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**FUNDING ALLOCATIONS FOR RESEARCH AT
NATIONAL INSTITUTES OF HEALTH**

HEARING
BEFORE A
SUBCOMMITTEE OF THE
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UNITED STATES SENATE
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FIRST SESSION
SPECIAL HEARING

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FUNDING ALLOCATIONS FOR RESEARCH AT NATIONAL INSTITUTES OF HEALTH

THURSDAY, MAY 6, 1999

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN
SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 9:05 a.m., in room SD-124, Dirksen Senate Office Building, Hon. Arlen Specter (chairman) presiding.
Present: Senators Specter, Gorton, Stevens, Harkin, and Murray.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

STATEMENT OF DR. HAROLD VARMUS, DIRECTOR

OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. Good morning. The Subcommittee on Labor, Health and Human Services, and Education will now proceed.

This is one of the regular subcommittee hearings on establishing our budget for fiscal year 2000. The crown jewel of the Federal Government is the National Institutes of Health. It may be that that is the only jewel of the Federal Government, and the subcommittee has taken a lead in substantially increasing the allocations for the National Institutes of Health over the past many years.

Two years ago the subcommittee started a recommendation that emerged intact from the full Senate for \$950 million, and that was reduced in conference slightly to \$907 million. We have found that when Senate resolutions come before the Senate, there is great generosity, a 98 to nothing vote to increase NIH funding by \$2 billion, but when it comes to actually putting the money up, the amendment offered by Senator Harkin and myself this year lost 52 to 48.

Last year the amendment lost again, but as a matter of priorities from our budget, we increased the NIH funding by some \$2 billion, and this year we are looking at a very tight budget, and we are going to do our very best to match that \$2 billion increase from last year. That is where we set our sights.

Later today there will be an allocation for this subcommittee and the preliminary news, candidly, is not good. The tremendous amount of money which had been expected from tobacco revenues

is going to be excluded. Legislation is pending, having passed the Senate to send all of that to the states, but this subcommittee leadership, Senator Harkin and myself, are determined to do everything we can, because NIH has done such marvelous things.

The stem cell research has the potential to conquer Parkinson's in 5 to 10 years, according to testimony addressed before this subcommittee, and there is a battle there as to whether that funding is prohibited from live embryos, and NIH has cut the Gordian knot by using private funding to extract the stem cells from live embryos so that the public funding comes only on the extracted stem cells.

This is really similar to the problem we had with fetal tissue a few years ago, where some objected to the use of fetal tissue for medical research on the grounds that it would promote abortions, but then it was established that fetal tissue left on discarded abortions, did not have any causal connection to abortions. I note Dr. Varmus nodding in the affirmative, let the record show, and I think the issue with embryos is very similar.

There has been some issue raised as to whether the Congress establishes how much should be spent for research on each disease, and the Senate does not do that and the Congress does not do that. That judgment is left to the National Institutes of Health, and we will have testimony today on that specific point.

The allocations among the various branches are very, very heavily lobbied. On a daily basis, my schedule is replete with visits from people who feel that more money ought to be allocated to their particular line, I had visits yesterday on that subject, and it is said that AIDS has a disproportionate share. It is a communicable disease and a great deal of effort has been directed there, and Dr. Varmus will take a look at it. The real answer is to have a larger total allocation, and that way the rising tide will lift all the boats, as the saying goes.

Last year there was an effort made to increase funding on prostate cancer, and notwithstanding the backing in the high quarters in the Senate, that was rejected, in accordance with the principle of having the allocations made by the National Institutes of Health.

Now, there was one exception with the Balance Budget Act of 1997, which made some specific allocations, but that came from the Executive Branch in conference, candidly, with the leadership of the House of Representatives, but it was not the practice of this subcommittee to try to determine the allocations, because we think that ought to be left in the hands of the experts.

There are some matters where public policy can come from the Congress is an appropriate comment, but the allocation of these funds has been for NIH, and we will proceed to hear the testimony on that.

But before doing so I yield to my distinguished colleague and ranking member, Senator Harkin.

OPENING STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. Thank you very much, Mr. Chairman. I want to associate myself with your remarks, and thank you for calling this hearing.

I am pleased in joining you and welcoming Dr. Varmus and the other witnesses today, and in particular, welcome to Dr. Mary Hendrix, a fellow Iowan, whose outstanding achievements have led her to be Head of the Department of Anatomy and Cell Biology at the University of Iowa, and who was recently elected President of the Federation of American Societies for Experimental Biology. I want to congratulate her.

Welcome also to Mr. Brad Margus. I have heard a great deal about what you and your wife are accomplishing on behalf of all families with children stricken with AT. So we applaud you and Vickie for your selfless efforts, especially as you cope with the illnesses of your two sons.

Again, Mr. Chairman, I applaud you for having this hearing today. As you said, the Senate went on record 98 to nothing to double the NIH budget over the next 5 years, but when we came down to the real money, they decided to cut and run. But we are going to keep going, and we are going to keep pushing to try to get that money, as much this year as we got last year. And we could not have a better person to chair this subcommittee, and to work to get that funding than Senator Specter.

I just want to say a couple of things. I know Dr. Varmus will agree with me when I say that there is no time in our history that we have been as close to major advances in the fight against killer diseases. Two things have sort of come together now, sort of like the time we finally split the atom and finally opened up a whole new era, not just in terms of warfare, but in terms of scientific research, and development, and applications.

The recent advances in stem cell research and our progress in uncovering the mysteries of the human genome present us with tremendous opportunities.

So now is the time to boost our investment to make certain that our nation's top scientists can turn these opportunities into reality. We can achieve so much in, I think, a very short span of time, if we do invest that money.

I can go on more about making sure we get that money. Senator Specter and I have said before that at least one or two pennies out of every health dollar in America ought to go to research. We are not even doing that yet. That would help us get some much needed money into research, and we will continue to push on that. But really the basis of this hearing was NIH funding allocations.

I agree wholeheartedly with our Chairman. When it comes to the decisions on how to allocate and invest the money that our taxpayers are investing in scientific research, this must be done through a time-tested and time-proven system of peer review. It must be done by those that understand the scientific basis of this research, and where we can focus our attentions.

However, we, too, have a responsibility on this end in terms of oversight, in terms of working with the scientific community, to try to determine how best we can fulfill our obligation to help set broad national priorities to answer the legitimate concerns of those that our Chairman just spoke to us about, whose families have illnesses, whose kids are suffering from AT, or from a variety of different illnesses, and who legitimately want us to focus on them. So

we have our obligations to be responsive, and that is what we try to do in exercising our oversight role.

I must say that it has been my experience, at least with the scientific community, that to a large extent both sides understand this. Now, there are some on this side who say we ought to be able to tell them everything, and there are some on the scientific side who say we ought not to say anything.

I think those opinions are on the margins and that the great bulk of those in the middle understand that there should be a consultative collaborative arrangement between NIH and the scientific community, and those of us in the Congress, in which we work together to try to respond to the societal needs and priorities that we hear, and yet to ask the legitimate questions about where can we make the most progress, and where can we get the most bang for the buck and then try to help move in that direction. This brings me to my final statement, and that is that we probably would not be here today if we really did have enough money in biomedical research.

If we had the kinds of funding for biomedical research that we are trying to get, in terms of doubling NIH's budget, I am not certain that we would have these kinds of concerns. So I come back to where I started, and where I think our Chairman started, and that is, we have to put more money into biomedical research in this country. Then we need to work in that collaborative arrangement with the scientists to try to decide how we answer the legitimate concerns of people's priorities, and to make sure that the scientists who have a system of peer review can apply for that money in the most logically consistent manner.

Thank you, Mr. Chairman.

Senator SPECTER. Thank you very much, Senator Harkin. We have been joined by the Chairman of the full Committee, Senator Stevens.

OPENING STATEMENT OF SENATOR TED STEVENS

Senator STEVENS. Good morning, Doctor.

Dr. VARMUS. Good morning.

Senator STEVENS. To me, this is a sad day, because today is the day I make the allocation under 602(b) of the Budget Act, and the news is not good. The bottom line is that we will have to have a substantial increase to fund the priorities that we know are there.

All I can tell you is that as the year wears on I hope that we can find some way to rectify this maladjustment of allocation of funds. I think the Chairman has indicated that we are quite—I am still quite interested in trying to achieve our goal of doubling the funding for research over the 5-year period.

That does not look like it is possible, unless we can get some basic readjustment of these priorities in the balance of this year, but do not blow a stack, but just hold on tight, we will see what we can do as the year goes on.

I do have a couple of questions that I want to submit to you for the record. I have to go to another hearing, but I want to drop by to tell you that what you are going to read in the papers is true, unfortunately.

Thank you very much.

Senator SPECTER. I would thank you, Senator Stevens, except for the acceptance of your comments. [Laughter.]

Senator STEVENS. Well, I expect to be the target of very sharp barbs from the chairman, and they will be well intentioned and well placed, and I will see what I can do to help. Thank you very much.

SUMMARY STATEMENT OF DR. HAROLD VARMUS

Senator SPECTER. Thank you for coming, sir. We now turn to Dr. Harold Varmus, the very distinguished Director of the National Institutes of Health. He has been at it since November 1993, more than 5 years now.

At the University of California, San Francisco, he earned the Nobel Prize for his work on a causative link between certain genes and cancer, which is the cutting edge today of medical research, graduate of Amherst, Harvard, and the Columbia Medical School. We welcome you, Dr. Varmus, and look forward to your testimony.

Dr. VARMUS. Mr. Chairman, thank you very much.

Senator SPECTER. Your full statement will be made a part of the record, and we have quite a number of witnesses, so we are going to use the lights for the five-minute opening.

Dr. VARMUS. Thank you. I appreciate your support and welcoming remarks, and thank you, also, Senator Harkin for your support. I appreciate the opportunity to review the decision-making processes that determine the spending patterns at the NIH.

As you know, there is great interest in these questions, because of our budgetary success, for which we hold you responsible, and because of the benefits of past work and the hopes for future discoveries that will benefit the health of this nation.

For that reason, there have been multiple hearings on this topic. There was recently a congressionally mandated report published by the Institute of Medicine on this topic. The NIH has issued a priority-setting handbook, and there has been much public discussion in the press and elsewhere.

I intend to be brief this morning, but I would like to consider quickly five issues to bring the subcommittee up to date on the way we think about these matters and to describe some of our responses to the recommendations in the Institute of Medicine report.

First, what criteria are used to allocate research funds? Everyone seems to agree, including the IOM report, that several criteria are involved in setting our spending plan, and at least five of those are worth reiterating here.

First, as Senator Harkin mentioned a moment ago, the quality of research matters. Expert peer review is essential to the process of allocating funds. Second, it is crucial to consider the prospects for important discoveries, discoveries that will advance our understanding of the human organism, and the prospects for making progress in our efforts to treat and prevent disease. We sometimes call that "scientific opportunity."

The third criterion is public health need, which is often estimated from disease burden. I will return to that issue in just a moment. The fourth consideration is maintaining a broad portfolio across all sciences relevant to health to ensure that we are maintaining adequate vigilance on all fronts.

You can see results of this consideration in this year's budget proposal when you look at our initiatives for sustaining allied disciplines—physics, chemistry, mathematics, computer science, and engineering—as they affect medicine. Or you can see it as you look at the many new initiatives that we have to sustain clinical research, a component of our research efforts that is under siege at the moment.

Finally, we have to pay attention to the infrastructure in which science is done. That includes maintenance of facilities, of equipment, and, of course, most important of all, our human resources, the people who do science. All of these factors and others need to be considered.

Let me second consider a question that is troubling to some, that is, is it possible to actually plan a scientific program? After all, discovery is unpredictable, and we know that top-down science of the sort that directs everyone in the trenches from above can be wasteful. We still believe it is possible to plan initiatives and to set broad programmatic goals.

We insist at the moment in building our budget that every institute present to the NIH director, a set of goals for the coming year. As of this year, every institute and center will be required to have a written strategic plan for the next 2 to 5 years.

Those of you who have had a chance to look at the summary of how we are going to spend the 2 billion extra dollars we have in 1999 know that there are many plans.

It is important to remember that the planning process entails a lot more than just attempting to assign dollars to diseases. Each institute and center has to consider which mechanisms for funding it is going to use, whether it is going to use certain kinds of grants or others, whether it is going to support centers or program project grants or supply money to the intramural research program.

Every institute needs to consider its various goals, research goals, goals to improve the infrastructure in which research is done, and goals in the training process. And each institute needs to think specifically about programs, many of which are not specific to diseases but, instead, involve developing instrumentation, or pursuing the genomes of mice or human beings or flies.

The third question is one that is addressed very specifically in the Institute of Medicine report, and that is, who provides advice to the NIH leadership and how is that advice actually provided? There are a broad range of advisors, and that has been true for many years. They include the scientific community, members of the NIH staff, patient advocacy groups, health care providers, other components of the public, and—very importantly—members of Congress and the Administration. There is a profound, complex dialog that has always gone on.

How is that advice provided? Well, we have scientific review groups that now often include public members as well as scientists. We have long-standing national advisory councils, and other advisory groups that are developed ad hoc to address certain issues. We hold workshops that address specific issues that are of contemporary concern. We have town meetings and other public events.

In response to the Institute of Medicine report, we have clearly identified in every institute and in my office an office of public liai-

son that tells members of the public exactly where to go to register their comments. And we have established very recently a council of public representatives that serves as a public body of advocates and other interested members of the public to advise me in a broad range of issues.

I have included in my written testimony many examples of special mechanisms used by individual institutes and centers to illustrate how they go about collecting information from the public, and there is variation, of course, depending on the missions of the individual institutes.

The fourth issue I would like to discuss very briefly is a particularly contentious one. Why do we argue that measurement of disease burden is an insufficient means to allocate research dollars? Let me make something very clear. NIH monitors disease burden extremely carefully. We do research—many millions of dollars worth of research—on this issue. We report to Congress. We consider disease burden carefully in budget formulation. There are many examples in our contemporary research that illustrate that point: The increased money for Hepatitis C, as a result of new findings of its prevalence and its link to liver cancer; our anticipation of the effects of aging on the population; our recognition of health disparities among different components of our population.

Moreover, as shown in a forthcoming article in the *New England Journal of Medicine* by Grosenthal, when the most comprehensive measure of disease burden, a measure called disability adjusted life years, is used, there is a reasonably good correlation between burden of disease and NIH spending, but we have to note many caveats here.

First, there are many possible individual measures of disease burden, and they give different answers, as shown clearly in the *New England Journal of Medicine* article that is forthcoming.

Second, when they calculate our spending by disease, while the calculations are consistent from year to year for a single disease, they may not be comparable between diseases. Third, many of our most important projects are not disease specific, even though they affect profoundly our understanding of disease. Fourth, we have to remember that we need to address not just the disease burden itself, but also the potential for reducing disease burden, as exemplified by our current emphasis on developing a vaccine against AIDS.

Finally, we need to consider other activities in other agencies and in industry. As a result, there is not and there should not be any absolute correspondence of dollars to disease burden, even when the best measures are used. Nonetheless, we continue to monitor and discuss disease burden. We are having a workshop on this topic in the fall, and we do consider this a very important component of the budget-building process.

My fifth comment concerns the question of whether money alone can drive discovery and progress against disease. We recognize that science is not a commodity—you cannot buy discoveries—but money is a critical resource. It encourages progress. It is not sufficient to make progress.

To make progress against disease, we need to attract talent and provide a suitable research environment. This is best done through

advertising our interests, developing workshops that spread the word about NIH's concern about certain conditions, and making imaginative collaborative arrangements.

PREPARED STATEMENT

This is a gradual process, and it profits tremendously from the close relationship that can exist among scientists, public advocates, NIH leadership, and the Congress.

Thank you, Senator, for a chance to present these views, and I look forward to receiving your questions.

Senator SPECTER. Thank you very much, Dr. Varmus.
[The statement follows:]

PREPARED STATEMENT OF DR. HAROLD VARMUS

Mr. Chairman and Members of the Subcommittee, I am Harold Varmus, Director of the National Institutes of Health. I am pleased to appear before you to discuss the research funding process at the NIH. I want to thank you for the opportunity to discuss this important issue.

The issues

Congress, patient/health advocacy groups, and the scientific community have a long-standing interest in how NIH sets priorities and allocates funds for medical research. These constituencies are concerned about how the NIH accounts for its funding decisions and the means by which the public can, and does, influence them.

A brief history

In 1997, I testified at two hearings on priority setting—the first in May, before the Subcommittee on Public Health and Safety of the Senate Committee on Labor and Human Resources, and the second in June, before the House Subcommittee on Labor, HHS, and Education, Committee on Appropriations. At both of these hearings, the criteria and processes by which NIH allocates research funds were examined and contrasted with the role of Congress in authorizing and appropriating funds for medical research.

After these hearings and in response to public and Congressional interest in how NIH sets priorities, I created the NIH Working Group on Priority Setting. This group, consisting of 15 senior NIH staff, was charged with developing a document that would clearly describe the principles and mechanisms by which NIH allocates its funds. In 1997, NIH published *Setting Research Priorities at the National Institutes of Health*. Although this booklet has been widely distributed and generally well-received (<http://www.nih.gov/news/ResPriority/priority.htm>), the public and members of Congress continued to express concern about the priority setting process and the means by which the public can influence NIH decision-making. In an effort to further address this issue, members of the Senate Subcommittee proposed, through the Fiscal Year 1998 Labor, HHS, Education Appropriations Act, that the Institute of Medicine (IOM) conduct an independent study of decision-making at the NIH and how resource allocation is influenced by Congress and the public.

The IOM Committee released its report, "Scientific Opportunities and Public Needs: Improving Priority Setting at the National Institutes of Health" in July of last year. The report contains twelve helpful recommendations for improving priority setting and consideration of public input at the NIH; ten of these recommendations were directed to NIH leadership, while two of the recommendations were directed to Congress. More recently, the fiscal year 1999 House Appropriations report encouraged the NIH to implement these recommendations and requested a report from the NIH on the status of implementation; the report was submitted to Congress in February of this year. (See Attachment)

What are NIH's Criteria for Allocation of Research Funds?

The allocation of funds to medical research is complex. Congress establishes the level of available resources to NIH through separate appropriation accounts for each research institute and center. Within these general parameters each institute and center must decide which specific applications to fund and whether to emphasize certain research topics within its authorized domain such as child health, cancer, cardiovascular disease, diabetes, or infectious disease. These decisions are also constrained by the commitment base, i.e., funding decisions made in previous years

which limit the number of dollars available for new grants or new initiatives. The net effect of these multiple processes and decisions determines how much of the entire NIH budget is devoted to work in certain scientific disciplines or on particular diseases.

There are five broad criteria that guide the planning and spending of the NIH budget; these criteria were fully endorsed in Recommendation 1 of the IOM Report. First, the NIH is committed to supporting work of the highest scientific caliber by ensuring rigorous peer review. Second, the NIH must seize those opportunities that offer the best prospects for new knowledge and for improving the prevention and treatment of disease. As important as it is that we fund research on specific diseases, we must also fund research programs, such as the Human Genome Project, that yield knowledge applicable to a broad range of biological questions and clinical problems.

Third, because we cannot know in advance exactly when and where major discoveries will occur, we also need to maintain a diverse research portfolio. For example, while we continue to pursue advances in cell biology and genetics, we are also expanding our effort in clinical research by initiating new training and career development programs for clinical investigators; increasing funds to General Clinical Research Centers; strengthening clinical research in the intramural program; expanding the number of clinical trials; and developing a Clinical Trials Database to ensure that patients and physicians know where and how to enroll in trials. Portfolio diversity is also evident in our commitment to train, support, and encourage scientists in allied fields, such as physics, engineering, chemistry, and computer science. This is accomplished by creating a Bioengineering Consortium; by supporting instrumentation development, such as the construction of new beam lines for structural biology; by developing interdisciplinary training programs for drug development; and by attracting and training young computer scientists into the growing field of bioinformatics.

A fourth criterion, and one that has drawn particular attention, is public health need as measured by the burden of disease. NIH gathers, analyzes, considers, and disseminates data on all of the factors that describe burden of disease, including incidence, prevalence, mortality, and morbidity, among others. These data are obtained from a variety of Federal agencies, such as the CDC, AHCPH, HCFA, the U.S. Census Bureau and voluntary health organizations. The NIH also funds longitudinal studies, short-term one time studies, and recurring surveys on disease risk factors, epidemiology, etiology, and natural history to ensure that we have all the necessary data to inform our decision-making.

Fifth, NIH must build and maintain the necessary infrastructure for the conduct of research. Productive science cannot be done without well-equipped laboratories, well-trained scientists or modern and safe research facilities. To this end, funds must be devoted to attracting, training and supporting young investigators and mid-career investigators who serve an important role as mentors. NIH funds must also be available to upgrade laboratories with state-of-the-art instrumentation, to construct and renovate laboratory facilities, and for the purchase of expensive equipment.

Does the NIH plan science and, if so, how?

Because research, by definition, is the attempt to discover what is unknown, it is unpredictable. And because it is unpredictable, there are genuine constraints on the ability to plan science. History has repeatedly shown the benefits of allowing research to be governed by the imagination and productivity of individual scientists, not by a formal plan for alleviating specific diseases we do not yet fully understand.

While it is not possible to plan for specific research outcomes, it is, however, possible to plan initiatives and set broad programmatic goals. Strategic planning has always been carried out at the NIH, although the processes within the ICs have not always been uniformly clear to the public. Some Institutes have formal planning processes and publish the results of these deliberations, while ongoing planning processes in other Institutes have been less visible. I have asked each IC to develop a 2-5 year strategic plan, which includes input from scientists, patient advocates, and health care providers with the goal of making these written plans available to the Administration, Congress, and the public early in fiscal year 2000.

There are many important yet competing factors that each IC must consider in planning how, and by what mechanisms, its funds should be spent. For example, how many dollars should be allocated to laboratory research vs. clinical research? to investigator-initiated research vs. targeted disease-specific research? to research project grants (RPGs) vs. contracts or centers? to intramural vs. extramural research? to training vs. instrumentation or buildings and facilities? These decisions

must be closely tailored to the IC's overall research objectives and to the specific scientific initiatives identified during the planning process.

How, and from whom, does NIH seek advice in setting priorities?

The factors that influence the planning and spending of budgets are multifaceted, so opinions about them are solicited and provided from many quarters—the extramural scientific community, patient advocacy groups, health care providers, Congress and the Administration, as well as the NIH staff. In an effort to ensure that we hear from all of those interested in, and affected by, medical research, we gather these opinions through many means and over the course of each year.

The ICs have many established means for reviewing scientific progress in their areas of responsibility, for developing long-range research objectives, and for formulating annual budgetary plans and research initiatives in consultation with scientists and the public. They use review groups composed of accomplished investigators (recently some have included lay members) to evaluate grant applications for scientific merit. Each year many conferences and workshops are organized to encourage scientists from diverse disciplines and lay disease advocates to come together to examine and stimulate new areas of research. IC Directors and NIH staff also frequently consult with members of other Federal agencies, with the OMB and DHHS, and with Congressional members and staff on a variety of common concerns. Some NIH ICs also engage the lay public by creating advisory groups like the NCI Director's Consumer Liaison Group, while others, such as NIDA and NIEHS, sponsor town meetings around the country to seek public input, involving community leaders and groups, local schools, and state or local government officials. In the past few years, the NIH has also made frequent use of extramural advisory groups to assess trans-NIH activities (for example, the intramural research program, the Clinical Center, gene therapy, clinical research, and AIDS research) and to recommend budgetary and programmatic changes in those areas.

Along with these long-standing efforts to seek advice, NIH has undertaken several new efforts which seek to build upon and improve both access to and communication from the NIH. For example, within the Office of the Director, the Office of Communications is being expanded and is now named the Office of Communications and Public Liaison which reflects its public liaison functions. Each IC has an Office of Public Liaison which provides information about an IC's research activities and ensures that each Institute has a conduit through which public voices can be heard in the Institute's deliberations on research directions and priorities. While the functions of these offices are not new—to communicate with the NIH's many constituencies—many of them have recently been renamed so as to clearly identify them to the interested public. The NIH also launched a new Web site to serve as a focal point for NIH public liaison activities (<http://www.nih.gov/welcome/publicliaison>). In addition, the new Director's Council of Public Representatives, which met for the first time last month, provides another avenue for greater public involvement in NIH's activities and policies.

Why is disease burden only a partial guide to spending NIH's research dollars?

In spite of NIH's extensive efforts to gather and analyze data, information on disease burden is imperfect. There is no common or accepted measure for disease burden. Morbidity, mortality, incidence, prevalence, the cost of direct health care services or the cost of unreimbursed family care, and loss of work productivity have all been touted as useful metrics for burden of disease. But each of these factors is incomplete. The nature of burden varies from one condition to another. Some diseases result in premature death while others result in diminished functioning. Some terminal conditions require short-term costly health care, while others cause pain and suffering over many years. To further explore the potential utility—and strengths and limitations—of disease-specific burden of illness, this summer we are convening a small group of experts to identify data sources, review models for the use of burden/cost of disease data, and explore how NIH might more effectively use this data.

Furthermore, estimates of spending by disease, while consistent from year to year for any single disease, often do not allow meaningful comparisons across diseases. The spending figures calculated for a specific disease are the result of a complex algorithm of laboratory and clinical research efforts, which appear to be related to that disease. In many cases, the most basic research on cellular function or gene expression may not be clearly attributable to a specific disease. Nevertheless, findings from such research often lead to real improvements in the prevention, diagnosis or treatment of that disease. For example, recent progress in developing effective therapies for patients with AIDS was based on much earlier cancer research on retroviruses found in chickens, mice, and other animals. We now use drugs designed to inhibit the enzymes made by HIV's genes, diagnose infection and follow the ef-

fects of therapy by measuring viral genomes in the blood, and study resistance to treatment by detecting mutations in viral genes.

Calculations of spending by disease also ignore a very important element of resource allocation—the importance of funding “enabling technologies.” These are knowledge and technology platforms that serve a broad range of scientific fields and disease-specific research. I already mentioned one such program, the Human Genome Project; others include the Trans-NIH Mouse Initiative and the Brain Molecular Anatomy Project. These programs are not easily assigned to diseases and yet they are critical components of much, if not all, disease-specific research.

In sum, the complexities of assigning dollars to disease-specific research inevitably lead to significant variations in the number of dollars spent on one disease as compared to another. And because public health need is one of several criteria NIH uses to allocate research funds, we can never expect a perfect correlation between disease specific funding and disease-specific burden.

Can money alone drive scientific advance?

Advances in science are not a commodity and cannot be purchased by the simple expenditure of dollars. Several important components of the research enterprise must be in place for new dollars to yield real progress. The elements can be defined, although they often are difficult to obtain. In the best case, public health need and scientific opportunity co-exist with highly trained, creative investigators and modern laboratories and research hospitals.

New scientific efforts are also driven by evidence that under-explored opportunities exist and that they can attract talented investigators—often newly trained scientists or scientists from other fields—who will then propose meritorious projects. To this end, the NIH employs a variety of means to recruit new talent to a scientific problem, including advertising an IC’s interest in making funds available to pursue a new scientific opportunity or a public health challenge through program announcements, requests for applications, and requests for contract proposals; inviting scientists from allied fields to workshops that highlight opportunities and needs in an underserved field of medical research; and supporting training programs to encourage new scientists to work in a designated area.

Mr. Chairman, I appreciate your providing a forum to present these views about an important, contentious, and complex issue. I would be pleased to answer any questions you might have.

NONDEPARTMENTAL WITNESSES

STATEMENT OF STEPHEN H. SMITH, CHAIRMAN, NATIONAL GOVERNMENT RELATIONS COMMITTEE, AMERICAN DIABETES ASSOCIATION

Senator SPECTER. We are going to proceed a little differently today. What we would like to do is call the other witnesses, we would like to have you remain. We are going to have some complaints from some of the people about the way you handle things, and when you are on hand we will be able to have the kind of dialog which will go right to the core of the issues.

So at this time I would like Dr. Mary Hendrix, Mr. Brad Margus, Mr. Stephen Smith, Dr. Stephen Spector and Dr. Purnell Choppin to step forward.

Let us begin with Mr. Stephen Smith, Chair of the Government Relations Committee of the American Diabetes Association. Mr. Smith is from South Carolina and has a degree from the University of South Carolina. The American Diabetes Association has been campaigning for \$827 million for diabetes research. The President's budget for fiscal year 2000 puts a figure of slightly in excess of \$462 million. The advances in diabetes research have been profound, a very effective public contact group. We know you would like more money, Mr. Smith. You would like a congressional mandate. Now tell us why.

Mr. SMITH. Mr. Chairman, thank you very much for having us here today.

Senator SPECTER. Anybody who has a statement will have it included in the record, and I am going to have to insist that we observe the 5-minute green light. Proceed, Mr. Smith.

Mr. SMITH. Thank you, Mr. Chairman and members of the committee. I am Chairman of the Government Relations Committee, and a member of the Board of Directors of the American Diabetes Association.

I have many people with me today. One special guest we have with us today is Mr. Edsall Ford, with the Ford Motor Company, who is joining in our efforts, right behind me.

Thank you very much. The American Diabetes Association is the largest volunteer health organization representing diabetes. I have Type I diabetes. The major focus of my remarks today is to talk about the new report, which I think has been submitted to the committee when it was released in February, called Cochran Diabetes.

I was a lay member of that committee, mandated by the Senate and members of the House of Representatives in 1997, in order to develop, using the best and brightest, minus one person, as a member of that committee, a comprehensive plan for diabetes. It identifies hundreds of scientific opportunities for treatment and a cure. It identifies the challenges associated with diabetes. It provides evi-

dence of the magnitude of the problem, and analyzes the Federal Government's commitment to research for diabetes. It established a 5-year organized plan to attack diabetes, and it is a peer-reviewed document.

My purpose here today is not to be critical of the distinguished director of the NIH. He is a very brilliant man and a great leader of NIH, and an asset to this country. Our purpose here today is to try to encourage you to send a signal to NIH and to the rest of the scientific community as to the benefits and the rewards of implementing this plan.

Public health need is a very important component of the decision process, and certainly if that is a component, not necessarily the most important one, as stated, but diabetes meets that.

We now have 16 million people in the United States with diabetes, 800,000 new cases per year, and it is projected by the World Health Organization that that will increase to 22 million by the year 2025. CDC has called it the epidemic of our time. It is the sixth deadliest disease in America, killing 190,000 per year.

It is the leading cause of blindness, over half of the new cases of kidney disease, causes 50 percent of lower limb amputations, increases my risk of heart disease and cardiovascular disease, it reduces my normal life expectancy, as a lucky diabetic with access to care and education, by 10 to 15 years.

So obviously, with a staggering \$105 billion cost to America, it is a very important component, as NIH sets its goals for spending. Does it meet scientific opportunity? As mentioned, the NIH assembled the leading researchers in the world, and we presented to you this report. It is divided into some areas of scientific opportunity.

Those include genetics for Type I and Type II, autoimmunity for the beta cell for Type I, cell signaling and regulation for Type II, obesity and clinical research. So the science is there in the document, Mr. Chairman and members of the committee.

The scientific opportunity is presented to you in a plan, but we are severely underfunded. Diabetes, as you have mentioned there, those that complain about their funding, we have three percent of the NIH budget, \$432 million, but this is a disease that affects seven percent of our population. Its complications and death rates have been rising. The inflation-adjusted growth and research budget has been less than two percent a year for diabetes.

So if the rising tide, respectfully, lifts all boats, ours is somewhere over in the swamp somewhere, because we start in the muddy waters, so to speak, with such a low commitment relative to or vis-a-vis the impact and the prevalence of disease.

Relative to our whole budget, diabetes research has decreased 30 percent, since 1981, in dollars, yet the death rate in diabetes, while the death rates for cardiovascular disease and others are going down, ours is going up.

PREPARED STATEMENT

Mr. Chairman, before you is the plan. We are not asking for a pot of money to be sent over to NIH with instructions. Mr. Chairman, we submit that this plan is an organized, comprehensive plan, which gives the science the prevalence, the impact, and we know that the members of the Senate have ways in which to send

messages, and we would simply ask you to insist, not only to NIH, but by sending a signal from this committee to the nation that diabetes is a priority and this plan is a way to go in the next 5 years in solving this debilitating disease, which is killing so many.

Thank you, Mr. Chairman.

Senator SPECTER. Thank you very much, Mr. Smith.

[The statement follows:]

PREPARED STATEMENT OF STEPHEN H. SMITH

Mr. Chairman and members of the subcommittee, thank you for the opportunity to testify today on the important issue of the National Institutes of Health (NIH) allocation process. I am Stephen H. Smith, Chair of the American Diabetes Association's Government Relations Committee. I have type 1 diabetes.

In 1997, Congress directed NIH to put together a team of "the best and the brightest" diabetes experts and develop a comprehensive plan that would lead to the elimination of diabetes. This spring, *Conquering Diabetes*, the final report of the Diabetes Research Working Group (DRWG), was presented to Congress. I was pleased to serve as a lay member of the DRWG.

Conquering Diabetes identifies the challenges associated with diabetes and provides compelling evidence attesting to the magnitude of the problem. It also analyzes the federal government's current commitment to diabetes research. Most importantly, *Conquering Diabetes* identifies hundreds of scientific opportunities that could lead to better treatments and hopefully, a cure.

Since 1997, the issue of how NIH allocates its multi-billion annual budget has been explored internally by NIH, by the National Academy of Science's Institute of Medicine and by a subcommittee of the Senate Labor and Human Resources Committee.

During this time, NIH has stated that it uses five criteria in setting research priorities:

- Public health needs.
- Scientific quality of the research.
- Potential for scientific progress.
- Portfolio diversification.
- Adequate support of infrastructure.¹

According to NIH, "two of the most important of these * * * are public health needs and scientific opportunities."² Each year, according to NIH, "deciding how and where to distribute [its] money * * * requires a fresh assessment of the nation's health needs and renewed evaluation of scientific opportunity."³

Based upon the findings of the DRWG, diabetes exceedingly meets these two criteria. Yet despite meeting them, the DRWG found that diabetes research has been, and continues to remain, significantly underfunded by NIH.

Pressing public health needs

In terms of incidence, severity and cost, there can be no doubt that diabetes imposes a significant burden on our nation and the world.

Incidence.—Sixteen million Americans have diabetes.⁴ Approximately 500,000 have type 1, formerly known as juvenile, diabetes and the rest, predominantly older Americans, have type 2 diabetes.⁵ Each year, another 800,000 will develop the disease.⁶

Since 1959, the number of Americans diagnosed with diabetes has increased nearly 700 percent.⁷ This trend will continue as our nation ages and becomes more sedentary. According to the World Health Organization (WHO), nearly 22 million

¹Institute of Medicine, "Scientific Opportunities and Public Needs: Improving Priority Setting and Public Input at the National Institutes of Health." National Academy Press: Washington, D.C.: 1998.

²"Biomedical Research Priorities: Who Should Decide?" Hearing before the Subcommittee on Public Health and Safety of the Committee on Labor and Human Resources, United States Senate. May 1, 1997, p. 8.

³"Setting Research Priorities at the National Institutes of Health," National Institutes of Health, September 1997: p. 7.

⁴Diabetes Research Working Group. 1999. *Conquering Diabetes: A Strategic Plan for the 21st Century*, p. 2.

⁵National Institutes of Health. *Diabetes in America: 2nd Edition*, 1995, p. 1.

⁶Diabetes Research Working Group. 1999. *Conquering Diabetes: A Strategic Plan for the 21st Century*, p. 2.

⁷*Ibid.*, p. 16.

Americans will have diabetes by 2025—a 37.5 percent increase.⁸ This has led the Centers for Disease Control and Prevention (CDC) to call diabetes “the epidemic of our time.”⁹

This epidemic is also evident worldwide. According to WHO, the worldwide incidence of diabetes is expected to rise from its current level of 135.5 million to 300 million by 2025. This growth will be especially pronounced in developing countries, which are expected to see a 170 percent increase in the number of people affected with diabetes over the next 25 years.¹⁰

According to WHO’s Director-General, Dr. Gro Harlem Brundtland, these statistics “are yet another scientific testimony of a transition the world is experiencing at the moment, the transition from communicable to noncommunicable diseases. In the 21st century,” she stated, “the impact of this transition on the public health and economic sectors will be especially noticeable in developing countries.”¹¹

Severity.—Diabetes is the sixth deadliest disease in America, killing over 193,000 Americans annually. Diabetes is deadly because it affects virtually every tissue of the body with long-term and severe damage. For example, in the United States:

- Diabetes-related eye disease is the most common cause of blindness in working age adults.
- Diabetes-related kidney disease accounts for 42 percent of new cases and is responsible for 100,000 cases of dialysis and transplantation each year.
- More than 50 percent of lower limb amputations, approximately 80,000 cases a year, are caused by diabetes.
- Heart disease death rates in adults with diabetes are 2,094 times greater.
- The risk of stroke in adults with diabetes is 2,094 times greater.
- The rate of major congenital malformations and death of the fetus and newborn are 3094 times greater in a woman with diabetes.¹²

Given the systemic damage diabetes imposes, it is no surprise that the life expectancy of a person with the disease averages 10–15 years less than that of the general population.¹³

Unlike cancer and other acute medical conditions, the damage caused by diabetes typically occurs over a period of years as opposed to months. Because a person with diabetes can live with the disease for years, it creates the mistaken impression that diabetes is not serious.

Medical research has shown that careful control of diabetes can diminish the individual’s risk for developing complications. But diminished risk is not equivalent to immunity from risk. As the DRWG correctly stated, “available treatments have only limited success in controlling its devastating complications.”¹⁴

Unlike other diseases and medical conditions, the DRWG found that diabetes has not experienced a diminution in the rate at which it kills. According to the U.S. National Center for Health Statistics, the age-adjusted death rates for cardiovascular disease and stroke have each declined more than 35 percent since 1980.¹⁵

Yet diabetes has not declined. According to the U.S. National Center for Health Statistics, the age-adjusted diabetes death rate has increased more than 30 percent since 1980.¹⁶ Furthermore, people with diabetes have not benefited equally from the national decline in heart disease death rates.

A recent study published in the *Journal of the American Medical Association* found that while heart disease deaths declined 36 percent in nondiabetic men from 1971–93, they fell just 13 percent in men with diabetes. The study also found that heart disease deaths rose 23 percent in women with diabetes despite a 27 percent drop in heart disease deaths in non-diabetic women.¹⁷

Cost.—In addition to the extraordinary personal burden, diabetes exacts an equally staggering economic burden on our nation. According to *Conquering Diabetes*, the

⁸ World Health Organization. GLOBAL BURDEN OF DIABETES: WHO Projects a 170 percent Growth in the Number of People with Diabetes in Developing Countries by 2025. September 14, 1998 Press Release.

⁹ 1999 Congressional Appropriations Justification, p. 45.

¹⁰ World Health Organization. GLOBAL BURDEN OF DIABETES: WHO Projects a 170 percent Growth in the Number of People with Diabetes in Developing Countries by 2025. September 14, 1998 Press Release.

¹¹ *Ibid.*

¹² Diabetes Research Working Group. 1999. *Conquering Diabetes: A Strategic Plan for the 21st Century*, p. 2.

¹³ *Ibid.*

¹⁴ *Ibid.*, p. 1.

¹⁵ *Ibid.*, p. 2.

¹⁶ *Ibid.*, p. 2.

¹⁷ Gu, Ken, Ph.D. and Cowie, Catherine C., Ph.D., MPH and Harris, Maureen I., Ph.D., MPH. “Diabetes and Decline in Heart Disease Mortality in U.S. Adults.” *Journal of the American Medical Association*. April 14, 1999.

cost of diabetes to the nation is over \$105 billion a year. The DRWG also found that more than 1 of every 10 health care dollars is spent for diabetes.¹⁸

The federal government is held hostage to these exorbitant medical costs. According to the DRWG, about one in every four Medicare dollars pays for the health care of people with diabetes.¹⁹ A recent study found that the federal government spends more than \$40 billion a year treating people with diabetes through Medicare, Medicaid, FEHBP and veterans programs.²⁰

If this \$40 billion was returned to the taxpayers through tax relief, it would provide a \$400 rebate to every working American or nearly \$600 to every American family. It could also be used to provide computers to every public school, save Social Security or help pay down the debt.²¹

How do the economic consequences of diabetes compare to other diseases? In 1998, NIH sought to answer this question in a report titled "HHS and National Costs for Thirteen Diseases and Conditions." The data in the following table is taken directly from the report.²²

[In billions]	
<i>Disease</i>	<i>Direct cost</i>
Heart diseases	97.9
Diabetes	44.1
Stroke	28.3
Cancer	27.5
Kidney diseases	26.2
Chronic pulmonary diseases	21.6
Depression	19.9
Pneumonia/influenza	17.5
Arthritis	15.2
HIV/AIDS	10.3
Septicemia	4.9
Acute respiratory distress syndrome	2.6
Chronic liver diseases	1.2

Clearly, diabetes imposes a significant burden upon our nation's health unlike any other and meets NIH's first criteria on determining how to allocate research funding. Diabetes also satisfies NIH's second criteria, the availability of scientific research opportunities.

Scientific Opportunities

In *Conquering Diabetes*, the members of the DRWG stated their conviction that "a significant investment in research today will greatly speed progress in understanding and conquering this disease and its complications." Their Strategic Research Plan set forth two goals:

- To understand the causes and define approaches to prevent the development of type 1 and type 2 diabetes and their complications.
- To develop methods for optimal management, treatment and ultimate cure of diabetes and its complications.²³

The DRWG's Strategic Research Plan is more than a "professional judgement" budget, the documents provided to Congress each year by NIH institutes that outline the maximum amount of money that could be spent in the upcoming year. Instead, it is a peer-reviewed document that sets forth a comprehensive plan of attack against diabetes.

According to the DRWG, exciting and rapid research advances in recent years have opened the door to a new understanding of diabetes. In their judgement, the next decade offers important research opportunities that, if seized now, can vastly improve the lives of people with diabetes.

Towards this goal, the DRWG identified five areas that offer extraordinary opportunities for making genuine and significant progress toward understanding, more effectively treating, and ultimately preventing and curing diabetes:

¹⁸Diabetes Research Working Group. 1999. *Conquering Diabetes: A Strategic Plan for the 21st Century*, p. 2.

¹⁹Ibid.

²⁰Economic Consequences of Diabetes Mellitus in the U.S. in 1997. *Diabetes Care*, February 1998: 296-309.

²¹The World Almanac and Book of Facts: 1999. World Almanac Books.

²²Department of Health and Human Services. February 23, 1998.

²³Diabetes Research Working Group. 1999. *Conquering Diabetes: A Strategic Plan for the 21st Century*, p. 3.

- Genetics of Diabetes*.—Because type 1 and type 2 diabetes have strong genetic determinants, defining the specific genes involved is essential to prevention and could lead to new and better therapies.
- Autoimmunity and the Beta Cell*.—Type 1 diabetes is an “autoimmune” disease in which the body’s own defense system mistakenly attacks the insulin-producing cells of the pancreas. Aggressive pursuit of the following areas could lead to dramatic improvements in diabetes therapy and prevention: (1) Define immunological basis of type 1 diabetes and develop methods for prevention. (2) Advance research on islet cell transplantation. (3) Develop methods to stimulate beta cell growth and regeneration.
- Cell Signaling and Regulation*.—Disturbances in cell communication are central to disturbances in insulin secretion and action. The DRWG has identified five areas of opportunity that warrant increased research: (1) Dissection of insulin and hormone signaling pathways. (2) Understanding and countering insulin resistance. (3) Defining mechanisms regulating Beta cell function. (4) Understanding metabolic staging. (5) Defining alterations in signaling pathways that lead to complications.
- Obesity*.—Obesity is a major risk factor for type 2 diabetes and results from an imbalance between energy intake and expenditure. New discoveries have provided a revolutionary understanding of obesity at the molecular level, thus leading to extraordinary opportunities in research.
- Clinical Research and Trials*.—Translation of basic research into human therapies depends on an active and vigorous clinical research program. A comprehensive program for tackling diabetes requires a major investment in order to document the safety and efficacy of different therapies and to increase the knowledge base of diabetes. There are two major needs to meet these goals: (1) The creation of an infrastructure to facilitate clinical trials in diabetes. (2) A commitment to these trials as a way to increase understanding of diabetes.

In addition to these extraordinary opportunities, the DRWG Strategic Research Plan includes two additional components necessary to make significant inroads against diabetes:

- Special Needs for Special Problems*.—Equally important, but more focused research areas, targeted to specific populations, complications and methodological approaches.
- Resources and Infrastructure Needs*.—A bold plan for increasing research manpower, technology and other infrastructure elements for diabetes-related research.

Conquering Diabetes provides NIH with the “scientific opportunities that offer the best prospects for new knowledge and better health.” Furthermore, being drafted by the world’s leading diabetes researchers, it virtually assures that, if funded, NIH will be able to keep its commitment to supporting “work of the highest scientific caliber.”²⁴

NIH Funding

In addition to outlining the magnitude of the problem and the scientific opportunities available in diabetes research, the DRWG thoroughly analyzed the current federal investment in diabetes research. They found that despite the pressing public health needs and the myriad scientific opportunities available to researchers, diabetes research is significantly underfunded at NIH:

- NIH funding for diabetes research has risen from \$134 million in fiscal year 1980 to an estimated \$442.8 million for fiscal year 1999. When adjusted for inflation, however, the actual amount of growth has been only 34.4 percent over 20 years, or less than 2 percent per year.²⁵
- From fiscal year 1980–99, the diabetes research budget, expressed as a percentage of the total NIH budget, has never exceeded 4.1 percent, although diabetes-related illness amounts during the same period represented 10 percent of the health care expenses in the United States.²⁶
- Diabetes research represents less than 3 percent of the NIH research budget. Although there is generally no accepted methodology for determining appropriate levels of research funding, this is a small investment for a disease that

²⁴“Biomedical Research Priorities: Who Should Decide?” Hearing before the Subcommittee on Public Health and Safety of the Committee on Labor and Human Resources, United States Senate, May 1, 1997, p. 8.

²⁵Diabetes Research Working Group. 1999. *Conquering Diabetes: A Strategic Plan for the 21st Century*, p. 3.

²⁶Diabetes Research Working Group. 1999. *Conquering Diabetes: A Strategic Plan for the 21st Century*, p. 49.

affects 6–7 percent of the population and accounts for about 10 percent of all health care dollars.²⁷

—Relative to the whole NIH budget, the amount devoted to diabetes research has decreased by more than 30 percent since 1981, at a time when the death rate due to diabetes has increased by 30 percent.²⁸

—Diabetes research represents only about \$30 per person affected with diabetes per year—less than two people might spend for a movie and a pizza.²⁹

Based upon their analysis of the federal government's current commitment to diabetes research, the DRWG concluded that:

Although federal support for diabetes research has produced a number of major advances in the past two decades, many scientific opportunities are not being pursued due to insufficient funding, lack of appropriate mechanisms and a shortage of trained researchers. Improvements in technology and the general growth in scientific knowledge offer unprecedented opportunities for advances that might lead to better treatments, prevention and possibly a cure.

While [funding for diabetes research] has increased steadily since 1981, there is a strong consensus in the DRWG that this funding level is far short of what is required to make optimal progress on this complex and difficult problem. In fact, the current federal budget for diabetes research represents less than one-half of one percent (0.5 percent) of the annual cost of diabetes to the U.S. economy. When compared with the 5 to 15 percent budgets for research and development in other high-technology sectors, this investment in diabetes research is trivial.³⁰

Conclusion

Mr. Chairman, I have attempted to summarize the science and data of the DRWG as a demonstration that diabetes research is severely under funded by NIH despite meeting its published criteria for allocation of resources.

As the DRWG concluded, “conquering diabetes and its complications represents a formidable task.” The budgetary recommendations of the DRWG are “not only more consistent with the impact of diabetes on the U.S. population from both human and economic perspectives, but is what would be required to have a robust and effective diabetes research effort—one which will reduce the rising burden created by this debilitating disease.”³¹

The American Diabetes Association strongly urges Congress to fully fund diabetes research at \$827 million, the amount recommended by the DRWG. We also urge Congress to ensure that the DRWG Strategic Research Plan is fully implemented by NIH throughout fiscal year 2004.

On behalf of the 16 million Americans with diabetes, I appreciate this opportunity to testify.

[Attachment 1]

ORAL TESTIMONY OF DORIS GILBERT, REPRESENTING THE AMERICAN DIABETES ASSOCIATION BEFORE THE HOUSE APPROPRIATIONS SUBCOMMITTEE ON LABOR, HHS AND EDUCATION

Mr. Chairman and members of the subcommittee, my name is Doris Gilbert. I live in Los Angeles, California and I am here representing the American Diabetes Association and the 16 million Americans with diabetes.

Thank you for having me here to tell about our family's experiences with diabetes.

17,000 shots! That's how many insulin injections my child took to stay alive, starting at age 6. It didn't save her. At 28 Laurie was dead from complications of 22 years of diabetes.

What is diabetes, anyway? It's a long-term condition in which if you take your insulin shots, or for adult onset diabetes, follow your diet, and if necessary, take medication, you'll be fine. Right? Wrong!

²⁷Diabetes Research Working Group. 1999. *Conquering Diabetes: A Strategic Plan for the 21st Century*, p. 3.

²⁸Ibid.

²⁹Ibid.

³⁰Ibid.

³¹Diabetes Research Working Group. 1999. *Conquering Diabetes: A Strategic Plan for the 21st Century*, p. 118.

At diagnosis when we learned the techniques and were told Laurie could live a normal life, we thought, being responsible parents * * *. We'll handle this and it'll be just fine. It just didn't end up that way.

What's it like for a parent living with a child with diabetes? At 7 I had to comfort her when her close friend told her she couldn't invite her to her birthday party because, "You might feel bad since you can't have cake, or you might get sick, or something." There was always an undercurrent of fear that she would have a sudden disabling low blood sugar reaction while alone.

At 12 she had numerous hospitalizations. Parents expect their children will get sick—and then get better. That's the way it always was. But once she was rushed to intensive care, and I remember staring out of the window, confronting for the first time that our child might die!

In her late teens she suffered from severe retinopathy, one of the common long-term complications which can lead to blindness. Once I watched the anesthetic preparation for a large amount of laser surgery. That 1½-inch needle looked 6 inches to me, and seeing it stuck in her eye made me cry.

What was Laurie like? She passionately wanted to make a difference in the world. She was an original, unforgettable. The creative urge enveloped her and she pursued her passions voraciously finding a voice to speak to the world.

In high school the discovery of art photography thrilled her. In college she wrote, published, directed, acted, devouring every opportunity she could, graduating with a degree in art and theater. She was sensitive, emotional, loving, insightful, a little outrageous, charismatic; she made us laugh!

At age 22 the long-term complications of diabetes began to become pronounced and initiated a protracted, miserable deterioration of health the last 5 years. Each year's birthday message was a variation on a theme. At first: "We're sure this will be a better year for you." Later—"We hope * * *." It never was.

Being admitted to the graduate program in screenwriting at UCLA realized a dream. The quarter began, and she lay in the hospital. Then she struggled to catch up. Increasingly she suffered from retinopathy, neuropathy, kidney and liver disease, severe hypertension, depression, and worst of all, gastroparesis, for her extremely painful and utterly debilitating. Flare-ups and hospitalizations happened over and over until she was just too ill to continue.

Rather than giving more depressing details, I'll let the hospital record tell the story. 1995—116 days in the hospital, 1996—156 days. 1997—she began the year in the hospital and never left alive. 28 years old! What a waste!

Laurie wanted so to leave her mark on the world. If her story can convince Congress to firmly commit to improving and saving the lives of thousands of people like Laurie with diabetes through research, she will continue to meet her aim to make a difference.

On behalf of the American Diabetes Association, and Laurie Gilbert, I strongly urge you to fully fund diabetes research this year at \$827 million. Thank you.

[Attachment 2]

TESTIMONY OF FREDERICK J. SPERLING BEFORE THE SUBCOMMITTEE ON LABOR,
HEALTH AND HUMAN SERVICES, EDUCATION AND RELATED AGENCIES

Chairman Porter, Members of the Subcommittee, sitting next to me is my ten-year-old daughter, Susan, who was diagnosed with insulin dependent diabetes just over three years ago. I still remember that first terrifying day after she was diagnosed when she was in intensive care and we feared for her life. But after she overcame this immediate threat, we learned about the more insidious threat posed by diabetes. As you know, diabetes—which afflicts more than 16 million Americans—is the leading cause of blindness, kidney failure, and amputation and a major contributor to stroke and heart disease. On average, diabetes shortens life expectancy by 15 years. Yet, by any objective measure, diabetes has not received its fair share of the NIH research budget.

Mr. Chairman, as you have recognized, funding decisions should be based on the number of people affected and the cost to our society. Our nation spends more than \$137 billion each year on diabetes and its complications, and the federal government alone spends more than \$40 billion on diabetes—one out of every four Medicare dollars. But only approximately one percent of that \$40 billion—less than three percent of the NIH budget—is spent on diabetes research. To put this in perspective, diabetes kills twice as many people per year as breast cancer and AIDS combined, yet it receives less than one-seventh of the research dollars devoted to these two diseases.

The last decade has been nothing short of a disaster for diabetes research. While the NIH budget increased by more than 100 percent, funding for diabetes research increased by only 35 percent. Because this was less than the rate of inflation for biomedical research, funding for diabetes research is actually worse off now than it was a decade ago. If funding for diabetes research had only kept pace with the growth of the overall NIH budget, nearly \$1 billion more would have been devoted to diabetes research over the past decade. Although this is a time of extraordinary opportunity for diabetes research, many researchers have left the field because of the lack of adequate funding.

The recently released report of the congressionally established Diabetes Research Working Group characterizes the government's commitment to diabetes research as "trivial." Why is this so? Perhaps in part because diabetes wreaks its havoc slowly, over years and decades, rather than immediately. Perhaps also because the members of the diabetes community have been too quiet and well behaved—they haven't disrupted meetings with tactics like shouting and spilling blood as advocates for research on other diseases have done. But I hope we can all agree that these methods should not dictate the biomedical research priorities for our country.

Even if you put aside the untold suffering and shattered lives caused by diabetes—if you only consider the economic cost to our society—the dividend in saved lives and dollars that a cure would yield makes diabetes research the best investment NIH could possibly make.

On behalf of my daughter Susan and the more than 16 million other Americans who are at risk for the serious complications that all too often occur, I ask that you implement the recommendations of the Diabetes Research Working Group that diabetes research be funded for the coming fiscal year at \$827 million rising to \$1.17 billion by fiscal year 2004. With adequate funding, the scourge of diabetes could be laid to rest within a decade. If our nation could send people to the moon and bring them back safely, surely we can do this as well.

To my continual amazement, through all the travails of the last three years—all the injections and all the rest—my daughter has never once asked "Why me?" or complained that "It's not fair." But she does have a dream. Her dream is to be among the first generation of people who have had diabetes and have been cured. And my dream is that we find a cure for her and the millions of others in our nation who fight the battle of diabetes every day before it takes its relentless toll and cuts short their lives. We ask no more than that you follow your own objective standards and—based on the number of people affected and the cost to our society—that you devote the resources necessary to find the cure for diabetes that is tantalizingly within reach.

DIABETES

Senator SPECTER. Just one brief comment before turning to our next witness. In our report last year, page 99, we said, "Diabetes affects 16 million Americans, leading cause of blindness, kidney disease, and heart disease." We went on to say that the committee further encourages increased research into the causes and treatments of juvenile diabetes.

If you are complaining that Dr. Varmus has not paid attention to you, you have company, but when we made that point as to diabetes, we made the point as to virtually every other ailment which has been called to our attention, but I appreciate your testimony.

STATEMENT OF DR. STEPHEN SPECTOR, MEMBER OF THE BOARD, AIDS POLICY CENTER FOR CHILDREN, YOUTH, AND FAMILIES

Senator SPECTER. I want to turn now to Dr. Stephen Spector. He has a very distinguished name.

Dr. SPECTOR. It is misspelled, though, Senator. [Laughter.]

Senator SPECTER. The reason you have a very distinguished name is because my son's name is Stephen, but he and I spell Spector differently. We spell it "er" and you spell it "or," but my Uncle Joe spelled it "or," too, he and his brother, Harry Spector.

My father spelled his name differently from—Spectorski, coming from a small town in the Ukraine, which we will not delve into fur-

ther, but we appreciate your being here, Dr. Spector. You represent the AIDS Policy Center for Children, Youth and Families. You are a professor of pediatrics at the University of California at San Diego, an M.D. from Tufts Medical School, and have been singled out consistently of those who come to argue for more money, the pro rata share for people who have AIDS, and why do we not have the same amount. If we gave diabetes the same it would be off the charts.

Dr. Spector, what is the justification for the pro rata high share for AIDS research?

Dr. SPECTOR. Thank you very much. Chairman Specter, and members of the subcommittee, thank you for inviting me to appear this morning. I am Dr. Stephen Spector, and I am testifying as a member of the Board of the AIDS Policy Center for Children, Youth, and Families.

I am a Professor and Vice-Chairman of the Department of Pediatrics at the University of California, San Diego, and Chair of the Executive Committee of the Pediatric AIDS Clinical Trials Group, PACTG. PACTG is the leading clinical research group in the world, dedicated to the prevention of mother-to-infant transmission of HIV, and improves strategies for treatment of HIV-infected children and adolescents. It is funded through the NIH.

The PACTG has been responsible for carrying out studies, demonstrating the transmission of HIV from an infected pregnant mother to her infant can be dramatically decreased by ACT treatment. It has been responsible for establishing new treatments for HIV-infected children, and for having changed HIV infection of children from an invariably fatal disease to a chronic illness.

I appreciate the opportunity to discuss the methods by which NIH allocates resources among the many disease research priorities and opportunities.

There are fundamentally three different categories of research that require support, basic science, studies of pathogenesis or transnational research, and clinical research, including clinical trials, epidemiology, behavioral, and social science research. An important quality of research at the basic transnational and clinical level is often what is observed in one area has broad implications for other areas of human illness.

Researchers from multiple disciplines must be encouraged to cross boundaries in order to provide the scientific synergies that are necessary to solve complex problems. Additionally, the ability of scientists to rapidly transition from basic research to clinical application provides the greatest opportunity for preventing and treating human illness. This is particularly true for research involving AIDS and HIV.

As an example, the ability of chemists to isolate protein crystals enable researchers to identify the crystal structure of an important HIV protein, the protease. With the knowledge of the crystal structure, drugs were developed that specifically inhibit the HIV protease.

These drugs have formed the cornerstone of new combination therapies that have significantly slowed the progression of HIV-related disease in adults and children. Moreover, these drugs often reverse the immunologic defects caused by HIV infection.

In HIV-infected children, as their immune systems have improved, we have come to a surprising realization. That is, we do not know in many situations what constitutes the normal immune response of healthy children. Thus, in order to evaluate the reconstituted immune system of HIV-infected children, we will also learn what constitutes a child's normal immune response. This knowledge will help us to better treat childhood cancers, congenital immune deficiencies, immature infants, as well as others.

Additionally, as potent combination therapies have been used in HIV-infected individuals, these same treatments are being given to HIV-infected pregnant women. Preliminary findings indicate that these combination treatments are even more potent than AZT by itself in interrupting transmission of HIV from a pregnant woman to her infant.

In addition to providing new knowledge of the normal immune system of adults and children, drugs that have been developed for the HIV infection and its complications have also found uses for treatment of other infections, including Hepatitis B, Hepatitis C, cytomegalovirus, herpes simplex virus, and many others. Patients with cancer, patients receiving transplants, including heart, lung, liver, and bone marrow, patients who have central nervous system diseases, and others have all benefited from the advances that have been made by AIDS research.

How NIH allocates resources among the many research priorities and opportunities is multi-factorial and must provide room for flexibility such that NIH is able to take advantage of emerging research opportunities and to fund the highest caliber science. This must be done within the context of responding to public health needs, and the taking advantage of those opportunities that have the highest likelihood of success while continuing to explore areas requiring fundamental advances.

Additionally, the world looks to the leadership of the NIH to provide new scientific insights in approaching new treatments and prevention of diseases, including tuberculosis, parasitic infections, and AIDS. We are a global society, and NIH-funded research must reflect global disease.

Senator SPECTER. Dr. Spector, your full statement will be a part of the record. If you could conclude by summarizing, we would appreciate it.

PREPARED STATEMENT

Dr. SPECTOR. In summarizing, I believe that NIH must be responsive to public health concerns, NIH must fund a broad range of basic transnational and clinical research, and NIH must have the resources and flexibility to take advantage of rapidly changing research opportunities.

I thank you for the opportunity to speak, and I will answer any questions you may have.

Senator SPECTER. Thank you very much, Dr. Spector.

[The statement follows:]

PREPARED STATEMENT OF STEPHEN A. SPECTOR

Chairman Specter and members of the subcommittee, thank you for inviting me to appear this morning. I am Dr. Stephen Spector and it is an honor to testify today

as a member of the board of directors of AIDS Policy Center for Children, Youth and Families.

AIDS Policy Center was founded in 1994 to help respond to the unique concerns of HIV positive and at-risk children, youth, women and families and their service providers. The Center conducts policy research, education and training for consumers and providers on a broad range of HIV/AIDS prevention, care and research issues. Affiliates include over 500 community-based organizations in 27 states, D.C. and Puerto Rico.

In addition, Mr. Chairman, I am a Professor & Vice-Chairman of the Department of Pediatrics at the University of California, San Diego, and Chair of the Executive Committee of the Pediatric AIDS Clinical Trials Group (PACTG). The PACTG is the leading clinical research group in the world dedicated to the prevention of mother-to-infant transmission of HIV and improved strategies for the treatment of HIV-infected children and adolescents. It is funded through a joint effort of the National Institute of Allergy and Infectious Diseases and the National Institute for Child Health and Human Development.

The PACTG has been responsible for carrying out the studies demonstrating that transmission of HIV from an infected pregnant mother to her infant can be dramatically reduced by AZT treatment, for establishing new treatments for HIV-infected children and for having changed HIV infection of children from an invariably fatal disease to a chronic illness.

I appreciate the opportunity to discuss the method(s) by which the National Institutes of Health allocates resources among the many disease research priorities and opportunities. In the broad perspective there are fundamentally three different categories of research that require support: basic science, studies of pathogenesis or translational research, and clinical research including clinical trials, epidemiology, behavioral and social science research. I would like to spend a few moments discussing each of these areas.

Basic research is the driving force behind new advances and most importantly new conceptual breakthroughs in biomedical science. By its very nature, it is unpredictable. By exploring what is unknown, basic research challenges what is known and questions long held dogma. It is most responsible for having revolutionized science in the twentieth century and will certainly impact on every facet of our lives in the centuries to come. Perhaps most importantly, the implications often cannot be predicted and frequently lead to significant benefit in areas far afield from the intent of the original research.

As basic research has become more complex, the challenge is often to recognize the potential implications of basic research to questions specifically relating to human disease. This research, most recently termed translational science, extends the findings of basic science in an attempt to understand how a disease is caused or to how an illness can be identified or monitored. It attempts to understand why patients have the symptoms that they do. Translational research often generates questions and important new approaches for clinical researchers. Thus translational research bridges the gap between basic science and clinical research.

Clinical research evaluates novel approaches for the detection, treatment or prevention of disease. The best clinical research is tightly linked to basic and translational research. Importantly, clinical research not only develops new treatments and prevention strategies, but also generates new questions that must then be examined by laboratory based scientists. Clinical research often, like basic science, overturns dogma in its search for the truth.

An important quality of research at the basic, translational and clinical level is that often what is observed in one area has broad implications for other areas of human disease. Researchers from multiple disciplines must be encouraged to cross boundaries in order to provide the scientific synergism necessary to solve complex problems. Additionally, the ability of scientists to rapidly transition from basic research to clinical application provides the greatest opportunity for preventing and treating human illness. This is particularly true for research involving AIDS and HIV. For example, the ability of chemists to isolate protein crystals enabled researchers to identify the crystal structure of the HIV protease. With knowledge of the crystal structure, drugs were developed that specifically inhibit the HIV protease. These drugs have formed the cornerstone for new combination therapies that have significantly slowed the progression of HIV-related disease in adults and children.

Moreover, these drugs have often reversed the immunologic defects caused by HIV infection. In HIV-infected children, as their immune systems have improved we have come to a surprising realization. That is, we do not know in many situations what constitutes the normal immune response of healthy children. Thus, in order to evaluate the reconstituted immune system of HIV-infected children, we will also

learn what constitutes a child's normal immune response. This knowledge will help us to better treat childhood cancers, congenital immune deficiencies, premature infants as well as others. Additionally, as potent combination treatments for HIV-infected individuals have become available, these same treatments are being given to HIV-infected pregnant women. Preliminary findings suggest that these new treatments are more effective than AZT alone in decreasing the transmission of HIV from a pregnant woman to her infant.

In addition to providing new knowledge of the normal immune system of adults and children, drugs that have been developed for treatment of HIV infection and its complications have also found uses for treatments of other infections including hepatitis B, hepatitis C, cytomegalovirus, herpes simplex virus and others. Patients with cancer, patients receiving transplants (including heart, lung, liver, kidney and bone marrow), patients with genetic disorders (such as those with sickle cell anemia), patients with diseases of the central nervous system (such as those with Alzheimer's disease, dementia and multiple sclerosis) have benefited from advances made by AIDS research.

How NIH allocates resources among the many disease research priorities and opportunities is multi-factorial and must provide room for flexibility such that NIH is able to take advantage of emerging research opportunities and to fund the highest caliber research. This must be done within the context of responding to public health needs and to taking advantage of those opportunities that have the highest likelihood of success while continuing to explore areas requiring fundamental advances. Additionally, the world looks to the leadership of the NIH to provide new scientific insights and approaches to the treatment and prevention of diseases including tuberculosis, parasitic infections and AIDS. We are a global society and NIH funded research must reflect global diseases. There is no road map for science so that many different approaches often involving many different disciplines is required to address the most challenging questions. Even then, the fundamental breakthrough often comes from totally unrelated projects and insights.

As a biomedical researcher and a pediatrician who specializes in infectious diseases, I am concerned by the suggestion of some that a mathematical formula could be used to determine research budgets for specific diseases. These models invariably reduce funding for children and pregnant women. Moreover, they fail to seize the research opportunities that can lead to the rapid development of strategies for disease prevention and treatments. Much has been learned from research that was first performed in children. The advances in childhood leukemia have been applied for the treatment of adult cancers. Similarly, the demonstration that the transmission of HIV from an infected pregnant mother to her infant could be interrupted through AZT treatment led to studies that demonstrated that similar approaches can decrease infection following needle stick exposure and have generated interest in the concept of other post-exposure prophylaxis. Additionally, history has taught us that as an infectious disease declines, if we become complacent and decrease funding for research, there is a resurgence of that infection. The recent resurgence of tuberculosis as a major health problem is one such example.

The multi-disciplinary nature of AIDS requires a coordinated effort. The Office of AIDS Research is a critical component to the successful prioritization and planning of NIH's AIDS research budget. The OAR must have the resources necessary to lead NIH's HIV/AIDS program. The PACTG intends to work closely with the OAR to develop future research priorities and initiatives, including vaccine and other prevention research and international priorities.

Further, AIDS Policy Center for Children, Youth and Families and the National Organizations Responding to AIDS Coalition support increased funding for AIDS research in the context of an overall increase in our nation's investment in research. We support a 15 percent increase for the NIH overall in fiscal year 2000 and a commensurate increase for AIDS research.

In summary, I believe that: NIH must be responsive to Public Health concerns; NIH must fund a broad range of basic, translational and clinical research; and NIH must have the resources and flexibility to take advantage of rapidly changing research opportunities.

Thank you again for the opportunity to speak to the subcommittee. I will be pleased to answer any questions.

STATEMENT OF BRAD MARGUS, PRESIDENT, AT CHILDREN'S PROJECT

Senator SPECTER. We now turn to Mr. Brad Margus. He is President and co-founder of the AT Children's Project. AT stands for ataxia-telangiectasia, a very rare genetic illness.

Mr. Margus has had the unfortunate personal experience of having two young children with AT, this is the so-called Orphan's Disease, and we have asked him to come here because it is an ailment which affects relatively few people, but obviously is very important. The issue is whether it is adequately funded, and this so-called Orphan's Disease is representative of many like it where NIH has to allocate resources on Orphan Diseases, such as hard cancer, Parkinson's, et cetera.

Mr. Margus, we appreciate your being here, and the floor is yours.

Mr. MARGUS. Thank you for allowing me to come today. I really appreciate it. I am definitely not a physician or a scientist, but as you know, about 5 years ago I was just a businessman in the shrimp business and my wife and I learned that two of our little boys had a disease, AT, ataxia-telangiectasia, as very few people can pronounce. It is a brutal disease.

Usually kids are normal until about the age of two, when they become wobbly and have slurred speech. Then they stay that way until about the age of eight when the loss of muscle control becomes much more obvious, and they begin to lose control of their legs and their arms, and eventually their eyes, and swallowing. My two boys Jarett and Quinn are now eight and ten. The eight year old, Quinn, is still walking; the ten year old is now in a wheelchair.

Besides losing muscle control and usually dying in their teens, AT kids, most of them have immune deficiency. On top of that, quite a few develop diabetes. Several have premature aging facets of the disease, and if that is not bad enough, about 40 percent of the kids develop cancer, usually leukemia or lymphoma.

On top of that, though we do not really care about it, in light of our family situation, we have also learned that AT carriers, like my wife and me, and probably some of you in this room, we do not know if you are, AT carriers have a higher likelihood than healthy people of developing some kinds of cancer.

Our family was devastated. It is an Orphan's Disease. I think the definition of an Orphan's Disease is something like less than a hundred-thousand cases, or something like that, but with AT we have only been able to find a little over 300 patients in the U.S., and that is not per year, but that is in total.

So we formed an organization called the AT Children's Project, and in the last 5 years have tried to raise a lot of money, accelerate research of the disease by having conferences, workshops, funding research grants, organizing cell banks and tissue banks to make it possible to share re-agents with other scientists.

Along the way we have established the Clinical Center for AT at Johns Hopkins and a cancer center at St. Jude's. Besides doing these things, the research has paid off. We pretty early on were able to identify the gene that causes AT. Of course, you would say, why in the world would anybody give a dollar to AT at NIH based on what we just heard about 16 million people with diabetes, and everybody with all the other diseases, but what is interesting, when that gene was found, they found out some interesting things about.

First of all, the protein that it encodes the instructions for, that protein plays a really important role in the cells of all people in

controlling their copy and divide cycle of the cell, and it activates or acts on another protein called p53, which is a very famous protein that has found to be misspelled in the majority of cancerous tumors. They just recently found that in the tumors of people with two types of leukemia and one type of B-cell lymphoma, the AT gene is misspelled. Very recently they found out that with the AT mice that we were able to develop that those mice are losing dopaminergic neurons, the same part of the brain that produces dopamine, that is important in Parkinson's, and that Parkinson's patients do not have, and they found that is true with AT mice as well.

So as you can see our rare disease suddenly is pretty big news in the science world, and suddenly our obscure little problem is now scientifically very intriguing, although at the same time all that complexity makes it really frustrating for us.

Our strategy, therefore, has not been to really pound Congress or lobby intensively to get funding for AT, but instead to try to engage scientists anywhere to think about AT, to know what AT is. At our workshops we always try to bring people from totally diverse fields in order to make them keep AT on their mind. If science and discovery really favors the prepared mind, then we want to have as many scientists in the world working on diabetes and cancer at least aware of AT so if they find something in a lab that could help AT kids, that would happen.

NIH is something I am eager to talk about. I am obviously not qualified, and as much as you might want me to, I would not dare take shots at Dr. Varmus, but at the same time I am a businessman, I think I have—

Senator SPECTER. We do not want you to. You might want to compliment him. You can say whatever you please.

Mr. MARGUS. This is definitely a golden opportunity to suck up to the NIH. [Laughter.]

If you want to ask me questions, there are things that I have observed, and I think as a businessman I would say that some of them are operational things that should be left to NIH directors; on the other hand, there may be sometimes, in business and perhaps at the NIH, where the board of directors, or in this case, congressional oversight could help Dr. Varmus make some changes that he himself or the NIH itself cannot make.

Those might be very large structural changes or re-engineering, or completely changing certain areas of the NIH that it is tough for a politically sensitive man to change by himself.

Some of those areas might include the world today of intramural programs compared to what it was supposed to be when it was started, some overlap with other areas that fund the same kinds of research, how the peer review is done, whether some institutes are still merited, or if they should be merged or broadened. There are a lot of things like that I would be glad to talk about here today.

The last point that I want to make is that, I do not know if NIH can ever do this, but please keep in mind that outside of Washington people like me before a disease entered my life do not know too much about what NIH is or what it does.

PREPARED STATEMENT

After you have stuck around here awhile where you have worked with NIH researchers a lot, you think about them all the time, and you realize the magnitude of all the diseases, all the ways of dealing with them, from education, to basic research, and the magnitude is amazing, and it is awesome, and the science that I have learned about from microbiology and the revolution in genetics is truly amazing, but for most of us outside Washington, Americans do not have a clue of what NIH is doing, and do not appreciate what it means to them personally, and I think some of the committees and councils that have been formed are good, but we probably have enough of those, and we do need to somehow to get the people in America to realize even if they are healthy that NIH funding really will impact their lives. I have some ideas about that, too.

Thanks again for inviting me.
[The statement follows:]

PREPARED STATEMENT OF BRAD MARGUS

Mr. Chairman and Members of this Sub-committee, my name is Brad Margus, and I can't tell you enough how much of an honor it is to have been invited to speak to you today. I am neither a scientist nor a physician. I am just a businessman and a father who in the last few years has come to appreciate the rapid advances taking place in medical research and the tremendous contribution our country is making to the health of the world by funding the National Institutes of Health. I certainly do not deserve to sit alongside the distinguished experts who will be addressing you after me today, but I nevertheless hope that you will find my perspective thought provoking.

My Family

About five years ago, I knew nothing about serious diseases, nothing about molecular biology and nothing about how my government spent money on research. I lived in Florida with my wife and three little boys, and I ran a shrimp processing company. Then one day, my wife and I learned that two of our young sons—Jarrett and Quinn—had been diagnosed with an extremely rare, obscure and brutal disease called ataxia-telangiectasia, or "A-T" for short.

A-T

That diagnosis was devastating. If you were to imagine a disease that combines the worst symptoms of muscular dystrophy, cystic fibrosis, immune deficiency and cancer into one disorder, you would be thinking about A-T. Children with A-T seem normal until they reach the age of two, when their walk becomes a little wobbly and their speech becomes slurred. Most of the time, they are misdiagnosed as having a mild cerebral palsy until a few years later when the progressive loss of muscle control and other symptoms become more obvious, or when another sibling is born with the same symptoms and it becomes clear that the problem is genetic.

By the age of nine or ten, A-T kids are dependent on wheelchairs. My son Quinn, who is eight, is still able to walk, but Jarrett, who is ten, cannot. Soon my boys, like other A-T children, will lose the ability to control their eyes for reading and will not even be able to feed themselves. Swallowing and coughing will become difficult for them and will probably cause lung problems that will ultimately contribute to their deaths.

In addition to the brain deterioration that makes children with A-T lose control of their muscles, most A-T children also have deficient immune systems, making them vulnerable to infections.

Diabetes is also quite common. And, there's still more. About forty percent of A-T children develop cancer, usually leukemia or lymphoma. Even if they escape the cancer, most children with A-T are completely debilitated by their mid-teens and die in their late teens or early twenties.

Like most diseases, A-T does not just affect the patients who have it. The disease has a tremendous impact on everyone in my family. Most A-T families like mine would tell you that they are perpetually exhausted from the efforts they must expend for everyday living and that they continuously struggle to keep their spirits up for their kids. As a father, the toughest part for me is knowing how much poten-

tial my bright sons were born with and knowing that today, we have no way to stop this disease from robbing my sons of their dreams and futures.

Besides the way A-T affects children with the disease, carriers of this disease, like my wife and me, appear to be at a higher risk than the general population of developing cancer.

The A-T Children's Project

Shortly after learning that our boys had A-T, my wife Vicki and I started a non-profit organization called the A-T Children's Project. During the last five years, we have done what many small disease organizations do, raising money through numerous grass-roots approaches such as walkathons, dinners and auctions. Then, with guidance from a respected board of objective scientists who themselves do not work on A-T, we have awarded this money to researchers around the world. Our grant decisions are made rapidly, and the awards are often used by scientists as "seed money" to support preliminary studies before the researchers can apply to the NIH for additional support.

Besides helping researchers with funding, we have also established tissue and cell banks so researchers who are interested in studying A-T can easily obtain patient tissue or DNA. And, to encourage collaborations and to generate new research strategies, we have held at least two scientific workshops or conferences each year, making a special effort to involve new scientists from diverse fields rather than just the same researchers who have been working on A-T all along.

A-T Research's Relevance to More Common Diseases

Early on, we funded research that led to the identification of the defective gene that causes A-T in children who inherit it. As a result, we now know that this gene, called "ATM," plays an extremely important role in the cells of healthy people. When working correctly, ATM instructs cells to make a protein that monitors DNA damage and coordinates the cell's response to that damage. This protein also interacts with many other proteins that are involved in the cell's copy-and-divide cycle, such as p53, a famous tumor-suppressor gene that has been found by cancer researchers to be damaged in the majority of tumors. Other researchers have recently published that the A-T gene has been found to be misspelled in the tumors of most patients with a particular form of leukemia, called "T-PLL," as well as a type of B-cell lymphoma. The cells of A-T children have also been found to have shortened telomeres, the ends of chromosomes that are known to shorten with aging.

More recently, we have helped several separate labs use genetic engineering to develop "A-T mice" that have many of the same symptoms seen in A-T kids. Two of these laboratories have now found that dopaminergic neurons—the same brain cells that are known to die in people with Parkinson's disease—are dying in the A-T mice.

As a result of these findings, my sons' previously obscure disease has now become very well known by scientists working on cancer, neurodegeneration and aging. I hope these scientific results demonstrate to you how research on a rare disease can benefit many more common diseases. And, I think this may also indicate that allocating funds to research based only on the number of people with the condition may not always be the smartest approach.

Sure, I would love to have you establish an RFA to set aside a billion dollars for A-T. But I have also tried to study the history of significant medical discoveries, and history teaches that the most important medical breakthroughs typically have critical roots in unrelated basic breakthroughs. Research on A-T would not be where it is today—honing in on pathogenesis—if it were not for many major background advances in molecular biology, stem cell biology, and neurobiology.

Today, we continue funding numerous research projects that try to figure out the function of the A-T gene and the corresponding protein that is missing in children with the disease. And besides funding, we have urged labs to share reagents, such as antibodies that have been raised against the human and mouse versions of the A-T gene.

We have also established an A-T Clinical Center at Johns Hopkins Hospital in Baltimore, as well as an A-T Cancer Clinic at St. Jude's Children's Research Hospital in Memphis. And this past year, we funded a small clinical trial that tested a drug on A-T children that had appeared to help the mice. The drug did not work any better than a placebo, but just reaching a point where we could apply a scientific discovery in a clinical setting was an important milestone for us.

Our Research Strategy

Unfortunately, we still do not have a single treatment that will slow the progression of this terrible disease in A-T children like my sons. Although we are clearly desperate for a cure, we have refrained from becoming bitter or irrational toward

the research establishment, although I fully understand why some parents do. Instead, we have channeled our energies into making as many scientists aware of this disease as possible. As I see it, because one can never predict from which area the next breakthrough will come, it is a good strategy to make sure that if an investigator discovers something that could help A-T children, they think of A-T right away.

The NIH

Early on, I began learning about the National Institutes of Health and about all the money it spent each year. Although I really wasn't sure what "lobbying" was, I visited Members of Congress and their staffs in hopes of persuading them to direct the NIH to shift some of those huge amounts of money toward research on A-T. But I also began visiting the scientists themselves at the NIH and quickly sensed that they resented having Congress dictate their funding priorities. From listening to the NIH leaders, I grew to believe that set-asides for diseases might by themselves not accelerate research progress on my disease. Instead, I decided, faster progress might be achieved by doing my homework first, and then visiting first-rate scientists and convincing them that working on A-T might not only eventually help A-T children, but presented the opportunity to make significant discoveries in biology that could impact many diseases. Through these visits, I was often able to persuade great scientists—who didn't even need my funding—to begin an experiment or two looking at some facet of A-T. And, I learned that money isn't the only way to engage a good scientist on my disease.

During the last year, my organization has worked more closely with the NIH than ever. We have held conferences together, compared notes on research ideas on A-T proposed by investigators, and Dr. Varmus was even kind enough to allow me to sit in on his advisory committee for one meeting. From this exposure to the workings of the NIH, I have developed a tremendous appreciation for the magnitude of the problems being tackled. Because A-T affects so many systems in the body, and because the obstacles to research progress on A-T are now often the same obstacles to progress faced by researchers working on more common diseases, I continue to keep a close eye on many NIH institutes. And, I frequently consider what might be changed to improve it.

Possible Improvements to the NIH

Perhaps here in Washington, it is easy to take it for granted, but for someone like me to be invited to speak before a Senate hearing in our nation's capital is an unbelievable experience and an opportunity I did not want to squander. Therefore, when I was called last week about speaking to you today, I began putting together a list of everything I wanted to say about the National Institutes of Health.

In particular, I wanted to bring up possibly needed changes that the NIH leadership would not be able to bring about by themselves—changes that I believe Congress would have to initiate. Some of my comments would probably sound naive to you; after all, I am neither a scientist nor a physician but a businessman from the for-profit world where things are often done differently. And, I would undoubtedly step on some toes, particularly if I suggested phasing out or reinventing the NIH intramural program, or if I proposed that because of the convergence of the scientific bases of disease, certain institutes should be eliminated or merged to cut administrative redundancy. I also have delicate questions about the funding overlap between the NIH, the National Science Foundation, the Veteran's Administration and the Defense Department and the increased bureaucracy undoubtedly created by having these different entities funding similar research. And, I have doubts about the level of rigor applied to reviewing grants for "politically correct" diseases that have been "fast-tracked" for funding.

Most of my concerns, however, would be about helping scientists. For example, basic researchers need more core services that are reliable and fast. A great deal of time and money is spent in different labs, duplicating efforts on generating reagents. Once a gene, like the A-T gene, is cloned, a full length cDNA must be made, antibodies generated, mutants made, expression patterns discovered, and so on. I think this could be systematically done for all genes by a central facility linked to the human genome project. Thus, scientists would spend more time investigating the function of the genes than developing reagents (developing these reagents for A-T research took much longer than I had hoped). This would be a tremendously cost effective way to speed scientific discovery for many diseases. It would give us a great "bang for the buck." But, the NIH itself probably is not up to imposing the organization that would be needed to carry out such an effort.

For example, the new "DNA chip" technologies for studying gene expression on a large scale have significant entry costs that can be absorbed by a larger group

sharing these kinds of facilities. I have heard that the NIH intramural program has cut a deal with a biotech company to make this technology available to individual investigators in the intramural program—but why not the extramural science world?

Another core service that is needed is for transgenic animals. Federally funded Jackson Labs is the most valuable resource in the world for mouse work, but I keep hearing that they are overwhelmed by the numerous mouse models being made these days. Making and characterizing a mouse takes a minimum of one to two years. Maintaining mouse colonies is expensive for individual labs, and it restricts a researcher's ability to obtain important mice quickly.

I have also wondered whether or not the NIH should put more effort into enforcing the existing policy that reagents generated using NIH funds which have been published must be provided to researchers for non-commercial use without strings attached. So many NIH-funded researchers do not comply with this policy.

There are some excellent examples of services that the NIH has provided to the research community. The work done by the NCBI on the DNA sequence database (GenBank) and the medical literature database (MedLine) demonstrate how government investment in a shared resource helps a much larger group of scientists make medical research move more quickly.

It is also important to me that new areas of study that hold promise for A-T children, such as neural stem cell research and nuclear transfer, are addressed quickly but are not restricted with broad stroke legislation simply because the ethical implications are complicated.

In addition, the NIH needs a creative way to attract the best investigators (who are also the most time-constrained) to participate on study sections in the grant review process, because we don't want second- or third-tier scientists calling the shots.

But, Dr. Varmus is obviously the person who is qualified to discuss these concerns, not me. And all of his institute directors have numerous advisors who regularly provide insightful advice on these kinds of things. Frankly, I'm probably not qualified to speak on these things. And, based on what I have heard from many scientists, the NIH is doing a much better job today than ever before of policing itself and of being responsive to the extramural scientific community. For example, I have repeatedly heard positive comments about the triage system implemented by the NIH. Clearly, the competing demands are incredibly large, and the decisions that have to be made are extremely difficult.

So instead, there are just two areas I would like to emphasize with you today.

1. *Save Clinical Research Centers at Academic Hospitals.*—First, I would like to urge you to increase your emphasis on “translational” research, the popular buzzword these days that refers to transferring basic scientific discovery from the lab bench to the clinical setting. The NIH, the Howard Hughes Medical Institute—everyone—seems to be talking about it, and as a parent waiting for a treatment to save my sons, I am wholeheartedly in favor of it. But I'm not sure what is really being done about it.

Translating the exploding knowledge from basic science to clinical relevancy is very difficult. I know from organizing my own scientific meetings that it is hard to find good physician-scientists who can straddle both worlds, bringing a good research background and scientific understanding, and creativity, to treating patients.

But even more urgent than finding these special kinds of research physicians is the need to keep our academic medical centers financially viable so that they can continue their academic pursuits instead of forcing them to compete with community hospitals to survive.

Because of managed care, academic institutions don't seem to be supporting physician scientists the way they did in the past. As a result, I believe there is a growing gap between funding of basic research and funding for drug development and clinical trials. This is especially difficult for rare, orphan diseases. Every time I speak to a researcher about conducting a clinical study for A-T, I hear that his or her institution does not have the money to do clinical research and pharmacology. Instead, the physicians at the academic hospitals seem to be focused on seeing more patients for economic reasons.

For children like my boys, who have rare diseases for which a drug or biotech company could never project a profitable market, academic research centers are our only hope. And without them, the important physician-scientists will not have a place to work, even after you have found or trained them.

2. *Show the Public Why We Need to Increase the NIH Budget.*—Second, the NIH, with your help as U.S. senators, needs to do a better job of reaching out to citizens so that they understand how important the NIH is to them. Think about what the world would be like without the NIH. Our best doctors, scientists and technicians rely at one point or another on this remarkable institution. The multi-billion dollar

biotechnology and drug industries owe a tremendous debt of gratitude to the NIH. And our country's biotech leadership position feeds the economy, provides jobs, fosters better education and most importantly, holds the potential to improve the health and welfare of every American. The NIH is, generally speaking, what sets American biomedical research apart from the rest of the world.

We have to do something about the public's ignorance about the NIH, especially outside of Washington. As a businessman who has now learned what the NIH does, I believe our country can justify a far greater expenditure on medical research. Just the aging of our population and the cost of taking care of our growing numbers of older citizens alone can present an excellent case for increasing our NIH budget. Throw in all sorts of unexpected, side discoveries—like the side discoveries made by NASA during the 1960s race to the moon—and enthusiasm should surge. And if those reasons aren't persuasive enough, let them meet my sons, Jarrett and Quinn, who are deteriorating every day as we wait for a breakthrough.

Health could be a much bigger priority in this country than it is now. I would like to see a day when most Americans—not just those of us who have been somehow affected by a disease—know what the NIH is, how funding decisions are made and how important their tax dollars are to the mission of the NIH.

My small organization, the A-T Children's Project, raises about \$5,000 per patient per year for my little known disease that no one has ever heard of and most people cannot even pronounce. If that much money were raised for each of the 8 or 9 million cancer patients in the U.S., the total would exceed \$40 billion per year. So it amazes me how much people have helped us with A-T.

You see, having only identified about 300 children with A-T in this country, we aren't able to depend on help from people who are personally affected by the disease. Instead, we have to persuade total strangers—people who have no personal connection to A-T—to reach out to help us, and they do. Why? Because we convince them that their support will have an impact, that we stretch every penny, that we make progress, and that research on A-T may help many other diseases, too. Our supporters also understand our urgency to save our children, and they believe that each dollar they give makes something happen that otherwise would not. They believe that we avoid bureaucracy, and that we are able to make difficult decisions, such as cutting off funding to a grant recipient who hasn't expended the effort that was promised in his or her original grant proposal.

Somehow, we need to make Americans feel the same way about the National Institutes of Health. I'm not just talking about courting the leaders of patient advocacy groups, but actually getting the message out to healthy, uninvolved people who do not yet realize how the NIH may impact their lives.

We could start by introducing America to the people who run the NIH, so it will not be perceived as a faceless agency of our government. And, we need to decide that it is okay to brag about them. Throughout the science world, researchers have quietly described NIH leaders like Harold Varmus and Rick Klausner as inspirational, passionate, brilliant scientists who are driven to make progress in healthcare and basic research and who really feel the burden of disease on families like mine. Many scientists seem excited about the course that Dr. Varmus has charted for the NIH. And, I can't count how many neuroscientists have raved about the new director of the NINDS, Dr. Fischbach.

But, the average non-scientist never hears these stories. For some reason, impressive CEOs of important American companies can have stories about them making the headlines every week, but NIH directors can't. Business leaders, even in biotech and drug companies, can be outrageous, visionary characters who don't fit in any mold but force the world to think a new way. But not at the NIH. I guess that it is politically precarious in academic science and in government to blow ones own horn. But there are many faces of heroes I have met at the NIH whom the public should meet. The only physician's face who Americans can recognize should not be C. Everett Coop!

Besides putting faces behind the NIH, we need to communicate clearly what additional funds allocated to the NIH would buy us. Most people like me do not understand how increasing the budget "x percent" or increasing the "grant success rate" will produce faster progress on health problems. We like to hear about simple, impressive goals, like when Babe Ruth pointed to the center field fence before hitting a home run over it.

And, we also have to make the public understand that irresolute, inconsistent support of the NIH destroys the groundwork laid for progress. Large budget increases, followed by cutbacks, followed by increases, cause tremendous uncertainty, and these uncertainties can convince promising young investigators that public support for research is far too unsure to build a life upon.

And finally, Senators, the next time you run for re-election, please consider making the NIH an even bigger part of your campaign platform. We need people to hear about it, and if you succeed in delivering the message, you'll receive greater support. If a person could run for Congress on only a single platform—such as quadrupling the NIH budget—I would even give it a shot. I would of course lose the election, but think of the attention I might be able to bring to health and medical research.

Again, I have a full-time job running a shrimp business, and I am only here today because my sons' brutal disease has made me understand the importance of your decisions involving the NIH. Families like mine are depending on you. I hope my comments have been helpful, and I stand willing to help you any way that I can.

Thank you.

Senator SPECTER. Thank you, very much, Mr. Margus. I think your testimony is very important, from somebody who has experienced a family tragedy.

We certainly extend our sympathy for your two young sons, one now in a wheelchair, and the prospects of a death in the teens. It is something we really want to work on, and I think if more people in the Congress could hear what you have to say, we would have less trouble getting the increase in funding, and many Americans will see your comments on C-Span. It carries to a lot of people.

STATEMENT OF DR. MARY HENDRIX, PRESIDENT-ELECT, FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY

Senator SPECTER. We now turn to Dr. Mary Hendrix, President-elect of the Federation of American Societies for Experimental Biology. She also serves as Head of the Cell Biology and Anatomy Department at the University of Iowa Cancer Center.

We welcome you here, Dr. Hendrix, and look forward to your testimony.

Dr. HENDRIX. Thank you.

Mr. Chairman, Senator Harkin, and members of the subcommittee, I am really a basic science researcher and a disease specialist in the area of cancer research. This work is currently supported by research grants from the National Cancer Institute.

I have also been recently elected as President-elect of the Federation of American Societies for Experimental Biology, we call FASEB, and it is in this role that I appear today to testify regarding the NIH's system for allocating funds among research priorities.

FASEB is actually a coalition of 17 societies, with a membership of more than 57,000 scientists. The message of FASEB in testimony before Congress has traditionally been a very simple one, investment in medical research is the first and critical step in prevention, treatment, and control of disease, which in turn will lead to longer, healthier, and more active lives.

The question posed by today's hearing, however, is a more complex one than that of adequate funding for the NIH. That question is: Below the aggregate level of funding for biomedical research, how should these funds be distributed among programs and diseases?

As the subcommittee well understands, the reason this question is so difficult is that the decision to increase funding for one area eventually and inevitably results in less for another. There are then two basic questions for the committee today.

The first is: Who should exercise this judgment? The second is: Once you decide institutionally where this decision making should

occur, is that institution carrying out its allocation process in the most informed, effective, and fair manner?

As the subcommittee reviews the first of these questions, FASEB's recommendation is that Congress maintain the existing balance of responsibility between Congress and the NIH in the allocation system. Under this system, Congress plays a critical role, through its hearing process, in reviewing allocations and in providing an opportunity for the public and congressional input into the NIH.

After this has occurred, Congress then sets overall funding levels, broken down by the institute, but the selection of specific research remains principally the responsibility of the NIH.

While not perfect, we believe the NIH, with proper public input, has the fullest understanding of the human economic costs of the disease, as well as the scientific challenges and opportunities that exist in specific areas.

It is FASEB's view that there is broad support for this general principle, that the NIH should be the main decision point in allocation decisions, but there is renewed debate about when exception should be made by Congress, based on the compelling nature of a particular disease, or the perception that existing allocations are inappropriate.

We recommend that you ask yourselves, what system will work best to produce positive results, not just for a particular disease, but for the improved overall health of the American people.

Senator SPECTER. Dr. Hendrix, do you believe the Congress then should intervene and change the policy of leaving it all up to NIH, and mandate allocations through Congress?

Dr. HENDRIX. Mr. Chairman, I believe Congress is very wise in allocating the funds to NIH to make the proper decisions, based on disease—

Senator SPECTER. So you think NIH should make the decisions—

Dr. HENDRIX. Yes.

Senator SPECTER [continuing]. As opposed to changing that to have Congress make the decision.

Dr. HENDRIX. Yes, I do.

Senator SPECTER. All right. I just wanted to clarify that point. I thought you said to the contrary, as to how much goes to Parkinson's—

Dr. HENDRIX. How much goes to each disease.

Senator SPECTER [continuing]. How much goes to Alzheimers, how much goes to diabetes—

Dr. HENDRIX. Yes.

Senator SPECTER [continuing]. And how much goes to AIDS, you think that is the proper decision for NIH.

Dr. HENDRIX. I think NIH is in the best position, with public input—

Senator SPECTER. I misunderstood your testimony—

Dr. HENDRIX [continuing]. To make that decision.

Senator SPECTER [continuing]. And I wanted to have it clarified. Thank you.

Dr. HENDRIX. Thank you. We also suggest that you consider the following factors. First, simple quantitative measures, while useful,

are inevitably incomplete and often flawed. No single comparison, such as morbidity, or mortality, or economic impact works across all diseases.

Second, basic science. The foundation of disease-specific research will inevitably suffer in a politically based system of allocating scarce dollars.

Third, it is important to remember the adage, no good deed goes unpunished. An increase in one area may do substantial damage to other equally deserving programs. Fourth, the quality of the leadership at the NIH is unparalleled in government. These leaders and administrators have broad knowledge of the science and the human aspect of these decisions.

Last, we believe that Congress is already quite effective in influencing the decisions that NIH makes. Committee reports, studies, and hearings already influence these allocation decisions. FASEB is sympathetic, however, to the views of the patient advocates, at the level of involvement of the outside community as advisors to NIH could be improved, and that factors of disease burden could be more effectively built into NIH's judgments.

PREPARED STATEMENT

In conclusion, Mr. Chairman, we at FASEB believe that the leadership at the NIH, in consultation with the Congress and with the public, is in the best position to set these biomedical research priorities. As one member of Congress said, let the science call the shots, not science that works in the vacuum, but science that works to cure disease, managed by some of the most broadly informed science managers in the world today.

I thank you for the privilege and the opportunity to address the committee.

Senator SPECTER. Thank you very much, Dr. Hendrix. We appreciate your being here.

[The statement follows:]

PREPARED STATEMENT OF DR. MARY HENDRIX

Mr. Chairman, Senator Harkin, Members of the Subcommittee: I am Dr. Mary Hendrix, professor and chair of the Department of Anatomy and Cell Biology at the University of Iowa. In this role I am both a basic scientist and a disease specialist, as most of my work is in the area of cancer. This work is supported by individual research project grants from the National Cancer Institute, which also supports the University of Iowa Cancer Center where I serve as Associate Director of Basic Research and Deputy Director. I also serve as Chair of an NIH Study Section.

I am a member of the Board of Directors of the Federation of American Societies for Experimental Biology, FASEB, and have recently been selected to be the Federation's president beginning in July of 2000. It is in my role as president-elect of FASEB that I appear today to testify during these important hearings regarding the National Institute of Health's system for allocating funds among different research priorities and diseases.

FASEB is a coalition of 17 societies with a combined membership of more than 57,000 individual scientists who work in biomedical research. The Federation was founded in 1912 to provide an organization that could represent the views of scientists in the research policy debates of its day. This remains more than 80 years later the fundamental purpose for the existence of our Federation.

Mr. Chairman, while patient advocacy organizations and basic research scientists each bring their own perspectives to this debate, all are here with one overarching goal—to make progress against the diseases and disabilities which continue to afflict our people and, indeed, the people of the world. FASEB's members are practitioners of molecular biology, biochemistry, anatomy, and other biological sciences,

but our cause is to apply our scientific research toward the reduction of human suffering from disease.

The message of our Federation in testimony before Congress has traditionally been a simple one. Investment in medical research is the first and critical step in prevention, treatment and control of disease, which in turn will lead to longer, healthier and more active lives. Without adequate funding of the NIH, progress will be slowed and suffering will be prolonged. This statement is the basis for our national advocacy. FASEB is enormously grateful for the leadership of yourself and Senator Harkin in our joint efforts. This leadership has changed the status of the NIH "Doubling" effort from a wish and a prayer to a goal that seems potentially reachable.

However, the question posed by today's hearing is a more complex and difficult one than that of adequate funding for the NIH. That question is, below the aggregate level of funding for biomedical research, how should these funds be distributed among the various programs, diseases and activities of the NIH.

As this subcommittee well understands, the reason this question is so difficult is that the decision to increase funding for one area inevitably results in less for another, even if in the current environment that means a smaller increase. This is true whether we are talking about another disease or another avenue of biomedical research. I believe most of us understand the difficulty with these decisions, which cannot be made using simple mathematical models, comparisons or other purely quantitative measures. While these factors provide useful benchmarks of relative effort, allocation decisions are fundamentally matters of "judgment." There are, then, two basic questions before this committee today. The first is who should exercise this judgment, who should make these Solomon-like choices? The second is, once you decide institutionally where this decision-making should occur, is that institution carrying out its allocation process in the most informed, effective and fair manner?

As the subcommittee reviews this important question, FASEB's recommendation is that Congress maintain the existing balance of responsibility in which Congress sets overall funding levels broken down by Institute, but the selection of specific research areas to be funded remains principally the responsibility of the NIH. While not perfect, we believe the NIH has the fullest understanding not only of the human and economic costs of a disease, but also of the scientific challenges and current opportunities that exist in specific areas, and more broadly in biomedical research.

It is FASEB's view, based on extensive discussions with members and staff from both the Senate and the House, that there is wide-spread support for this general principle, but renewed debate about when exceptions should be made and where on the continuum of shared responsibility the dividing line should be drawn.

This committee not only has every right to review this question, but, in fact, has a duty to do so on behalf of your constituents and colleagues who are sincerely asking whether the current mix of spending among diseases is appropriate. However, in carrying out this review, as biomedical research advocates we ask that you continuously ask yourselves what system will work best to produce positive results not just for a particular disease but for improved overall health of the American people. We ask you to make this the standard, no matter how powerful the advocacy or how emotionally compelling the case before you regarding a particular disease. We believe that if this is the standard which is applied, the current approach of delegation to NIH will emerge as the most efficient and productive.

We also suggest as you carry out your review that you consider the following factors:

- First, simple quantitative measures, while useful, are inevitably incomplete, often flawed and subject to manipulation. For example, NIH's own tables regarding spending levels for various diseases, have no common definition of direct and indirect spending which makes it specific to a particular disease. No single quantitative comparison—morbidity, mortality, expenditures per case, years of life lost, or economic or budgetary impact—works across all diseases for allocation purposes. None take into consideration the nonquantifiable element such as the degree of human suffering.
- Second, basic research, recognized universally as the foundation of most advances in disease specific research, will inevitably suffer in a politically based system of allocating scarce dollars. If disease specific criteria assume disproportionately large roles in allocation decisions, we are concerned this will create a disincentive to critical long-term investments in basic science, which generate new knowledge that cannot always be immediately correlated to a specific disease.
- Third, it is important in looking at Congress' role in allocating funds to remember the adage, "no good deed goes unpunished." Without a thorough understanding of the impact an increase in a particular disease or program area will

have over multiple years, data seldom available to Congress, an increase in one area may do substantial damage to other equally deserving programs.

—Fourth, the quality of the leadership at the NIH is unparalleled in government. Institute directors and the NIH staff are extremely dedicated career civil servants at the top of their professions. These leaders and administrators have broad and deep knowledge of the science and of the human aspect of these decisions.

—Lastly, we believe there is much evidence that Congress is effective within the existing system in influencing the decisions NIH makes. Committee reports, studies and hearings are taken seriously by the NIH, and influence, where appropriate, allocation decisions.

On the second question—is NIH carrying out its allocation responsibilities in the most informed, effective and fair manner—we believe that the answer is fundamentally, but not unequivocally, “Yes.” We would note that this is a question both of the reality and the perception of NIH’s efforts. It is our experience as investigators and members of NIH study sections, that patient advocates have considerable access to NIH and that the science leaders within NIH are committed to NIH’s disease-related core mission.

FASEB is sympathetic, however, to the views of many patient advocates that the level of involvement of the outside community as advisers to NIH could be improved and that factors of disease burden could be more uniformly and effectively built into NIH’s judgements. These are areas of concern expressed in last year’s Institute of Medicine Report, Scientific Opportunities and Public Needs. We believe that the IOM recommendations for increased public input through a new Council of Public Representatives and expanded public liaison efforts within each of the institutes are entirely appropriate.

The Federal Funding Consensus Conference held by FASEB last December endorsed greater public input into the process noting that “Human health will be advanced most effectively when patients, health care providers, medical researchers and the public have opportunities for input into research priorities.” This view is shared broadly within the advocacy community. In June of last year a group organized by FASEB representing scientists, academic health centers and patient groups made a similar statement. Among the 12 principles these “stakeholders” endorsed, number V specifically recommended greater input by disease groups. We are pleased that NIH has moved to implement these recommendations, including those of the IOM. As you know, the first meeting of this new COPR Council was held on April 20.

In conclusion, Mr. Chairman, we at FASEB believe that the leadership at the NIH, in consultation with the Congress and with the public, is in the best position to set biomedical research priorities. As one member of Congress said, let “the science call the shots”—not science that works in a vacuum but science that works to cure disease, managed by some of the most broadly informed science managers in the world today.

I would be pleased to answer your questions.

STATEMENT OF PURNELL CHOPPIN, PRESIDENT, HOWARD HUGHES MEDICAL INSTITUTE

Senator SPECTER. We turn now to Dr. Purnell Choppin, President of the Howard Hughes Medical Institute, where he has served since 1985. He is an urologist by training, vice president of the Rockefeller University, where he conducted research on the influenza and the measles virus.

He has headed up the group which has made an analysis of allocations, and we are very pleased to have him here today to give his professional judgment on the support, which I understand he has for the current system, where NIH makes the allocations, as opposed to Congress.

Dr. Choppin, welcome, and the floor is yours.

Dr. CHOPPIN. Thank you very much, Mr. Chairman. As President of the Howard Hughes Medical Institute, I am associated with the largest private non-profit funder of biomedical research in the country, and science education. NIH is a wonder institution.

It has been extremely well directed and managed, enormously successful in its mission, and would undoubtedly continue to do so, if given the proper support, which Congress has always generously provided in the past.

The setting of priorities in an institution that is as large and as complex as the NIH and which has so many calls upon it is a truly daunting task. The NIH budget, no matter how large, will never be large enough to meet every need or support every research opportunity, thus difficult choices will always have to be made and made in a context of continuously changing demographics, health problems, and research opportunities.

The IOM committee report supported the criteria that the NIH has used for priority setting, and recommended that NIH continue to use these in a balanced way. The setting of priorities for research should be largely left to scientists who not only understand the problems presented by disease, but also the research approaches and the scientific opportunities that will lead to the greatest benefit, given the current state of knowledge and capabilities.

The committee made a number of other recommendations. First, NIH should make clearer the mechanisms that it uses to set its priorities and evaluate their effectiveness. This recommendation is a reflection of the general theme and major message of the report; that is, there is the need for NIH to better explain its processes and to set up improved mechanisms for receiving input from the public and for providing information on its activities.

Two other recommendations dealt with the use of health statistics and data on funding of specific diseases and research areas. NIH should strengthen its analysis and the use of health data, such as burdens and cost of diseases, and the impact of research on health. It should be emphasized that there is no simple way to calculate disease burdens. One cannot simply count the number of cases or deaths. Factors such as age of onset, duration, level of disability, pain, et cetera, are all part of the equation.

Furthermore, disease burden, no matter how well estimated, is only one factor in the priority-setting process. I do not think NIH should set up a new large data gathering organization, but should increase its effort to assemble and analyze the information that does exist, and that is being gathered by other agencies, such as the National Center for Health Statistics, and I was pleased at Dr. Varmus's earlier comments this morning.

A related recommendation was that NIH improve the quality and analysis of data relative to spending on specific diseases, and include not only expenditures directly related to that disease, but to the best of its ability, expenditures indirectly related. The attribution of indirect basic research expenditures to specific diseases is particularly complex.

Indeed, the same basic research might contribute to more than one disease, and thus, attribution of these expenditures could generate in its some people's mind double-counting. Nevertheless, increased efforts in this area are desirable, and if improved data can be obtained and communicated effectively, the very good job that NIH is doing in setting priorities would be better appreciated by the public.

I would like to end this section of my presentation by noting that NIH has been responsive to the committee's report, particularly in setting up offices of public liaison and the Director's Council of Public Representatives.

I will say a few words about the Howard Hughes Medical Institute, and how it sets its priorities. HHMI is not a foundation, but an operating medical research organization. It supports 317 scientists, called Hughes Investigators, and 70 medical schools, universities, and research institutes across the country.

These investigators are faculty members of the institutions where they are based, but they are HHMI employees, receiving full salary from HHMI, as well as support for supplies, equipment, personnel, and in many cases, construction or renovation of their laboratories. We have spent more than \$340 million in construction of laboratories and renovation in the past decade.

We have selected five major areas for research, genetics, cell biology, immunology, neuro-science, instructor of biology, and these are broadly interpreted. I have in my written remarks something about the contributions of that research.

Importantly, we regard HHMI as a complimentary institution to the NIH, not as a duplicative one. I could cite examples of collaborative and cooperative effects, if there is interest.

The main difference in the way that we approach funding is that HHMI supports people, not projects. We identify outstanding scientists, try to give them adequate funding, and review them rigorously approximately every 5 years. The system works well. Five of our investigators have won Nobel Prizes, and seventy-three are members of the National Academy of Sciences.

Our budget for this year is approximately \$556 million, and although, as I said, we are the largest private not-for-profit funder of medical research and plurality of support is important, that is both government and private support, its budget is, of course, only three-and-a-half percent of that of the NIH.

Thus, the health and medical research, and, therefore, the health of the nation, is inexplicably tied to the success of NIH, and I trust that support for it will prosper, so that the superb work that it carries out cannot only continue, but grow. Thank you very much for the opportunity to be with you today.

Senator SPECTER. Thank you very much, Dr. Choppin. The issue is about activity by the subcommittee or the full Congress on what NIH ultimately does—Bettilou Taylor has compiled some of the statistics here. We have 67 pages of report language, covering about 253 separate ailments, as we transmit information to NIH. I mentioned the request last year for earmarking \$175 million for prostate cancer, and it is worth just a comment or two.

Now, that request came from Senator Stevens, as the chairman of the full committee. And Senator Stevens has a greater awareness of prostate cancer because he is recovering from prostate cancer. A fair number of our Senators are.

Senator Stevens asked that this earmark be obtained last year, and the subcommittee considered it, and notwithstanding the recommendation, we decided it ought not to be done. The subcommittee decided not to deviate from our existing policy of leaving the specification to NIH.

In full committee, chaired by Senator Stevens, and we are telling you what happens inside the beltway, \$175 million was added, and nobody challenged it on the Senate floor, it came out of the full committee report, but then our system is to go to conference with the House, and it has to be approved by the House as well, and it was dropped in conference. So notwithstanding that level of recommendation, we left it to NIH to make the choice. I might share with you parenthetically a story. Senator Dole came back when he was majority leader, after he had a prostate cancer operation, Senator Harkin did not hear this, he is in the wrong caucus, but Senator Dole addressed the Republican caucus and he said, "I just had a prostate operation, and one man out of nine are saved," and he said, "Senator Stevens just had his prostate operation," and then he pointed over to Senator Thurmond, who was 94 at the time, 96 now, and he said, "And Strom is too old to get prostate cancer."

I tell you that story for a slight purpose, and the purpose is that there is a little more awareness of prostate cancer in the Republican caucus, maybe even in the caucus attended by Senator Harkin, but notwithstanding that, we have not elevated our own views to take over from what NIH has to say.

Dr. Varmus, my first question is: Applying the standards which you have articulated, and I am not disagreeing with your allocation to AIDS, but why do you give on a pro rata basis so much to AIDS, say, compared to other ailments?

Dr. VARMUS. Let me backtrack a second, Senator, if I could, to think about the appropriation process more generally, and then come back to the question about AIDS, and maybe even deal with the issue you raised about prostate cancer.

It is written in law that the Congress appropriates not to the NIH overall, but to individual institutes. They are separately authorized, and they receive their separate appropriations.

In the course of building our budget, we have every institute prepare a set of plans that would be appropriate for different levels of funding, and we come to you each year with the President's request, after extensive deliberation with components of the Administration, and an overall distribution among the institutes in a corps, with an overall level for the NIH.

In the course of hearings and markups and conferences, the Congress determines what it can afford to spend on the NIH, and consults with us—we are very appreciative of that consultation—to ask what we would think to be the ideal distribution among institutes at a certain level of funding. And we provide that to you. It has been a very great benefit to us that you listen to us and take our recommendations very seriously.

Senator SPECTER. Well, when you say we consult with you, you really mean we take your recommendations.

Dr. VARMUS. Yes, you do, and you—

Senator SPECTER. It is more of a matter of notification.

Dr. VARMUS. Importantly, the budgets for the individual institutes have not been subject to directives concerning which grants we should support, or which institutions we should support, or exactly which projects we should undertake. That has been extremely helpful.

Senator SPECTER. So you are the \$15 billion man.

Dr. VARMUS. But within the domain of each institute, it is not just me, Senator, it is each institute director who has built a plan for that institute, to include basic research, clinical research, transnational research, training—

Senator SPECTER. Those judgments are made by the individual institutes.

Dr. VARMUS. They are made in consultation with their public, as I have described, in a major planning process that also includes consultation with me and with the Administration.

Senator SPECTER. But the ultimate decisions are made there—

Dr. VARMUS. That is correct.

Senator SPECTER [continuing]. Without a congressional mandate.

Dr. VARMUS. We are extremely grateful to you and to your counterparts in the House for taking our advice so seriously, because you do, of course, as the representatives of the public—we are a public institution, and we are responsive to your suggestions.

Now, I would point out, for example, that in the context of the discussion of prostate cancer, we are aware of the toll that prostate cancer takes, we see many new scientific opportunities to study prostate cancer, and we hear the general concern among individuals who have the disease that we have not been paying adequate attention to it. We have written, as you know, a detailed plan, which we will soon present to you in a hearing, that lays out our plans for studying prostate cancer. There is no doubt that the investment in that area is increasing. We very much appreciate having the flexibility to determine the actual spending level, based on the quality of the applications we receive and the determination of a precise plan.

Senator SPECTER. Well, my red light is on, so I will conclude with a final observation or perhaps question, but just as you get inputs on prostate cancer from the public, et cetera, you have the flexibility to make the final decision. That is the same way it applies to other ailments, right?

Dr. VARMUS. Yes, sir.

Senator SPECTER. Senator Harkin.

Senator HARKIN. Mr. Chairman, thank you. Sometimes one of the best ways of enlightening a process and developing a good dialog is to challenge your friends, so I am going to challenge one of my friends. I want to challenge Dr. Hendrix.

In your testimony for FASEB, you talked about the allocation decisions are fundamentally matters of judgment, and there are two basic questions. First, who should exercise this judgment, make these Solomon-like choices, and then second, once you decide where this decision making should occur, is that institution carrying out its allocation process in the most informed, effective, and fair manner, and then you go on to say that NIH is the repository of this. Well, again, there is no one who has more respect and admiration for the people that guide and direct NIH, not only the present director, but the ones that have come before him, and the institution directors who are there, and the ones before them, than I have.

They are among some of the brightest, most capable people I have ever met, but they are not Gods. They are human beings, with the same prides, and prejudices, compassion, and conceit that any other human being has.

So, therefore, like any institution, NIH, or any institute therein, is subject to what I call institutional inertia, and especially in this area of scientific research, people tend to focus narrowly. We want them to focus narrowly. We want them to focus on their areas, and as such, as any human being, and you failed to take into account some broader principles, perhaps.

Now, I have said many times, Dr. Hendrix, that NIH stands for the National Institutes of Health, it does not stand for the National Institutes of Basic Research, a much broader, much broader language than just basic research.

So whoever said, I do not know who it was, that we have to look at global implications, what is happening globally, yes, we do. I saw a person who returned from Africa, and they told me there are 16,000 people a day coming down with HIV in Africa—16,000 every single day. Now, should NIH be concerned about that? I think so. I think so.

But then again, NIH, as an institute, is going down a direction. Now, for example, in the early nineties, we did a GAO study, I happened to be involved in that, since I was chairman of the subcommittee at that time, a couple of Senators had come to me with certain information, and we asked GAO to do a study of NIH in terms of how it was focusing on women's health.

Guess what we found? Gaping holes in the focus on women's health issues at NIH. They were not giving appropriate attention to it. It is well documented that women were not included in studies. So we stepped in and we changed it.

Now, had we not done that, would NIH have done it on their own? I do not know. Maybe, maybe not. It had started down a certain path, institutional inertia being what it is, that is the way they go.

In the early nineties we doubled Alzheimer's research. Now, was that wrong for us to do that or was it right? We created the Arthritis Institute. We did not have one. NIH fought it. That was before your time.

Back in the eighties I looked around and found that we were doing deafness and communication research in a bunch of different institutes, and so Congress created the National Institute on Deafness and Communication Disorders. NIH fought it, said we should not have it, do not need it, but we created it anyway, and quite frankly, I think it is doing a pretty darn good job, as I think the National Institutes on Arthritis is doing a good job, too.

So where am I headed on this? Where I am headed on this is to say that, look, I think we ought to give quite a bit of reign to those directors at the institutes and to the director, but I still believe we have a role to play in oversight, in guidance, in direction, in challenging, and yes, in funding certain things, if we believe that is in the best interest of the public, even though the NIH director may say no.

Now, this NIH director and I have had a running battle on complimentary and alternative medical research. Is he right or I am wrong, or is he wrong and I am right? I do not think either one. I think we have different ways of viewing it, but out of this I think will come some better research, guidance, and direction for the people in this country on this hugely burgeoning area of alternative

medicine, but left to its own, would have NIH have done it? I do not think so. Maybe. But this Congress, I do not just say me, but this Congress, Senator Specter was involved in that, and the people on the House side said we need to focus in this area, and we need to have some effort in that area.

So I guess I am by discourse, not so much with a question, but again, I am saying that as long as we are charged with this responsibility that we have, we are going to be involved in NIH, and we are going to be involved in its decisions. We will, of course, listen to that.

Give us all the best information you have, and we will work with you in a collaborative manner, but sometimes it is going to come down to the point where we are going to say, I am sorry, you are just not doing enough in diabetes and we are going to put more money there, because we are looking at a broader aspect of public health than the narrow or the constrained focus of one institute. I did not mean to pick on diabetes here.

I happen to believe that there is a legitimate role for us to play. I would be shirking my responsibilities if I simply turned over or voted to turn over \$15 billion a year to NIH and said, "Do not talk to me now. I do not want to know anything about it. You make the decisions." So that is where I think we are.

Now, if some people in the media think that is wrong, they can go after me. If some people in the scientific community think I am wrong, you can go after me, too, but this is what I believe, this is what I have come to believe in all my years here, and in working with NIH, and I will continue to exercise that responsibility and role. I will be involved.

As long as I am here on this committee and in the Senate, I will be involved in the decisions, and in the decision-making process, and in the allocations of money, not whether it goes to one specific disease or another, or how these are—that is for the peer review process. I am talking about this general overview pattern of where we are going to focus these public health dollars.

Is it a sharp line? No. It is a big grey area, and in that grey area we move back and forth. Thank you very much.

Senator SPECTER. Thank you very much for that question, Senator Harkin. [Laughter.]

There is no doubt, as Senator Harkin has said, that the Congress has very extensive responsibilities. The Congress created the National Institutes of Health, and Tom and I took the lead many years ago when he was chairman and I ranking, by creating the women's division—

Senator HARKIN. Yes. That is right. That is right. Women's health.

Senator SPECTER [continuing]. And we have made suggestions on alternative medicine, and we do make suggestions from time to time, but I think Senator Harkin puts his finger right on the center of the target when he said, when it comes to the specific allocations among the diseases, it is a matter for peer review and it is a matter for the professionalism for NIH.

CONCLUSION OF HEARING

Now, that concludes our hearing, and we thank you all very much. The subcommittee will stand in recess subject to the call of the Chair.

[Whereupon, at 10:20 a.m., Thursday, May 6, the hearing was concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]

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