NCMHD has been effective because, in its two years of existence, it has made significant accomplishments by meeting all of the mandates contained in the authorizing legislation (establishing its congressionally mandated programs, strategic plan and annual report). The NCMHD is continuing to meet all of its goals outlined in the strategic plan.

Through its mandated programs and collaborations throughout the country, the NCMHD is committed to building a solid and diverse national biomedical research enterprise of individuals and institutions dedicated to eliminating health disparities and ensuring the health of all Americans. The Center's top priority is to expand these programs and develop new ones to meet the ever increasing health needs of minority and medically underserved populations in the United States. Since its inception, the NCMHD has established the *Centers of Excellence Program*, the *Research Endowment Program* and the *Loan Repayment Program*.

In collaboration with the Director of the NIH, the Directors of the other NIH Institutes and Centers (ICs) and the National Advisory Council on Minority Health and Health Disparities, the NCMHD has developed two very important reports to the Congress that were mandated by Public Law 106-525 - the *NIH Strategic Research Plan and Budget to Reduce and Ultimately Eliminate Health Disparities, Fiscal Years 2002-2006* and the *NIH Fiscal Year 2001 Annual*

Report on Health Disparities Research. Both reports were submitted to Congress.

The Institute of Medicine has suggested that NIH consolidate certain centers to promote efficiency. At this time, I do not envision such a consolidation involving the NCMHD. The structure of NCMHD has been established. Critical to enhancing the NCMHD's effectiveness are staff needed to fill key positions within the Center. Efforts are underway to recruit and hire an Associate Director of Scientific Programs and a Director of the Office of Community Based Research and Outreach.

In addition to its mandated programs, the NCMHD funds a broad range of collaborations with the other NIH ICs and other Federal agencies. Over years 2002 and 2003 cumulatively, NCMHD co-funded, with other NIH ICs, and other agencies, more than 450 awards totaling \$128.9 million for projects related to minority health or health disparities research and training. The *NIH Strategic Research Plan and Budget to Reduce and Ultimately Eliminate Health Disparities*, spearheaded by the NCMHD, serves as the NIH blueprint to conduct and support research aimed at reducing and eliminating health disparities. The *NIH Annual Report on Health Disparities* will inform the planning of future health disparities research projects across the NIH.

NCMHD has an Office of Outreach and Public Liaison in its Division of Scientific Planning & Policy Analysis. This office (1) disseminates information on scientific and policy developments related to the mission of the Center; (2) plans and implements a comprehensive information and communications program; (3) coordinates with the NIH ICs on minority health disparities research and research on other health disparities for the purpose of serving as a clearinghouse and focal point for disseminating information on the goals and advances in these programs; (4) maintains liaison with the NIH Office of Communications and Public Liaison; and (5) provides oversight for the maintenance of the Center's website. NCMHD also has an Office of Community-Based Research and Outreach, in its Division of Research and Training Activities, for which it is in the process of hiring a new Director.

NCMHD strives to ensure access to information for the communities it serves. Therefore, the Center focuses primarily on disseminating information through its grass-roots networks, its website and by participating in various conferences and local meetings. As a critical component of the Center's work, outreach has been built into one of its most extensive research programs, the Centers of Excellence in Partnerships for Community Outreach, Research on Health Disparities and Training (Project EXPORT), which was originally launched in fiscal year 2002. In fiscal year 2002, NCMHD established 21 Project EXPORT Centers and funded 6 planning grants at biomedical and behavioral research institutions located in three regions and Puerto Rico. Twelve (12) Centers in the South, 3 in the Northeast, and 5 in the West. In fiscal year 2003 the Center established 23 additional Centers and funded 10 new planning grants at biomedical and behavioral research institutions in six regions of the country and Puerto Rico. Three (3) Project EXPORT Centers were established in the Northeast, 9 in the South, 5 in the Southwest, 2 Centers were established in the West, 1 in the Frontier States, and 2 in the Midwest regions of the country and 1 in Puerto Rico. With its 60 programs, Project EXPORT is central to the NCMHD's investment strategy for addressing disparities in health status. In addition to

broadening NIH's commitment to research and research training, Project EXPORT will strengthen community involvement in understanding the causes/origin of health disparities and available treatments.

The effects of the environment on our health is becoming increasingly apparent in our everyday life – whether we are talking diseases like asthma or diabetes. Our goal to better our health and understand the environmental contributions must span across all our research efforts. Could you describe how the National Institute for Environmental Health Sciences will work with other institutes and how it could better serve our public? I would like to see the research and recommendations from this Institute become a part of our everyday life so that we can work on *preventing* diseases. How can this Institute further that goal?

Environmental contributions to disease cut across every organ system and disease represented at the National Institutes of Health. Genes, environment, and behavior are all important components of our health status, but environmental causes have proven the most amenable to change and to prevention. Even when talking about obesity, a condition which has devastating effects on our health and for which behavioral changes have been so difficult for people to make, it is the environment which offers the best chance for improvement. In the case of obesity, the man-made components of our environment (lack of sidewalks, pedestrian-unfriendly environments) are a major underlying cause and the one that best lends itself to change.

Although many ICs may support projects related to the environment and health issues, the lead for environmental health sciences resides with the National Institute of Environmental Health Sciences (NIEHS). Thus coordination is needed and must extend beyond the NIH. NIEHS has standing coordinating committees among numerous federal entities, including the Environmental Protection Agency, the Food and Drug Administration, and the Centers for Disease Control and Prevention. At the NIH, NIEHS representatives sit on a number of coordinating committees that deal with environmental factors on health and disease. The National Children's Study, for which the NICHD has the lead, was one area in which the NIEHS' contribution was sought. The NINDS also makes use of the expertise at NIEHS relative to environmental influences in neurodegeneration, and NIEHS is represented on the NIH Parkinson's Disease Coordinating Committee. At the same time, when NIEHS seeks new approaches to finding environmental contributions of diseases such as Parkinson's and breast cancer, it solicits the ideas, input, and collaborative funding of its sister ICs. In fact, the NIEHS has been particularly creative in finding ways to leverage resources. For example, when the NCI developed a cohort to investigate environmental causes of cancer among farmers, the NIEHS joined in so that the benefit of the existing NCI cohort could be expanded to include non-cancer endpoints such as birth defects, infertility, diabetes, macular degeneration, Parkinson's Disease, and other conditions. Similarly, when the NIEHS sought to establish its Collaborative Centers for

Parkinson's Disease Environmental Research, it capitalized, in part, upon the existing Udall Centers supported by NINDS.

In these and many other ways, the NIEHS is doing an outstanding job of furthering our knowledge of environmental contributions to disease. As the results of these studies become known, they will be incorporated into public health and regulatory policy so that prevention of disease, rather than treatment, will be more common.

Representative Towns

It is my understanding that Dr. Bernard Schwetz is no longer Director of the Department of Health and Human Services's (HHS) Office of Research Protections. As you know, this office was formerly at NIH and was elevated to the office of the secretary of HHS because of intense congressional concern about patient protections in human subject research. This position plays a pivotal role in assuring that intramural and extramural research conducted by NIH or supported by NIH grants. Can you tell me: 1) the progress of the search process to replace Dr. Schwetz and what kind of active recruitment is being done to assure that the person who heads this office has a commitment to patient protections; and 2) until a replacement is found, what assurances can you offer about patient protection and NIH's ongoing commitment to assuring the integrity of the IRB process?

On January 31, 2003, Secretary Thompson appointed Dr. Bernard Schwetz to be Acting Director of the Office for Human Research Protections (OHRP), following the departure of Dr. Greg Koski, who stepped down as OHRP's first director on November 30, 2002. Dr. Schwetz continues to serve as the Acting Director of OHRP and to lead the department's efforts to ensure the responsible conduct of research involving human subjects. As you know, in June 2000, the Department's human research protection functions were transferred from the National Institutes of Health (NIH) to the newly established OHRP in the Office of Public Health and Science (OPHS) within the Office of the Secretary. OPHS is under the direction of the Assistant Secretary for Health.

Regarding your first question about what kind of active recruitment process for an OHRP Director is in place, a vacancy announcement for that position was published/posted on September 16, 2003 and closed on October 15, 2003. Efforts are under way to select a highly qualified applicant.

Regarding your second question about what assurances the Department can offer related to patient protection, ensuring that human subjects who volunteer to participate in research are adequately protected continues to be a high priority for HHS. OHRP is and will continue to be HHS's focal point for leading, coordinating and implementing the Department's responsibilities to protect human research subjects.

The processes in place at the NIH for the oversight of human subjects protections will continue unabated. There have been periods of time in the past that OHRP has not had a permanent Director, and there has never been any interruption in our carrying out the responsibilities that we take very seriously. Our peer reviewers continue to exercise stringent review of all aspects of human subjects research proposed in applications for support, and if concerns are identified, funding cannot be forthcoming without resolution of those concerns. This process continues independent of OHRP. Institutions understand their responsibilities regarding their Institutional Review Boards' oversight of human subject research and provide assurances to that effect in every application. Again, no award can be made without that documentation.

Representative Green

Two years ago, NCI researchers found that women with breast implants were twice as likely to die from brain cancer, three times as likely to die from lung diseases, and four times as likely to die from suicide, compared to other plastic surgery patients. European studies have now found similar risks of suicide and lung disease for women with breast implants. What studies does NIH plan to conduct to examine these findings further?

Analyses are currently underway to assess relationships with connective tissue disorders. NCI researchers plan to continue to follow the cohort to update the mortality data over time, which may shed light on the observed excess risks of lung and brain cancers, and of suicide. The FDA is also studying some of the women for implant ruptures.

Two researchers at the National Institute of Environmental Health Sciences (NIEHS) have conducted research indicating that women with silicone implants have "undesirable immune responses" that warrant further study. What research does NIH plan to do to learn more about the impact of these immune problems?

The NIH will consider carefully the results of the research currently underway at the NIEHS in order to help determine further directions for research in this area.

In addition, the NIH will continue to welcome investigator initiated projects that propose to further delve into immune responses to silicone implants and other related scientific questions.

Dr. William Katzin of Case Western Reserve Medical School has conducted research indicating that women with silicone gel breast implants have silicone in their lymph nodes. Of course, this means the silicone can migrate throughout their bodies. What does NIH plan to do to examine the health effects of leaking silicone implants?

Again, the NIH will welcome investigator initiated research proposals that can help to elucidate some of the continuing areas of concern related to silicone implants.

Senator DeWine

The reorganization of NIH--both in the Secretary's Roadmap and the NAS study--focuses on the restructuring and reshaping of centers and programs. Please explain how this reorganization will benefit specific areas of research---such as pediatric research? I would appreciate learning of specific examples.

The components of the NIH Roadmap are part of a well-thought out national portfolio of research to meet the health demands of the 21st century; these initiatives are not disease-specific, nor do they focus on gender-specific areas of research. The purpose of the NIH Roadmap is to deepen our understanding of biology, stimulate interdisciplinary research teams, and reshape clinical research to accelerate medical discovery and improve people's health. The NIH Roadmap provides a framework of the priorities that the agency as a whole must address in order to optimize its entire research portfolio. It presents a vision for a more efficient and productive system of medical research. It identifies the most compelling opportunities in three main areas: new pathways to discovery, research teams of the future, and re-engineering the clinical research enterprise.

The Pediatric Research Initiative, which my colleagues and I plan to reauthorize next year, is currently housed in the Office of the Director of NIH. Is this the best place for the initiative or is it better suited in another NIH institute?

Public Law No. 106-310, The Children's Health Act of 2000, was signed into law on October 17, 2000. Title X of the Act directs the Secretary of the Department of Health and Human Services to establish a Pediatric Research Initiative (PRI) in the Office of the Director of the National Institutes of Health (NIH). As established, among the purposes of the PRI are to increase support for pediatric biomedical research within the NIH, and to enhance collaborative efforts among NIH Institutes and Centers (ICs).

The Act also requires an annual report to Congress and the public on the extent of the total funds that NIH obligates to pediatric research generally, as well as the support allocated through the PRI. These reports, the most recent of which (for Fiscal Year 2002) was sent to Congress in July 2003, demonstrate the breadth of interest and support at NIH for pediatric research. In 2002, 21 of the 27 ICs at NIH reported providing research support for some aspect of pediatric research. In addition, in 2002, 11 of those ICs received additional funding from the NIH Director's Discretionary Fund to support research activities through the PRI. Clearly, no one IC is the locus for all pediatric research activities.

After receiving the mandate from Congress to establish the PRI, the Director of NIH formed the NIH Inter-Institute Committee on Pediatric Research to encourage the development of new research activities, including collaboration among the ICs, for new pediatric research conducted and supported by NIH. Committee members are the Directors of the six Institutes with the largest pediatric research portfolios: the National Institute of Child Health and Human Development, the National Cancer Institute, the National Heart, Lung and Blood Institute, the

National Institute of Allergy and Infectious Diseases, the National Institute of Diabetes and Digestive and Kidney Diseases, and the National Institute of Mental Health. Reflecting the NICHD's longstanding mission of improving and promoting children's health and development, the Director of NIH requested that the Director, NICHD, chair the Inter-Institute Committee.

This Committee has been functioning well since its inception. When additional funds were available for the PRI, the Committee selected outstanding proposals to receive funding, through a competitive process and with additional scientific and outside input. The Committee, under the direction of the NICHD, annually requests information on the research activities identified by each of the ICs as part of the PRI, for NIH's report to Congress. Because pediatric research is so widely distributed across NIH, this collaborative approach appears to be the most efficient at this time.

Increasing pediatric research is a priority of mine. I think the practice of pediatric research should be elevated and encouraged among young doctors and physician researchers. What can be done to enhance the quality and quantity of pediatric research?

NICHD has taken the lead in encouraging young clinicians and researchers to enter and stay in the field of pediatric research through a variety of mechanisms:

The objective of one of our longer-running programs, the Child Health Research Career Development Award Program, is to establish centers of excellence in research in pediatric departments throughout the country. The vital need for this career development program, which is aimed at increasing the number of pediatrician-scientists who devote the majority of their professional efforts to disease-oriented and prevention-oriented investigation, became apparent in the late 1980s. Funding began in 1990 with the support of six centers; nineteen centers were funded by 1992. Recently, a third three-year application cycle was completed. Successful applicants, comprising research-oriented pediatric departments, demonstrated longstanding track records or great potential for the development of young investigators.

The Institutional National Research Services Awards (T32), designed to address the current shortage of training opportunities, are intended to further develop successful academic pediatric scientists who will remain committed to research in pediatrics. This program provides an intensively monitored research experience for two to three years. The goal is to prepare the trainee to transition successfully to other junior faculty development opportunities. The trainee positions are intended for pediatricians who are in their third year of residency. While receiving funding, trainees spend full-time conducting research in the areas of basic pediatric science or clinical research. The first Request for Applications for this new program was issued in 2001, and in FY 2002, NICHD funded 24 institutional training grants.

A third program, the Pediatric Physician Scientist Program Award (K12), is a postdoctoral career development training program sponsored by the Association of Medical Schools Pediatric Department Chairs in conjunction with NICHD under a cooperative agreement. The program was designed to bring basic science into specialty areas of pediatrics by placing pediatric fellows

in mentored research environments as they begin training in basic, translational, or health policy research. For each pediatrician selected for a fellowship, a minimum of two years of basic research training in highly selected research laboratory settings is funded by the program; fellows whose progress is exemplary compete for a third year of support. Trainees have an excellent record of remaining in academic pediatrics, and a significant percentage of them are Principal Investigators on grants from NIH.

Authorized by the Children's Health Act of 2000, the Pediatric Research Loan Repayment Program was established in 2001 to provide additional encouragement to qualified health professionals to conduct pediatric research for at least two years in exchange for a substantial repayment of their educational loans. Each recipient of an award receives up to \$35,000 a year toward paying off an educational loan, depending on his or her total debt. In addition, these awards include another 39 percent of an award to offset the recipient's tax liability. In FY 2002, a total of \$8 million – to 168 individuals -- was awarded under this increasingly popular program. **How will the re-organization facilitate furthering translational and basic research into diseases with a genetic basis that have become increasingly important in pediatric care and in determining predictors of diseases with onset in childhood that become major health issues in adults?**

NIH is still evaluating the Institute of Medicine recommendations regarding re-organization of the agency. However, the Roadmap Initiative embraces an increased emphasis on translational research. The achievement of the mapping of the human genome, as well as the application of new technologies such as expression microarrays and proteomics, will lead to new prevention strategies and public health programs. As science becomes more interdisciplinary and complex, NIH plans to expand collaborations among the ICs, and encourage new initiatives, that will support the infrastructure needed to harness these emerging technologies and advances in molecular biology and molecular genetics. This, in turn, should enhance our ability to develop the knowledge and treatments for a vast new range of conditions, including those that begin during fetal development or childhood.

From conception through fetal development, childhood and adolescence, patterns are established that determine individual susceptibility of disease. Although genetics and related biological factors provide the initial blueprints, environmental, developmental, and social traits, beginning during fetal development, interact with and modify this "imprinting." How and when these factors interact may determine whether individuals start life on a healthy and fully functional path or experience disease manifestations not only in childhood but throughout life. Furthermore, we now believe, the cumulative effect of these events can be passed down to future generations. Research in this arena will provide insight into the pathogenesis of disease by defining pathways from mutant genes that lead to disease phenotypes or by identifying the role of "modifiers" in the disease process. These modifiers include gene-gene interactions, epigenetic factors (i.e. factors that can affect the phenotype of an organism without affecting the genotype), or environmental influences.

Led by NICHD, in collaboration with other NIH Institutes and Centers, the Centers for Disease

Control and Prevention, the Environmental Protection Agency, and many other agencies across the Federal government, a major planning effort is underway to design the National Children's Study. As the study is implemented, it stands to achieve enormous progress in understanding and directing strategies to prevent a range of childhood and adult diseases by linking broadly defined childhood environmental exposures with health and development outcomes from birth into early adulthood. Utilizing research conducted to date (as well as taking advantage of forthcoming research findings) that identify genes of interest and suggested risk factors, the longitudinal cohort design of the National Children's Study will be able to substantiate long-sought causal factors to resolve questions such as whether the fetal environment may lead to the development of obesity and diabetes. As the various environments children live in interact with the genes with which they are born, analysis across a plethora of exposures and wide range of genotypes will permit a more complete picture of what may cause and, in turn, what may prevent disease.

NICHD is also embarking upon an exciting multidisciplinary and collaborative initiative that will allow us to develop new ways to expand screening of newborns for over 300 genetic defects. Besides adapting emerging microarray chip technology to implement this effort, we will work with state health departments and others to develop national longitudinal databases. These will be used to study the natural history of genetic conditions, many of which have no treatments readily available. Once the natural history is understood, and appropriate populations can begin to be more easily identified, new therapies can be developed. As a result, many genetic conditions that once promised to curtail not only the quality of life, but the actual lifespans, of newborns, can be prevented.

How does the re-organization [referring to Roadmap] address the increasing need for complex and state-of-the-art core services that empower and facilitate individual research programs?

The discovery of new strategies to prevent, treat, and cure disease depends on understanding how biological processes of different organ systems function and how they interact. Effectively and efficiently dealing with this new level of complexity requires new and innovative approaches to facilitating biomedical research.

The NIH Roadmap initiative on Molecular Libraries will offer public sector biomedical researchers access to small organic molecules which can be used as chemical probes to study cellular pathways in greater depth. It will provide new ways to explore the functions of major components of the cell in health and disease. It is hoped these NIH Roadmap initiatives will speed the development of new drugs and agents to definitively detect and treat common and rare diseases by providing early stage compounds that encompass a broad range of novel targets and activities. The development of such libraries will also enhance the discovery of small molecules for molecular imaging – the imaging of molecules or molecular events in biologic systems that span the scale from single cells to whole organisms. Obstacles to routine clinical use of this promising technology include the need for more sensitive probes for use in imaging systems, the need for a single database of probes and the need for centralized probe production.

By embarking on the Bioinformatics and Computational Biology initiatives, the NIH Roadmap is paving a future "information superhighway" dedicated to advancing medical research. A central focus of the initiative will be a set of National Centers for Biomedical Computing. As the centers begin to generate the software and data management tools to serve as fundamental building blocks for 21st century medical research, individual scientists will be funded to work together with the centers. "Big science" and "small science" will work hand-in-hand to advance all of science. Through these efforts, researchers will be able to share data gathered from large experiments. The best minds will be able to work together more efficiently to tackle unsolved biomedical mysteries, such as the role of heredity in individuals' different responses to medicines and the complex interplay of genetic and environmental factors in common diseases such as heart disease, cancer and diabetes.

Key to building a strong infrastructure will be to increase interactions between basic and clinical scientists, and ease the movement of powerful new tools from the laboratory into the clinic. In one approach aimed at accomplishing this, NIH is exploring development of regional translational research centers. These centers would provide sophisticated advice and resources to better enable scientists to master the many steps involved in bringing a new product from the bench to clinical use. Such steps involve laboratory studies to understand a therapy's mechanisms of action and animal studies to determine how well a therapeutic agent is absorbed into the body, how it is distributed to target tissues, how effective it is, and how likely it may be to cause unanticipated side effects.

The practical benefit of pediatric research is vital to the lives of many American children. How will the NIH reorganization ensure that new discoveries and updates to pediatric research findings will be more quickly disseminated to the field?

NIH is currently reviewing the Institute of Medicine's recommendations regarding reorganization. However, in the meantime, the dissemination of research results to appropriate audiences – whether that means health care professional organizations and scientific societies, research advocacy groups, patients and their families, or consumers and the lay public – in a timely, accurate, and complete manner is a critical function in improving and maintaining the health of children and their families. To accelerate its program of communicating the practical research results from pediatric research conducted or supported by the NICHD, several steps will be taken. To reach clinicians, NICHD will continue to present research results at national, regional and community professional conferences, a key source of information for practicing clinicians and allied health professionals. The NICHD also will focus its research dissemination activities on developing tailored background statements for specific practice groups such as pediatric immunologists or pediatric hematologists. The Institute will continue to work with both professional and community organizations to disseminate research results into groups and individuals that stand to benefit from the information. For example, over the next several months, NICHD will build on its collaboration with patient organizations such as the Jeffrey Modell Foundation (to promote understanding and recognition of primary immunodeficiency), and community organizations such as the Coalition of 100 Black Women (to help reduce racial disparity in infant mortality/Sudden Infant Death Syndrome).

The NICHD also will build upon its current program to work with national consumer media including broadcast, cable, and newspaper organizations to promote important clinical and public health information directly to the public. For instance, a recent article on the front page of the *New York Times*, reprinted by papers around the country, reported a significant advance in reducing the risk of premature birth. Such articles have an effect similar to direct-to-consumer pharmaceutical advertising. High visibility media stories about a clinical advance prompt many patients to ask their clinicians about it and prompt clinicians to seek background information and journal articles on the findings and the potential applicability for their patients.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892**Enclosure 2**

The Honorable W. J. "Billy" Tauzin
Chairman, Committee on
Energy and Commerce
United States House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

Over the past year, Members of Congress have expressed concerns about research on human sexuality supported by the National Institutes of Health (NIH). Because of the sensitivity of this subject in general, as well as inferences that might be made following a perusal of the titles of research grants, I can understand why some Members have questions. Congressional offices have asked NIH to justify grants that appeared inappropriate to some observers. Last year, these concerns led to a proposed amendment to the House appropriation bill for NIH to defund several grants that had already been approved through our well-established, independent peer-review process. During my appearance on October 2, 2003, before a joint hearing of the Senate Health, Education, Labor and Pensions Committee and the House Energy and Commerce Committee, several Members raised similar concerns based on specific descriptions and characterizations of several NIH-funded grants.

I believe that it is my duty to ensure that any and all concerns expressed by Members of Congress be fully and transparently addressed. My goal is to preserve your trust in NIH and that of the public you represent. This trust has to be based on the historic ability of NIH to properly determine research priorities in response to current and future public health challenges and to maintain, through our world-renowned peer review system, the exceptional quality of U.S. biomedical research.

I directed NIH officials to conduct a comprehensive review of the human sexuality research that we support with a particular focus on the lists of grants that have been cited by some Members of Congress. I asked the Directors of the relevant Institutes and their staff to review each and every grant to help answer the following questions, which summarize, I believe, the essence of the objections raised by some Members.

- 1) Are these grants relevant to the public health needs of our country; i.e., is this research a good use of taxpayers' dollars and why?
- 2) Are the research and its methods scientifically and ethically appropriate?
- 3) Was the integrity of the process by which these grants were reviewed and funded at NIH compromised?

4) Is the funding for this research area disproportionate relative to the burden of sexually related diseases as compared to that of other diseases?

I will begin with the basic mandate for NIH contained in Section 301 of the Public Health Service Act, which requires that we conduct and support "research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man."

Much of the success in improving the Nation's health is attributable to research advances furthering the understanding of human biology. The constant battle against illness and disease, however, cannot be limited to biological factors but has to include behavioral and social factors as well. Unhealthy human behaviors have been estimated to be the proximal cause of over half of the disease burden in our country. Smoking, overeating, abuse of alcohol and illicit drugs, the spread of sexually transmitted diseases, and sex-related or other violent behaviors are at the core of many of the illnesses we are trying to prevent and control in our diverse society today.

Based upon the enclosed summary of the findings of the Institute Directors, I fully support NHI's continued investment in research on human sexuality, and I believe that the peer review process, which is fundamental to the ability of NIH to conduct effective and high quality research, has worked properly and provided a level of valuable and independent review in this important area of research. While the enclosure specifically addresses only a few of the hundreds of grants examined, we would be pleased to answer any questions about any individual grant not addressed.

Congress plays a critical role in authorizing and appropriating funds to us, as well as overseeing all of our activities. Both Congress and the Administration have an important role in priority setting. We at the NIH must be accountable to both, as well as to the American public. To that end, I am initiating discussions with NIH Institute Directors about mechanisms we could establish to ensure that this research is better presented to the public so that they may understand the relevance of this research to public health and that it is in fact prioritized appropriately.

Your views, and those of other Members, are very important to me, and as we take steps to follow up on concerns we have heard, I would welcome any additional thoughts you may have.

Sincerely,

/S/

Elias A. Zerhouni, M.D.
Director

Enclosure

SUMMARY OF INSTITUTE DIRECTORS' FINDINGS**PUBLIC HEALTH RELEVANCE**

Sexually transmitted diseases (STDs) are common in the United States, with an estimated 15 million new cases reported each year. Nearly 4 million of the new cases occur in adolescents. More than 65 million people in the United States are living with incurable sexually transmitted diseases. Women generally suffer more serious STD complications than do men, including pelvic inflammatory disease, ectopic pregnancy, infertility, chronic pelvic pain, and cervical cancer from the human papilloma virus.

Between 800,000 and 900,000 people living in the United States are infected with HIV. The majority of them were infected through sexual contact. After years of progress, the transmission of the disease appears to be increasing again, not only in new generations of sexually active people but even in seniors. Alarming, the Centers for Disease Control and Prevention (CDC) recently reported that the rate of one STD, syphilis, increased in 2002 for the second consecutive year, following a decade-long decline of the disease. CDC also reported a high rate of co-infection of HIV among men diagnosed with syphilis.

The situation is much worse outside our borders. Worldwide, more than 42 million people are living with HIV/AIDS.

The vast majority of the grants that have raised the concerns of some Members are related to our efforts against HIV/AIDS and the at-risk populations we have targeted to prevent further spread of the disease. Understanding the risk factors posed by prostitution and illicit drug use, in addition to preventing initiation of sexual activity in teenagers, remain important to controlling the HIV/AIDS epidemic in the United States. Members have expressed concern that NIH seems to fund a number of similar scientific studies with the only difference being the ethnic origin or type of special population being studied. Unlike prevention or treatment interventions for diseases in which a single type of vaccine or medication can be applied to all patients, behavioral interventions have to take into account the cultural and social environment of the groups being studied. This is why we need to study all patients, including minorities, people living in different regions such as rural areas, people at different stages of life, and those of different gender identities. The context in which people live may be as important as the condition studied for scientific interventions to be discovered and effective.

Unfortunately, prostitution remains a major source of transmission of HIV/AIDS and is responsible for the spread of many diseases. Some Members have questioned the use of taxpayer dollars for the study of prostitutes. For example, some have questioned the value of studying this problem in relationship to trucker networks and their impact on disease transmission. I would like to share with you the analysis of that grant which our staff performed:

Grant Title: *Trucker Networks, Drug Use, and Disease Transmission*

Grant Number: *ROIHD042972-02*

Principal Investigator: *Yorghos Apostolopoulos*

Institution: *Emory University*

Description:

This project studies a potentially important mechanism for the spread of HIV/AIDS and other diseases in the United States. Scientists have shown that in sub-Saharan Africa, India, Southeast Asia, and other regions where HIV/AIDS is predominantly a heterosexual disease, long-distance truckers played a significant role in the spread of HIV/AIDS and other sexually transmitted and blood-borne diseases. This study examines the potential for a similar mechanism of disease transmission here in North America. There are more than 3.3 million U.S. and 300,000 Canadian long-haul truckers operating in the United States today. This research will produce estimates of the number of long-distance truckers currently infected with HIV/AIDS and other sexually transmitted and blood-borne diseases and will produce information about the situations and circumstances that are associated with long-distance truckers engaging in activities that put them--and tens of millions of others with whom they interact--at risk of being infected with HIV/AIDS and other diseases. Early results suggest that most HIV/AIDS transmission among long-distance truckers is primarily through heterosexual contact between truckers and women other than their wives and girlfriends during lengthy periods of time away from home, as well as through the use of intravenous drugs.

Public Health Impact:

The purpose of this grant is to produce scientific knowledge that can be used to reduce the number of people infected with HIV/AIDS and other sexually transmitted and blood-borne diseases every year in the United States. According to the CDC, as of 2001, 57,396 women in the United States have been infected with the HIV/AIDS virus through heterosexual contact. A significant share of these women is believed to have been infected by their husbands. Some of them pass on HIV/AIDS to their children; as of 2001, 8,284 children in the United States appear to have been infected in this way. This study will produce concrete, scientific findings that public health and law enforcement officials will be able to use to develop effective prevention programs to reduce the spread of HIV/AIDS and other diseases by long-distance truckers.

Research Questions:

- | *What is the role of long-haul truckers in spreading sexually transmitted and blood-borne infections in the United States?*
- | *What factors affect whether long-haul truckers are exposed to and expose others to sexually transmitted and blood-borne infections?*
- | *What is the seroprevalence of HIV, Hepatitis B, Hepatitis C, syphilis, gonorrhea, and chlamydia among long-haul truckers and the people with whom they interact?*

This is just one example of the increasing vulnerability we know exists because of national and

international sex trafficking in an interconnected world. Other grants in this category seek to stop the spread of disease by developing effective interventions. In order to intervene, we must first understand how to prevent transmission by prostitutes of different ethnic and cultural backgrounds, and these people are hard to reach. We are certainly not promoting an illegal activity such as prostitution, as some have suggested, but we are trying to stop the devastation it can unleash on the spouse or child who becomes infected because of this activity. Indeed, this work could highlight the health risks associated with prostitution. Our goal is to help law enforcement and policy makers develop more effective approaches to reduce this risk. This is an important area of research in the best interest of the American taxpayers, given its potential costs--financial and human--to society if more effective methods are not deployed.

The consequences of sexual behavior involve more than just the transmission of infectious diseases. Some Members of Congress have also expressed concerns about a small number of studies of human sexuality and behavior unrelated to either STDs or HIV/AIDS sexual behavior. One example of an important public health issue addressed by these studies is teenage pregnancies, a problem that increases the risk of low-birth-weight babies by 50 percent, increases the risk of child abuse and neglect, increases school dropout rates, and even increases the risk of incarceration. Sexual crimes against adults and children, such as rape, incest and molestation, are also major public health concerns.

Sexual dysfunction, which affects tens of millions of American men and women and contributes to many societal problems including divorce, is another public health problem related to human sexuality. Over 43 percent of women and 31 percent of men experience sexual dysfunction each year. It is one of the least understood areas of human psychophysiology. It has an enormous impact on the stability of families and is a major cause of divorce. I share with you below our review of one of the grants some have questioned as unjustified:

Grant Title: Conference on Reproductive Psychophysiology

Grant Number: 1 R13 HD043068-01

Principal Investigator: Erick Janssen

Institution: University of Indiana

Description:

This conference grant provided partial funding for a research meeting on sexual psychophysiology--the relationship between the physical and psychological factors underlying sexual functioning and behavior. The purpose of the conference was to review the research that has been conducted in this field, to review methods used in research on sexual psychophysiology, and to explore future research needs.

Public Health Impact:

Research on the physical and psychological factors underlying sexual functioning and behavior is relevant to the NIH mission to support research on healthy development. Sexual dysfunction affects 43 percent of women and 31 percent of men each year. In addition to harming marriages,

it can signal the presence of disease and mental health problems. Problems of sexual dysfunction prompt many patients under treatment for hypertension and depression to discontinue needed medications. Research on sexual function can help to identify treatments that, like Viagra, can improve the lives of millions of Americans. Research on the psychophysiology of sexual behavior also informs efforts to stem the spread of sexually transmitted infections such as HIV. Unhealthy decisions about sexual behavior result in part because decision-making capabilities can be compromised by the physiological effects of sexual arousal. Understanding these effects and their consequences for sexual abstinence will strengthen prevention efforts critical to our public health mission.

Research Question:

- | *The objective of the conference was to review the research that has been conducted in the field of sexual psychophysiology, to review methods used in research on sexual psychophysiology, and to explore future research needs.*

NIH-supported research is attempting to understand all the mechanisms involved in risky or violent sexual behavior such as rape or sexual abuse of children. This research is aimed at understanding physiological as well as psychological mechanisms involved. Research supported by NIH and the private sector is having positive results: prevention programs have substantially reduced the spread of HIV; school and family-based programs designed to promote academic success and better family bonding have delayed sexual activity in teenagers and reduced risky sexual behavior. Researchers have identified similar brain reactions to both erotic cues and illicit drug use, pointing the way towards possible new approaches to reduce the rate of teenage pregnancies.

We also have been questioned about the wisdom of spending research dollars on one grant researching the sexual behavior of older men. As our population is aging, we need to understand the impact of these demographic trends. For example, CDC is now reporting an increasing incidence of STDs and HIV/AIDS in seniors. Our analysis of this research follows.

Grant Title: Longitudinal Trends in the Sexual Behavior of Older Men

Grant Number: R03 HD39206

Principal Investigator: Andre Araujo [formerly C. Johannes]

Institution: New England Research Institute

Description:

Although it is well known that mens sexual function declines with increasing age, the reasons for this decline are not well understood. Declining sexual function may be the result not only of physiological changes linked to age but also of potentially modifiable non-physiological changes. These include, for example, health behaviors, psychosocial factors such as anger and depression, social ties and marital status, and the use of medications. This project studied changes over time in a range of behavioral and cognitive factors associated with male sexual function and behavior. This study was a secondary analysis of data collected in the

Massachusetts Male Aging Study (MMAS). It described and compared estimates of cross-sectional age trends in sexual behavior in two waves of the study and estimates of longitudinal changes in sexual behavior that occurred in this cohort of men as they aged. It sought to determine to what extent the age-associated decline in sexual function results from age-associated changes in lifestyle, social status, social ties, psychosocial factors, etc., that may be amenable to modification.

Public Health Impact:

Healthy sexual function among men ages 40 and older has important implications for families. Nearly one out of ten new babies are born to fathers aged 40 and older, and these men are parenting well into their sixties. Sexual function and satisfaction are important for the continuity of marriages and the likelihood that children can experience stable two-parent families while they are growing up. Age-related changes in sexual function involve not only changes in cell tissue and endocrine function that occur at the oldest ages, they also involve biological, environmental and social factors that can occur at any age. Without a better understanding of age-related changes in men's sexual function, physicians may mistake the signs of disease for normal declines in function or they may miss modifiable factors that detract from sexual health. This research provides a cost-effective way of increasing knowledge relevant to an important aspect of healthy human development.

Research Question:

- 1 *How do health and social status, medication use, lifestyle (e.g., smoking, exercise), psychological factors, and other modifiable factors influence cross-sectional and longitudinal age-trends in sexual function and behavior?*

We have far more to learn about human sexuality and its association to diseases and illnesses. Some of the research involves behavior that is criminal, such as prostitution and illicit drug use. Other research involves individual populations of people living in the United States who are particularly linked to the transmission of disease or illegal behaviors. Some of this research has unseemly titles because, frankly, the research involves looking at difficult, albeit real, components of the human condition.

THE REVIEW PROCESS AND QUALITY ASSURANCE

Research into human sexuality also undergoes the scrutiny of independent peer review and must adhere to all human subject protection requirements. The NIH peer review process includes a system of 170 chartered study sections and standing special emphasis panels. We have over 11,000 external experts participating in review panels, each of whom is nationally recognized for his or her area of expertise. These individual peer review groups, which examine each application for scientific and technical merit, are composed of 20 or more scientists. The members of each NIH study section are carefully chosen to represent a diversity of backgrounds, regions of the country, and scientific expertise. Membership on these review panels is not permanent; typically, members are appointed for four-year terms and consequently rotate off

approximately every four years in an overlapping fashion. It is highly unlikely that such diverse and constantly changing groups would conspire to favor unduly one type of grant over another. Finally, before awards can be made, applications must be considered by an Institute's advisory council, which by law is composed of at least one-third lay or community members. The process is highly competitive--less than a third of all applications are funded.

Prior to award of funding for any study that will involve participation by human research subjects, an Institutional Review Board (IRB) at the institution where the research is to be conducted and is covered by an assurance filed with the Office for Human Research Protections, Department of Health and Human Services, must review each grant application, research protocol, and Informed Consent document. These IRBs, which always include outside members representing the public, are charged with ensuring that the benefits of the proposed and ongoing research are weighed against the potential risks. Their review ensures that potential subjects will be provided with a comprehensible and accurate description of the risks and anticipated benefits of participating in the research and that appropriate safeguards are in place to protect the rights and welfare of human participants in research.

Also, please be aware that in research involving human subjects, federally funded researchers may compensate the subjects, not as an inducement but as a remuneration for their time for participation in research. This compensation is subject to the review and approval of local IRBs to ensure that a subjects decision to participate in research will be truly voluntary and that consent will be sought only under circumstances that provide the prospective subject...sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence."

All of the grants associated with human sexuality underwent the standard peer review and IRB review process, without deviation. All of them are scientifically justified and received independent review scores in the fundable quality range. Each of them is connected to clear public health priorities.

In addition, most individual medical research does not lead directly to prevention or therapy. Most research results in findings that function as small pieces of a large puzzle that, combined, achieve the benefits the public desires. Sometimes it is difficult to understand the relevance of individual research until we see the entire picture.

RELATIVE PRIORITY

Behavioral research on human sexuality has led to enormous progress in understanding the behavioral causes of HIV and other sexually transmitted diseases that have caused death and suffering, destroyed entire generations across the world, and added enormous fiscal costs to America and the international community. Nearly everyone, regardless of his or her status in life, is vulnerable to the health risks associated with sexual behavior. NIH supports research into the causes and consequences of sexual behaviors due to the substantial burden on society of the related diseases and dysfunction that affect millions. Clearly, this has to be considered as one of our highest priorities in light of the enormous suffering and costs of illnesses associated with sexual behavior. Even so, the NIH investment in this area of research is only a very small part of our overall budget.

NIH/OD – January 26, 2004

