FUNDING BIOMEDICAL RESEARCH PROGRAMS

Contributions of the Markey Trust

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

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Committee for the Evaluation of the Lucille P. Markey Charitable Trust
Programs in Biomedical Sciences

Board on Higher Education and Workforce
Policy and Global Affairs Division

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

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COMMITTEE FOR THE EVALUATION OF THE LUCILLE P. MARKEY CHARITABLE TRUST PROGRAMS IN BIOMEDICAL SCIENCES

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Preface and Acknowledgments

In response to a request by the Lucille P. Markey Charitable Trust, the National Research Council (NRC) of the National Academies, through the Board on Higher Education and Workforce (BHEW), is conducting an evaluation of the Markey Trust's grant programs in the biomedical sciences. During an interval of 15 years, the Markey Trust spent more than $500 million on four programs in the basic biomedical sciences that support the education and research of graduate students, postdoctoral fellows, junior faculty, and senior researchers. This study addresses two questions: (1) Were these funds well spent? and (2) What can others in the biomedical and philanthropic communities learn from the programs of the Markey Trust? To accomplish these goals, the committee overseeing the project

- Has examined the General Organizational Grants program, intended to catalyze new ways to train Ph.D. and M.D. students in translational research;
- Convened a conference of Markey Scholars and Visiting Fellows in 2002;
- Is reviewing the Research Programs Grants, which provided funding to institutions to support the work of senior investigators;
- Conducted a workshop to investigate methods used to evaluate funding of biomedical science by philanthropic donors; and
- Will evaluate the program for Markey Scholars and Visiting Fellows, which supported young biomedical investigators in their early careers.

This is the third of a series of reports that document the activities of the Markey Trust. This report examines the Research Programs Grants, the largest component of the Markey Trust's funding activities. During the 12-year interval beginning in 1985 the Trust awarded more than $325 million to 92 research organizations. These awards were made to able investigators with a major commitment to the life sciences to assist in the establishment, reorganization, or expansion of significant biomedical research centers or programs. The Trust initially identified the target of Research Program Grants as institutions with a major commitment to the life sciences. The grants usually involved funding for the recruitment of new faculty, pre- and postdoctoral support, completion or renovation of laboratory space, purchase of new equipment, and additional technical assistance.

NRC staff has obtained data and information from Markey archives and databases, solicited materials from grant recipients, and conducted site visits to a sample of institutions' grant recipients. The study assesses the impact of these grants on the centers and programs they funded, focusing on program development, program sustainability, research productivity, faculty development, and the impact of the funded program on the host institution.

Previously published reports that detail the activities of the Markey Trust are *Bridging the Bed-Bench Gap: Contributions of the Markey Trust*, which examines the General Organizational Grants program, and *The Markey Scholars Conference Proceedings*. The latter summarizes presentations and abstracts from the 2002 Markey Scholars Conference held as part of the National Academies evaluation. Both reports are available through the National Academies Press. Additional reports will assess the Markey Scholars and Visiting Fellows programs and publish the proceedings of a workshop on evaluation practices in philanthropic and public organizations that support biomedical scientists.

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

We wish to thank the following individuals for their review of this report: Peter Bruns, Howard Hughes Medical Institute; Barry Coller, Rockefeller University; Samuel Herman, Consultant; Hedvig Hricak, Memorial Sloan-Kettering Cancer Center; Henry Riecken, University of Penn-

sylvania; Lydia Villa-Komaroff, Whitehead Institute; and Robert Woolard, Brown University.

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by Edward Perrin, University of Washington and James Wyche, University of Oklahoma. Appointed by the National Academies, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

The production of this report was the result of work over a sustained period of time by the study Committee. George Reinhart, study director; Elaine Lawson, program officer; Patricia Ellen Santos, senior program assistant; and Heather Begg, program assistant ably assisted the committee in this study. Enriqueta Bond, Ph.D., who earlier served as chair of the committee, was instrumental in the early development of both the study and this report.

Lee Sechrest
Chair
Committee for the Evaluation of the
Lucille P. Markey Charitable Trust
Programs in Biomedical Sciences

Contents

Summary

The Lucille P. Markey Charitable Trust was created as a 15-year, limited-term philanthropy in support of basic medical research by the will of Lucille P. Markey who died on July 24, 1982. Mrs. Markey wished that a trust be established "for the purposes of supporting and encouraging basic medical research." The Trustees, who provided governance for the Markey Trust, targeted its programs to specific needs within the biomedical sciences where funding could potentially make a difference. Three main categories, which emerged over the life of the Trust, were targeted to the following:

1. Supporting of young researchers in the biomedical sciences
2. Funding the establishment, reorganization, or expansion of major biomedical research programs or centers led by established investigators
3. Providing training opportunities in translational research for graduate and medical students.

The Markey Trustees were also aware that their approach to philanthropy could potentially provide a model for others. Their approach had the following key attributes:

- Distribute all of the assets of the Trust over a limited period of time, allowing more funds to be distributed in a given year and larger awards to be offered;
- Operate with a small core staff, thereby reducing administrative

costs and allowing a higher proportion of funds to be awarded to grantees; and

- Provide funds with only a minimum of required reporting, thereby freeing recipients from the burdensome paperwork often associated with grants.

These three mechanisms for operating a grants program were successfully used by the Markey Trust and provide a model for other foundations. However, future funders of programs in the sciences should consider comprehensive program evaluation and prospective monitoring of outcomes as an integral part of the overall design of a project.

During the 15 years following its creation, the Lucille P. Markey Charitable Trust spent more than $500 million on three basic biomedical sciences grant programs that supported the education and research of predoctoral students, postdoctoral fellows, junior faculty, and senior researchers. In response to a request by the Markey Trustees, the committee is evaluating the Markey Trust's grant programs in the biomedical sciences. This evaluation addresses two questions: (1) Were the Trust's funds well spent? and (2) What can others learn from the programs of the Markey Trust both as an approach to funding biomedical research and as a model of philanthropy?

MARKEY GRANT PROGRAMS

The Markey Trust made awards reflecting the three main stages of a biomedical research career: basic training, development of young faculty, and research by experienced scientists. These three categories became referred to as the following: (1) General Organizational Grants, (2) Markey Scholars and Visiting Fellows Awards, and (3) Research Program Grants. However, some grants do not fall neatly into one of these categories and for evaluation purposes were assigned to one or another of the programs.

General Organizational Grants

The growth of a gap between biomedical research and its clinical application has been recognized. The Markey Trust funded awards to provide training in translational research to diminish this gap, including (1) programs that provided significant opportunities for M.D.s to engage in basic research during and immediately following medical school and residency, and (2) programs that provided significant clinical exposure for Ph.D.s while they were predoctoral or postdoctoral students. General Organizational Grant programs were funded for approximately five years and were not renewable.

Markey Scholars and Visiting Fellows Awards

The Trust adopted several mechanisms to fund selected scholars early in their careers. The two most important were (1) the Scholar Awards in Biomedical Sciences, by which a total of 113 Markey Scholars were supported for up to three years of postdoctoral training followed by five years of support as a junior faculty with both salary and research funding provided, and (2) the United Kingdom and Australian Visiting Fellows Awards , which supported outstanding young scientists from the United Kingdom and Australia to spend two years as postdoctoral fellows at American research institutions.

Research Program Grants

Research Program Grants were awarded to enable established investigators to address important issues in the biomedical sciences by developing new approaches or expanding continuing approaches to the study of basic biomedical research questions—in short, providing flexible dollars for innovation and growth. In some instances, the awards permitted the development of new programs or the complete reorganization of existing programs. In other cases, the awards enhanced existing programs and research endeavors.

This report covers only the Research Program Grants program. The General Organizational Grants programs were assessed earlier and can be reviewed in *Bridging the Bed-Bench Gap: Contributions of the Markey Trust*, published by the National Academies Press. The committee will publish a report in 2006, giving its assessment of the Markey Scholars and Visiting Fellows program. This is the only Markey program that lends itself to a data-driven, prospective evaluation with a comparison group. Unfortunately, formal evaluation was not built into the planning for the heterogeneous awards that constitute the programs funded by the Markey Trust, the subject of this and the previous report. In the case of these two reports, the committee is well aware of the limitations that are intrinsic to rendering judgments based on information that could be collected by such activities as site visits and progress reports but believed that its expert judgment would be useful to other funders of scientific work.

The committee sought to understand whether the grants made to develop centers or programs resulted in program creation and development, program sustainability, research productivity, and faculty development, and positively integrated the funded program with the host institution. Unfortunately, the committee was not able to assess adequately the scientific quality or impact of the Research Program Grants on biomedical research or the impact of the program on the research centers and projects

that it funded. This inability stems from one of the Research Program Grant's strengths, its flexibility in not imposing stringent reporting requirements on grant recipients. As a consequence, information that would be useful to an evaluation of the impact of the Research Program Grants was not systematically collected.

The committee used three approaches to assess the Research Program Grants. First, all grantees were required to submit annual progress reports to the Trust. Although there was little uniformity among these progress reports, the committee was able to use them to document some milestones for the grantees, including data on staffing changes, construction and renovations, and purchase of major equipment.

In addition, the committee and NRC staff made 19 site visits; conducted 12 telephone interviews with principal investigators, some of whom also received site visits; and analyzed letter reports from two grantees. These data provided the committee with valuable insights into how funds were used within a particular institution. However, the committee found that it was difficult to generalize the insights garnered from these sources, although it was clear that in almost every instance funds had been used to fund good scientists, buy needed equipment, and develop programs.

The third source of information came from analysis of the Lucille P. Markey Charitable Trust Records. As the Trust was entering its final years, it arranged for all Trust documents to be stored at the Rockefeller Archives Center in Sleepy Hollow, New York. Following the conclusion of the Trust in 1997, all of its documents were transferred to the center, classified, and microfilmed. These archival data are a rich source of information on all aspects of the Trust and will be made available to the public in 2007.

COMMITTEE CONCLUSIONS AND OBSERVATIONS

The Committee used its expert review combined with assessment of annual reports, site visits, and review of the Markey Trust archived records to evaluate the Research Program Grants program and arrive at the following conclusions and observations.

- The Research Program Grants were an appropriate mechanism to carry out the wishes to invest in the biomedical sciences articulated by Mrs. Markey to spend down her trust with minimal administrative overhead. Through this mechanism, more than $325 million in funding was awarded to 92 principal investigators in academic medical centers, hospitals, research universities, and research institutes or centers.
- By design, awards made through the Research Program Grants

award mechanism differed from those made by the National Institutes of Health (NIH) and National Science Foundation (NSF) in terms of both the size and flexibility of the award and in the selection process used to make the grants. The process focused on people with established records of success in science rather than the research proposal per se.

- Dollars provided by the Research Program Grants were invested in recruiting young scientists and provided start-up packages. These grants also funded equipment, infrastructure development, and research by leading scientists. However, it is impossible to assess the outcomes of individual awardees.
- The size and focus of Research Program Grants awards changed during the tenure of the Trust. A program of large awards to enhance infrastructure development and create new programs at academic medical centers evolved into one where smaller awards were made to individual investigators to further their research.
- The Trust developed procedures that maximized the flexibility of the awards, and this flexibility—according to those interviewed—led to efficient uses of Trust funds. The Trust focused on minimizing the bureaucracy in its administration of Research Program Grants awards.
- The committee believes that the Trust's goal of funding high-risk biomedical research, research that would not ordinarily be funded by NIH, NSF, or other funders, was met. Although examining the portfolio of grants in terms of whether they were high risk was beyond the scope of this evaluation, the committee noted that a number of grants supported research programs in their nascent stages.
- Finally, the committee believes that a number of aspects of the Markey model of philanthropy, including its design as a limited-term trust, are worthy of consideration by other funders interested in fostering biomedical research.

Through the Research Program Grants, the Markey Trust created a program that identified established leading scientists with promising ideas and models, provided them with substantial funding, and minimized administrative barriers in order to maximize their potential to take risks, support good young scientists in their labs, buy equipment, and build infrastructure to advance biomedical research. The need still remains for funding basic biomedical research whose outcomes are neither ensured nor predictable.

Introduction

In the world of philanthropy, there is a growing concern that assessment and evaluation may take a back seat to managing the ongoing programs of the organization. Trustees may have concerns that evaluation of programs is complex, takes time, and can be quite costly. This is especially relevant for smaller funds. On the other hand, evaluation of award programs may generate useful information to guide better decision making by organizations.

In response to a request by the Lucille P. Markey Charitable Trust, the National Research Council (NRC) of the National Academies, through the Board on Higher Education and Workforce (BHEW), is conducting an evaluation of the Markey Trust's grant programs in the biomedical sciences. During an interval of 15 years, the Markey Trust spent more than $500 million on four programs in the basic biomedical sciences that support the education and research of graduate students, postdoctoral fellows, junior faculty, and senior researchers. This study addresses two questions: (1) Were these funds well spent, and (2) What can others in the biomedical and philanthropic communities learn from the programs of the Markey Trust. To accomplish these goals, the committee overseeing the project

- Has examined the General Organizational Grants program, intended to catalyze new ways to train Ph.D. and M.D. students in translational research;

- Convened a conference of Markey Scholars and Visiting Fellows in 2002;
- Is assessing the Research Programs Grants, which provided funding to institutions to support the work of senior investigators;
- Conducted a workshop to investigate methods used to evaluate funding of biomedical science by philanthropic donors; and
- Will evaluate the program for Markey Scholars and Visiting Fellows, which supported young biomedical investigators in their early careers.

The Committee for the Evaluation of the Lucille P. Markey Charitable Trust Programs in Biomedical Science,[1] with the assistance of the staff from the BHEW, is evaluating the three major components of the of the Trust's philanthropy: (1) the General Organizational Grants, (2) the Markey Scholars and Fellows program, and (3) the Research Program Grants.

This report examines the Research Program Grants, which funded research centers or programs addressing fundamental questions in the biomedical sciences. The Trustees awarded 92 Research Program Grants ranging in size from $500,000 to $13 million for a total of $325 million. The awards were made to assist in the establishment, reorganization, or expansion of significant biomedical research centers or programs and to fund established leading investigators with major commitments to the life sciences. NRC staff obtained data and information from the Lucille P. Markey Charitable Trust Records archived at the Rockefeller Archive Center, examined Markey databases, solicited materials from grant recipients, and conducted site visits to a sample of grant recipients. The committee sought to understand whether the grants made to develop centers or programs resulted in program creation and development, program sustainability, research productivity, and faculty development, and positively integrated the funded program with the host institution. Unfortunately, the committee was not able to assess adequately the scientific quality or impact of the Research Program Grants on biomedical research or the impact of the program on the research centers and projects that it funded. This inability stems from one of the Research Program Grants' strengths, its flexibility in not imposing stringent reporting requirements on grant recipients. As a consequence, information that would be useful

[1]The Committee for the Evaluation of the Lucille P. Markey Program in Biomedical Sciences is the proper name of the NRC Committee that will assess the Markey Trust's activities. Hereafter it will be referred to as the "Markey Committee" or the "Committee."

to an evaluation of the impact of the Research Program Grants was not systematically collected.

This is the third in a series of reports that document the activities of the Markey Trust. The previously published, *Bridging the Bed-Bench Gap: Contributions of the Markey Trust*, examines the General Organizational Grants program, while *The Markey Scholars Conference Proceedings* summarizes presentations and abstracts from the 2002 Markey Scholars Conference held as part of the National Academies evaluation. Both reports are available through the National Academies Press. Additional reports will assess the Markey Scholars and Visiting Fellows programs and publish the proceedings of a workshop on evaluation practices in philanthropic and public organizations that support biomedical scientists.

Just as each of the Markey programs varied in terms of goals and focus, so did the committee's approach to assessment and evaluation. The Markey Scholars program was evaluated prospectively and is amenable to greater methodological rigor than this assessment of Research Program Grants or the previously published examination of the General Organizational Grants. This report relies on expert judgments and on the information gathered in site visits. It is organized into several sections and a set of appendixes, beginning with a history of the Markey Trust and the Markey grant programs. It continues with a discussion of the methodological issues related to evaluating these programs as a whole and the Research Program Grants in particular, and it briefly describes each of the 92 Research Program Grants funded by the Markey Trust. It concludes with potential lessons for funding organizations or individual philanthropists with analogous interests in supporting biomedical research. The appendixes summarize the site visits and telephone interviews with principal investigators conducted by the committee, expert consultants, and NRC staff.

History of the Markey Trust[2]

Lucille P. Markey executed her will creating the Lucille P. Markey Charitable Trust[3] in 1975. Mrs. Markey's wealth, which later endowed the Trust, was derived from the family of her first husband, Warren Wright. In 1888, with an initial investment of $3,500, Warren's father, William Wright, founded the Calumet Baking Powder Company, which he built over the ensuing decades into the leading company in the industry. In the late 1920s, Warren sold Calumet to Postum (later General Foods) for about $32 million. This fortune, along with Calumet Farms, purchased by the elder Wright in 1924, was the foundation of the Wrights' wealth, the bulk of which passed to Warren. When Warren Wright died in 1950, his estate was valued at approximately $20 million, about half of which was in securities and a quarter in oil and gas interests in seven states that would appreciate significantly in later years (Auerbach, 1994).

One of the valuable Wright-owned oil fields was the Waddell Ranch located outside of Odessa, Texas. Under typical oil lease arrangements, the lessor—in this case Gulf Oil Company—paid all costs and received seven-eighths of the proceeds, while the property owner received one-

[2]The History of the Markey Trust is largely a duplicate of the same section that appeared in *Bridging the Bed-Bench Gap: Contributions of the Markey Trust*. The committee wants each of the five reports produced in this evaluation to exist independently; consequently some sections are repeated in each report.

[3]The Lucille P. Markey Charitable Trust is the institution's official name. In this report it will be referred to as the "Markey Trust" or the "Trust."

eighth. In 1925, Gulf Oil leased the Waddell Ranch for 50 years, which was unusual because most oil leases are for perpetuity or for as long as the land is productive. In 1975, following the oil embargo and consequent rapid increase in oil prices, the leases expired. Through a series of court cases, Gulf fought to have the leases extended at the old 1925 rate, but eventually the Wright heirs and the other Waddell Ranch owners were victorious and the income from the new leases, which were then part of Mrs. Markey's estate, increased dramatically. Prior to his death, Warren Wright had amply addressed the needs of his children through a trust arrangement. Lucille Wright, who subsequently married Eugene Markey, realized that her estate would go either to charity or taxes. Mrs. Markey concluded that she was not interested in leaving her money to charity as broadly defined, but rather to something that would be immediate and specific (Auerbach, 1994).

Mrs. Markey's decision to leave her estate to medical research evolved slowly. Her illnesses and those of Gene Markey stimulated her interest in research that could impact human health. Realizing that health research is a broad field, Mrs. Markey asked Louis Hector, her attorney, to explore whether something more specific could be identified to guide the work of the charity. Hector visited the Robert Wood Johnson Foundation, which was established in 1972 as a national philanthropy devoted to improving the health and health care of all Americans, and the Rockefeller University, which focuses on medical research, to learn more of their activities. After hearing of the work of both institutions, Mrs. Markey concluded that the clinical aspects of health care were covered by other institutions, and that her estate should be dedicated to the promotion of biomedical research. Because of this decision the term "basic medical research" was inserted into her will.

> It took her quite a while to wrap her mind around the idea of basic medical research," says Hector, "but once she did, that was it. The money, she decided, should go for square-one stuff, to solve the most elemental and perplexing puzzles. (Fichtner, 1990).

The mission of the Markey Trust, thus was "For the purposes of supporting and encouraging basic medical research" (Lucille P. Markey Charitable Trust, 1996).

Although she had not previously been a generous benefactor, Mrs. Markey began to respond to solicitations from a variety of local institutions. The following anecdote reveals how her giving began with the University of Kentucky:

> When Dr. Roach first approached Lucille Markey in the late 1970s for a contribution toward the construction of a cancer center on the campus of the University of Kentucky, she said graciously, "Of course, Ben, we'll

> help. We'll give you $1,000." In response, Gene Markey chimed in, "Dear, he doesn't want a thousand dollars, he wants a million." The next morning Mrs. Markey called Dr. Roach and said, "We're going to give you one million in cash for your center." (Auerbach, 1994:95-96).

She subsequently gave a number of gifts totaling $5.25 million to the Ephraim McDowell Research Foundation to build a cancer center at the University of Kentucky. In 1984 and 1985, the Markey Trust gave nearly $8.1 million to the University of Kentucky to continue programs Mrs. Markey had initiated before her death (Lucille P. Markey Charitable Trust, 1996).

In addition to settling on a substantive focus for her Trust, Mrs. Markey also determined that she did not want to create a permanent foundation that might change or drift away from her own mission. Rather, she wanted to disperse her estate quickly so that the work of the Trust would not change over time, particularly as the Trustees changed. Louis J. Hector, who became chairman of the Trust, once told *The Chronicle of Higher Education* that when he and Mrs. Markey were working out the details of the Trust, the heiress told him, "I want the money out there doing a job, and I think what the trustees ought to do is spend it in a reasonable amount of time and then shut down" (Nicklin, 1997).

Mrs. Markey elected to limit the term of the Trust to 15 years and the number of trustees to five. Her decision was based on four guiding principles (Dickason and Neuhauser, 2000:2):

1. She felt it was important to apply as much money as possible to achieving the Trust's purpose in as short a time as possible.
2. She wanted to know who would be involved in the management of the assets and distribution of her largess. She named five trustees, all of whom she knew well. Four of them were alive at her death and three continued to serve throughout the life of the Trust.
3. She wanted her money applied to grants, not to support a permanent bureaucracy.
4. She believed that the purpose and goals of any foundation could become obsolete over time; a time limit could help to prevent such obsolescence.

When Mrs. Markey died on July 24, 1982, the Lucille P. Markey Charitable Trust was incorporated as a Florida nonprofit organization with 501(c) (3) status. The initial meeting of the Board of Trustees occurred in October 1983, and the Trust's Miami office opened January 1, 1984. The trust completed all activities on June 15, 1997.

Four trustees attended the initial 1983 meeting (Dickason and Neuhauser, 2000):

1. Laurette Heraty, who had served Mrs. Markey and her first husband, Warren Wright, in their Chicago office as a secretary since 1937. She retired from the board in 1989.

2. Louis Hector, who was Mrs. Markey's attorney and drafted her will. He served as a trustee of the University of Miami, Rockefeller University, and the Lincoln Center and is a member of the American Academy of Arts and Sciences.

3. William Sutter, an attorney and expert in oil and gas leasing issues, who worked for Mr. Wright and Mrs. Markey from his Chicago office in the law firm of Hopkins and Sutter.

4. Margaret Glass of Lexington, Kentucky, who worked so closely with Mrs. Markey over the years that she was seen as an effective custodian and interpreter of her wishes.

Two additional trustees were named during the life of the Trust:

1. George Shinn, a financial expert (elected to fill the position left vacant by the death in 1980 of Gene Markey) was president of Merrill Lynch & Co., CEO of First Boston Corporation, and a member of the Board of Governors of the New York Stock Exchange.

2. Robert Glaser, a physician with experience in both academic medicine and philanthropy (elected in 1989 following the retirement of Laurette Heraty), was the Trusts's Director of Medical Sciences from 1984 until 1989. He was past president of the Henry J. Kaiser Family Foundation and dean of the University of Colorado Medical School and Stanford University School of Medicine.

The structure and the function of the Markey Trust were guided from its inception by Louis Hector's vision of supporting and encouraging basic medical research. This vision was consistent and unwavering throughout the duration of the trust and guided the selection of grantees, advisers, reviewers, and funding mechanisms.

Dr. Glaser also played an important role in guiding the implementation of the Markey Trust programs. In 1984, he was asked to become the director of medical sciences for the Trust. Some of his initial recommendations to the Trust included the idea of supporting basic (as opposed to targeted) research. "Medicine was going through an exciting period," Glaser recalled. "There were new fields like structural biology and developmental biology coming along and with substantial resources such as the Trust enjoyed, they could do a very important thing by offering support that was flexible to people and/or programs over a period of time" (Glaser, 2002). Dr. Glaser also recommended that the Trust provide enough support to bright young people to allow them protected time to

establish their research careers. His expertise and vision were to become the major force in the foundation.

The Trust began distributing funds in 1984 to institutions that Mrs. Markey had supported during her lifetime. At the same time, the Trust began to plan a long-term strategy for its programs. In 1984, the Trust held a series of three "think tank" meetings with distinguished biomedical researchers in California, New York, and London. These sessions produced a number of recommendations, the most important of which was the idea of long-term financial support for postdoctoral fellows and young faculty members. In 1984 the Trust announced the creation of the Markey Scholars Awards in Biomedical Sciences, which became the Trust's best-known program. The initial cohort of Markey Scholars was appointed in February 1985. In the fall of 1985, the initial Research Program Grants were awarded. Later, in 1988, the Trust began making what would later be classified as General Organizational Grants. Each of these award mechanisms is discussed in greater detail later.

In 1985, most Trust activity ceased because of complicated litigation involving the pricing of natural gas. The litigation involved the Federal Energy Regulatory Commission, the California Public Service Commission, and a number of major oil and gas companies. The case was eventually settled in Texas courts. However, during the two years of court proceedings, the Trust funded no new research grants and was able to continue funding only for the Markey Scholars program and for a few small miscellaneous and related grants. During this hiatus, the Trustees continued to receive new grant proposals and conducted selected site visits. Moreover, the value of the Markey Estate and Trust grew substantially, benefiting from investment income as well as the continued oil and gas income. In the fall of 1987 the litigation was resolved, and the Trust resumed awarding Research Program Grants. During its 15-year lifetime, the Markey Trust gave a total of $507,151,000 to basic medical research and research training. Administrative and operational costs amounted to $29,087,000, or approximately 5 percent of the total Trust. A recent study by the Urban Institute indicates that foundations of similar size and scope have average operating and administrative expenses of about 8 percent (Boris, et. al, 2005). Additional expenses included $10,529,000 for direct investment costs and mineral depletion costs. The total value of the Trust was $549,520,000, which included $149,565,000 in investment income (Dickason and Neuhauser, 2000).

Grant Programs

The Markey Trust made awards in the three main stages of a biomedical research career in which "supporting and encouraging basic medical research" can occur.

1. General Organizational Grants were directed to improve the education and training of both Ph.D.s and M.D.s planning careers in basic clinical research and research in molecular medicine.
2. Markey Scholars and Fellows Awards identified and supported outstanding younger researchers in the biomedical sciences, providing them with long-term financial assistance early in their careers.
3. Research Program Grants provided funding opportunities for established scientists with proven records of excellence in biomedical research.

A few grants that fell outside the above categories were put into a miscellaneous category. The distribution of funding is shown in Figure 1. The Markey Scholars and Visiting Fellows Awards, which will be the subject of a subsequent full-length evaluative report, and the General Organizational Grants program, which has been described in *Bridging the Bed-Bench Gap: Contributions of the Markey Trust*, are described only briefly here. A thorough description of the Research Program Grants is presented in the next section of this report.

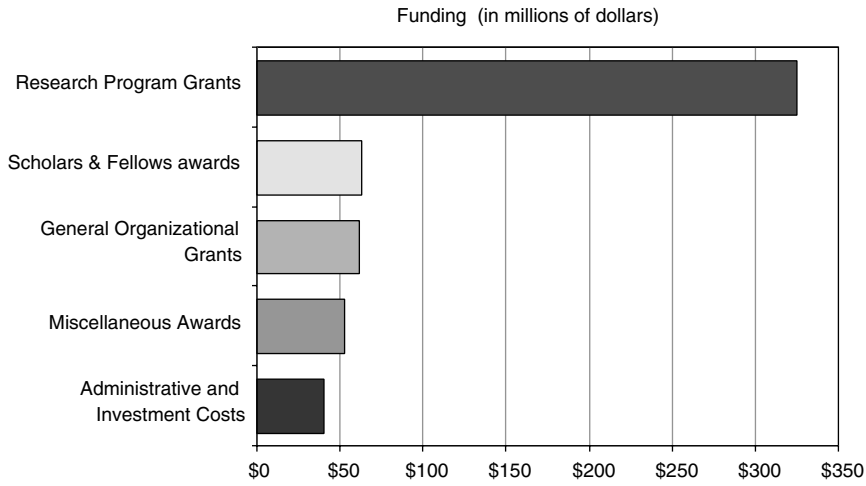

FIGURE 1 Distribution of the Markey Trust programs and grant making.
SOURCE: Lucille P. Markey Trust, 1996.

MARKEY SCHOLARS AND VISITING FELLOWS

The Markey Trustees recognized the importance of providing funding to young biomedical scientists to launch their careers. The Trust dedicated $63,093,900 to fund the Scholar Awards in Biomedical Sciences and the United Kingdom and Australian Visiting Fellows.

Scholar Awards in Biomedical Sciences

By establishing the Markey Scholars program in 1984, the Trustees recognized that top priority should be given to the support of young researchers as they moved from postdoctoral into junior faculty positions. The goal was to enable the Markey Scholars to conduct independent research early in their careers. Between 1985 and 1991, 113 Markey Scholars were supported for up to three years of postdoctoral training followed by five years as beginning faculty members. This support included both salary and research funding. Scholar awards ranged from $570,000 to $711,000 depending on the length of the postdoctoral experience. The Markey Trust was unique in providing support for young scientists for up to eight years. The total funding for Markey Scholars was $59,795,900.

United Kingdom and Australian Visiting Fellows

In addition to the scholars program, the Trustees supported outstanding young scientists from the United Kingdom and Australia by enabling them to spend two years as postdoctoral fellows at American research institutions. A total of 36 Visiting Fellows—26 from the United Kingdom and 10 from Australia—was elected between 1986 through 1994. Total support amounted to $3,298,000.

GENERAL ORGANIZATIONAL GRANTS

Almost at its inception, The Markey Trust had become cognizant of a growing gap between biomedical research and clinical application. In 1989, input was sought from a number of biomedical scientists on directions for Trust funding during its remaining term. They advised that there was general concern in medical schools about the "bed-bench gap" and that plans were emerging in many universities to develop new curricula and teaching techniques to close the gap between laboratory research and research based on clinical observation.

The Markey Trust indicated that it would be responsive to proposals to address the development of training programs designed to bridge the "bed-bench" gap. The trustees received a number of proposals that fell into two categories: those that provided significant opportunities for M.D.s to engage in basic research during and immediately following medical school and residency and those that provided significant clinical exposure for Ph.D.s while they were predoctoral or postdoctoral students. The first of these awards, classified as General Organizational Grants, was made in 1992. These grants were designed to close the widening gap between rapid advances in our understanding of biological process and the translation of that knowledge into techniques for preventing diseases (Lucille P. Markey Charitable Trust, 1995).

General Organizational Grant programs were funded for approximately five years, although due to the flexibility of the Markey grants, many grant recipients were able to extend the grant's duration. Because of the limited term of the Trust, General Organizational Grants could not be renewed. Between 1988 and 1995, 22 General Organizational Grants amounting to $62,121,700 were awarded. The average amount awarded was about $2.8 million, but award amounts ranged from $50,000 to $13,750,000.

MISCELLANEOUS AWARDS

During its tenure, the Markey Trust made a number of awards that did not fit into the three major award categories. These awards continued

support made by Mrs. Markey during her lifetime, funded endowed chairs, provided scholarships to biomedical researchers, and funded related research support. These award programs, totaling $53,606,232, are listed below.

Lucille P. Markey Basic Medical Research Funds

To memorialize the Trust's support for the training of biomedical scientists, endowments totaling $14,000,000 were made to seven institutions. These institutions established permanent endowments known as the Lucille P. Markey Basic Medical Research Funds to provide support for promising predoctoral and postdoctoral fellows and junior faculty.[4]

Markey Predoctoral Fellows

In its early years the Trust provided $9,400,000 to 15 academic institutions to assist predoctoral students in biomedical science programs. These graduate students were known as Markey Fellows.

Other Grants for Career Development

The Trust provided $3,030,000 to six research institutes to fund summer seminars and short courses for potential scientists in basic medical research.

Continuation of Programs Initiated by Mrs. Markey

These awards were made in 1984 and 1985 to the University of Kentucky and University of Miami and totaled $8,700,000.

Endowed Chairs

Between 1985 and 1996, the Markey Trust provided $11,500,000 to fund endowed chairs.[5]

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[4]These seven institutions were: Harvard University; Johns Hopkins University; Rockefeller University; Stanford University; University of California, San Francisco; University of Michigan; and University of Texas Southwestern Medical Center.

[5]The endowed chairs were: Rockefeller University, Henry G. Kunkel Professor; University of Kentucky, Warren Wright, Sr.-Lucille Wright Markey Chair, Gluck Equine Research Center; University of Kentucky, Lucille P. Markey Chair in Oncology Research; University of Kentucky, Warren Wright, Sr.-Lucille Wright Markey Chair, Gluck Equine Research Center (supplement); University of Miami, Markey Professorship in Biochemistry and Molecu-

Research Support and Related Grants

Between 1985 and 1997, the Trust provided $6,976,232 to fund 56 miscellaneous grants to support smaller research projects and to encourage or facilitate basic medical research.

RESEARCH PROGRAM GRANTS

Research Programs Grants represented the largest component of the Markey Trust's funding activities. During the 11-year interval from 1985 to 1995, 92 organizations were awarded a total of $316, 248,175. In fiscal years 1996 and 1997, the Trust made supplementary awards of $500,000 each to 18 grant recipients in recognition of outstanding progress by Markey-supported investigators. Consequently, awards in the Research Program Grants program totaled $325,248,175. They ranged in amount from a low of $500,000 to a high of $12, 613,000.

The Trust initially defined the purpose of Research Program Grants as follows:

> Research Program Grants are made to institutions with a major commitment to the life sciences to assist in the establishment, reorganization, or expansion of significant biomedical research programs or centers. The grants usually involve funding for the recruitment of new faculty, pre- and postdoctoral support, completion or renovation of laboratory space, purchase of new equipment, and additional technical assistance (Lucille P. Markey Charitable Trust, 1988).

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lar Biology; Washington University in St. Louis, Markey Professorship in Basic Biomedical or Basic Biological Sciences; and Yale University, Lucille P. Markey Professorship in Biomedical Sciences.

Background of the Research Program Grants

In order to understand how best to make significant contributions to the advance of biomedical research, the Markey Trustees held a series of meetings with experts in the biomedical sciences. The first meeting took place in Menlo Park, California, in April 1984 and was quickly followed by a similar meeting in New York City in May 1984. A third meeting was held in Dallas, Texas, in February 1989. The information collected from these meetings was used to focus and guide the three primary funding activities of the Trust. The first two meetings were especially important in identifying potential targets for Trust funding. The California conference was concerned primarily with what would emerge as the Markey Scholars program, and nine target areas were identified as appropriate for Markey funding (Lucille P. Markey Charitable Trust Records, 1984). These target areas included the following:

1. Research training
2. Support for young promising investigators
3. Support for established investigators
4. Funds for laboratory equipment
5. Discretionary funds to support promising research opportunities and fields of investigation
6. Identification and support of small groups of investigators already established and recognized for outstanding biomedical research
7. Support of promising fields of investigation
8. Funds for important but not popular research fields

9. Long-term support for ongoing research endeavors where the current track record presages future payoffs. Such as support provided by the Medical Research Council, University of Cambridge.

The Markey Predoctoral Fellows, the General Organizational Grants, and Markey Scholars programs addressed the first two targets. All of the remaining targets were addressed through the Research Program Grants. The Trustees wanted the Research Program Grants to have a major impact on biomedical sciences and used input from meeting participants to direct funding. Participants concluded that the flexibility to change directions in basic research to pursue new leads and ideas was vital. Although the level of private sector funding in biomedical sciences was lower than federal funding in an absolute sense, this greater flexibility would complement and augment federal funding. In addition, the support for equipment, construction, and renovation—which are generally not covered by federal funding—would provide infrastructure not generally available from other funding sources that was essential to establish or grow new programs. Finally, the relatively large grants would provide sufficient funding for bold efforts and usually represented a significant portion of the recipient's basic research portfolio (Lucille P. Markey Charitable Trust Records, 1984).

A consensus emerged among experts who advised the Markey Trustees that the focus of the Research Program Grants should be to fund research and infrastructure that would ordinarily not be funded by NIH or NSF. Rather, awards should be directed to proven, able individuals or to small groups working in areas that seemed promising, but might not have preliminary data nor show immediate applied results. The Trustees desired "to encourage the development of programs in biomedical research going beyond the reach of others—things that otherwise might not be done, but should be done" (Lucille P. Markey Charitable Trust Records, 1984). The experts recommended funding long-term support for ongoing research endeavors in which the track record of the individuals in a leadership position predicted major payoffs. They urged the Trustees to emulate a model based on the Medical Research Council Laboratory of Molecular Biology at Cambridge that had provided such support with extraordinary results.

Consequently, the Trustees identified a set of elements to guide the selection of awardees that might predict success and maximize the impact of Markey Research Program Grants. Although all tenets were not applicable to Research Program Grants, they provided guidelines for the selection of grantees by the Markey Trust (Lucille P. Markey Charitable Trust Records, 1989). By the third meeting in Dallas, these characteristics were crystallized into six basic tenets:

1. Investigators were encouraged to eschew conservatism in the choice of research topics, to take risks, and to pursue longer-term objectives than is the rule under conventional grant support.

2. Research environments were strengthened and enhanced by the establishment of new state-of-the-art laboratories and sophisticated multiuser resources.

3. Intellectual capital was made available for new ventures and for exploring emergent and unexpected research opportunities.

4. New faculty were given start-up funds for carrying out pilot research, gathering data, and positioning themselves to compete effectively for external funds from other sources.

5. Financial incentives were provided for dissolving departmental barriers, creating joint programs, and sharing graduate students. Indeed, it is difficult to exaggerate the catalytic effect of the Markey mode of support in fostering interaction and interdisciplinary research.

6. Investigators were encouraged to propose their best ideas for funding rather than having the Trustees specify program themes for grant awards.

SELECTION PROCESS FOR RESEARCH PROGRAM GRANTS

Ninety-two Research Program Grants were awarded between fiscal years 1986 and 1995. These grants varied in terms of size, duration, and approach. This diversity is described in Appendix A, which presents brief descriptions of each of the programs. The following material reviews the selection process and provides a history of events that occurred.

Selecting the Initial Grants

Early in its tenure, the Trustees recognized that they needed to establish a systematic procedure to rationalize the selection of Research Programs Grants that underwent a thorough review process. They quickly came to the conclusion that a considerable number of applications could not be funded either because the applicants were not legally qualified or because the purpose of the application was clearly outside the purposed of the Trust. The Trustees decided that such applications should be denied as promptly as possible by the staff in Miami.

Additional consideration was given to applications that were broadly within the field of biomedical research but which were not basic biomedical research. In some cases this discrepancy may have been apparent to the Miami staff, but in some instances professional judgment would be required. The Trustees decided that, in such cases, decisions would be made either by conference call with the Director for Medical Science or by

forwarding the application to him. Notification of denials would be made by the Miami staff except for a few denials that would require a letter from the Director for Medical Science.

Moreover, the Trust received some applications that were within the field of basic biomedical research, but were not in accordance with the policies established by the trustees. These applications included requests from re-grant organizations, requests for conference travel, requests for endowments, and requests for construction and renovation unconnected with a funded project. The Trustees decided that such applications should be denied by the Miami staff with a proviso that the Director for Medical Science, and if necessary, the Trustee Executive Committee be consulted in advance in cases in which the application of the policy might be unclear.

The goal of this screening process was to eliminate as many applications as possible without requiring review by the Director for Medical Science and expert consults. Nevertheless, the Trust received a large number of proposals for basic biomedical research that did not violate any of the previously established Trustee policies. The Executive Committee concluded that such applications could be denied by the Director for Medical Science, with appropriate advice from the expert consultants, or any one or more of the following general policy reasons:

- The National Institutes of Health would normally fund the proposal, but the proposal had not been submitted to NIH or had been submitted and had not been approved.
- The proposal substantially duplicated other research projects that appeared to have greater prospects of success.
- The proposal appeared to have no real expectation of important results.

In summary, the Trustees identified 16 denial codes classified into three categories. These included:

1. Denials under the provisions of Mrs. Markey's Will
   - Requests from an individual
   - Requests from a for-profit organization
   - Requests from an organization not in the United States
   - Requests for other than biomedical research
   - Requests for biomedical research that is not basic
2. Denials by policy established by the Trustees
   - Requests from re-grant organizations
   - Requests from private foundations

- Requests for support of travel to a conference
- Requests for endowment unconnected with a project
- Requests for construction/renovation funds unconnected with a project
- Requests for fellowships, scholarships, or similar programs

3. Denials as a result of review
   - Request denied, but a revised proposal requested
   - Request denied on merit
   - Request denied as the proposal would be funded by NIH
   - Request denied as the proposal substantially duplicates other research
   - Request denied as the proposal has no realistic expectations of significant or important results

The Markey Trustees never prepared a formal solicitation for Research Program Grants. Applicants were required to submit a preliminary letter of not more than four pages, briefly outlining the plans and objectives of the program for which support was sought and an estimate of the required budget. Curriculum vitae and a listing of current research support for investigators from NIH, NSF, and other funding agencies were also required. (Lucille P. Markey Charitable Trust Records, 1989). These guidelines were published by the Trust in 1991 as program information and guidelines (see below) but not as a formal solicitation:

> Research Program Grants are made to institutions with a major commitment to the life sciences to support in whole or in part new biomedical research programs or centers. Emphasis is placed on interdisciplinary efforts by groups of able investigators who are addressing fundamental questions in biomedical science. Research Program Grants support new initiatives in fields such as cellular and molecular biology, developmental biology, structural biology, neurobiology, immunology, genetics, virology, and related areas of basic science. (Lucille P. Markey Charitable Trust, 1991)

If the application survived the previous screens, Trustees reviewed the preliminary letter, and if they found that the proposal met the requirements for a Research Program Grant, additional information was requested. Following receipt and approval of the additional information, arrangements were made for the applicant to meet with the Trust's director for medical science. In some cases a site visit was also scheduled. At this point, the Trustees turned to five senior consultants to judge the merit of an application. These senior consultants, utilized throughout the duration of awards, included the following:

- Michael S. Brown, M.D., University of Texas Southwestern Medical Center
- Joseph M. Davie, M.D., Ph.D., Biogen, Inc.
- Arno G. Motulsky, M.D., University of Washington School of Medicine
- Elizabeth F. Neufeld, Ph.D., University of California, Los Angeles, School of Medicine
- Eric M. Shooter, Ph.D., Stanford University School of Medicine

Based on the advice of the senior consultants and the director for medical science, the initial Research Program Grants were made in August of 1985 to Carnegie Mellon University and the University of Texas Southwestern Medical Center and in November 1985 to the University of Chicago, Stanford University, and the California Institute of Technology. These five grantees were competitively selected from more than 100 proposals submitted. Because of problems associated with the natural gas pricing litigation, Trustees restricted the number of awards made in the fall of 1985 to those that could be funded from available funds. No awards were made in 1986 and 1987. After favorable resolution of the litigation, Research Program Grants awards resumed in 1988. In that year, 21 awards were made for a total of $105,120,402.

At the end of fiscal year 1988, the Trustees realized that there was an expectation at biomedical research institutions that grant activity by the Trust would continue at the 1988 level. The Trustees knew, however, that this level of annual funding would be reduced sharply because declines in oil and gas revenues had reduced the Markey Trust dollars. Consequently, a large number of meritorious proposals were unable to receive funding. The Trust calculated it could make approximately $25 million in new Research Program Grants awards annually for the next six years. In fact, over the next four years, 29 awards were made for a total of $118,590,000, an average of $30 million per year.

By 1992, the Trustees recognized that they needed to change their focus from Research Program Grants awards to General Organizational Grant awards. Consequently, in fiscal year 1993, the Trust made only five Research Program Grants awards to proposals that had been received and approved earlier for a total of $14,000,000.

From 1993 on, the focus of the Research Program Grants changed. The Trustees were increasingly aware that the Trust would have to close out its activities and considered two alternatives. First, the Trust could restrict the remaining funds to institutions that had not received support or could allocate remaining funds to previous grant recipients who had made exemplary use of funds. Second, the Trust could make awards to

new applicants—either relatively few grants in the $3 million to $6 million range or a larger number of grants in the in the $1 million to $2 million range. Contemplation of these strategies was tempered by the uncertain market for the remaining oil and gas revenues, which meant that the Trustees had only estimates of funds available for distribution.

After careful consideration, the Trustees had concluded that the best use of the remaining funding would be to award a larger number of Research Program Grants in the $1 million to $2 million dollar range. The Trustees reasoned that grants in this range were large enough to have an impact, particularly given the Trust's willingness to permit flexibility in the use of awards. Recent experiences indicated that established investigators were successful in targeting funds to high-priority areas so as to enhance the impact of relatively smaller awards. Therefore, the Trust sent a letter to a number of Research Program Grants applicants explaining the new program of smaller awards and requesting updated proposals in the $1 million to $2 million dollar range. In the fall of 1993, it budgeted $32 million for these smaller Research Program Grants and gave preliminary approval to the first batch. The Trustees' strategy was to make a large number of smaller awards in fiscal year 1995 and then to determine a strategy for any remaining funds. During the 1995 fiscal year, they made awards to 26 institutions for a total of $31,400,000.

As the Trust neared its closing date, the Trustees began planning for the final distribution of funds. In the spring of 1994, Louis Hector recommended that the Trust complete the funding of the $1 million to $2 million smaller Research Program Grants applications; pause for a while, saying nothing about the potential for extra funds being available; and then late in 1995 or early in 1996 announce one final round of grants—whether new, continuation, or otherwise. The Trustees were not sure exactly how much funding would be available for distribution and did not wish to make any announcements until they had a good estimate of funds available to distribute.

In the fall of 1995, the Trustees concluded that the best utilization of funds would be to (1) create a series of endowment grants to endow chairs and (2) develop continuation/special consideration awards to previously funded Research Program Grants awardees that had exhibited outstanding progress addressing important problems in biomedical science. These awards would be for $500,000 each. The Director for Medical Science and Eric Shooter, a special advisor to the Director for Medical Science, identified 22 previous Research Program Grants awardees worthy of consideration for these continuation/special consideration awards. In February of 1996, the Trustees awarded continuation/special consideration awards to 12 institutions. In September 1996, sufficient funds were

available to award an additional six continuation/special consideration awards. With these awards, the funding for Research Program Grants came to an end.

Because of the extensive review process, the Markey Trustees were less concerned about the supervision of grantee awards. Continuation of funding in subsequent years was dependent upon the receipt of an annual progress report, but the level of monitoring and evaluation was minimal. All Markey Research Program Grants awardees received second- and additional-year funding following receipt of an annual report. The Trustees allowed a great deal of flexibility in the timing of distribution of funds, and budget lines could be moved without returning for Trust approval. Many grantees were able to extend the period of funding beyond the initial tenure of the grant. This changing nature of program emphasis and lack of an evaluation plan make it difficult to assess the impact of the program.

Assessing the Markey Research Program Grants

Three different approaches were used to assess the Research Programs Grants. First, all grantees were required to submit annual progress reports to the Trust. No specific format for the annual reports was imposed with the consequence that progress reports varied greatly in what and how they reported. The progress reports of some grantees provided a detailed insight into the outcomes of the research conducted, as well as a diary of the process used to reach these outcomes. The progress reports of some grantees were less detailed and provided only thumbnail descriptions of activities conducted by the recipient organization. Despite the unevenness of the progress reports, the committee was able to use them to document some milestones for the grantees, including data on staffing changes, construction and renovation, and purchase of major equipment.

In addition, the committee and NRC staff made 19 site visits, conducted 12 telephone interviews with principal investigators, and received two letter reports. The selection of institutions for site visits was based on an intersection of several constructs. First, the committee recognized that there was neither the time nor the resources to visit all awardees. Second, the committee wanted to visit sites that received both large and small awards and sites that were infrastructure development and investigator initiated awardees. Third, the committee wanted to restrict site visits to those programs for which the principal investigator was still actively engaged with the program. One site was unable to participate as all staff with any institutional knowledge of the grant had left the institution.

Finally, in order to preserve resources, the committee concluded that, whenever possible, site visits should be made in clusters, minimizing travel time and expenses. Telephone interviews were used to augment the site visits. In two cases, NRC staff were unable to schedule a time for the telephone interview with the principal investigator, who submitted a letter report in place of the telephone interview. From some grantees telephone interviews and site visits and/or letter reports were obtained. Ultimately, data were obtained from 25 recipients.

These data provided the committee with valuable insights into how funds were used in a particular institution. The committee found, however, that it was difficult to generalize the insights garnered from these sources because of the diverse nature of the problems studied by grantees and the variety of awards made. The committee came to the conclusion that Research Program Grants were awarded to a heterogeneous group of investigators at a number of different universities within differently configured research centers.

The committee recognized that, at a minimum, Markey Research Program Grants awards could be classified into two categories: infrastructure development and investigator-initiated awards. The infrastructure development awards were used to create, expand, or enhance an existing department, center, or program or to develop new centers that focused on a particular aspect of the biological sciences. For several recipients, the awards resulted in the development of multidisciplinary departments within the biological sciences. Investigator-initiated awards focused on one or more particular research projects tied to a particular investigator or team of investigators. In addition, the committee classified Research Program Grants awards on a second dimension—the size of the award. The award amounts varied from less than $1 million to more than $13 million. The committee, somewhat arbitrarily, designated $4 million in total funding as the boundary between large and small awards. These awards are shown in Table A.

Infrastructure development awards tended to be made during the initial years of the Trust's philanthropy and were, in general, large awards—that is, in excess of $4 million. Investigator-initiated awards tended to be made during the concluding years of the Trust's philanthropy and were, in general, smaller awards—less than $4 million. However, there was sufficient variability in these awards that they overlapped in size with those for infrastructure development. Site visits were made to evaluate both infrastructure development and investigator-initiated awards and to recipients of both large and small awards.

A good example of such an intersection of dimensions is one of the earliest awards made by the Markey Trust to the University of California, San Francisco. This award of nearly $14 million enabled the university to

TABLE A

Grant Recipient	Award Amount	Years of Funding	
		Beginning	Ending
Large - Infrastructure Development			
California Institute of Technology	$13,000,000	1986	1991
Case Western Reserve University	$5,500,000	1988	1997
Cold Spring Harbor Laboratory	$4,500,000	1991	1996
Columbia University	$6,500,000	1988	1996
Cornell University Medical College	$4,000,000	1992	1997
Duke University	$8,000,000	1990	1994
Florida State University	$4,500,000	1991	2000
Fox Chase Cancer Center	$4,000,000	1991	1996
Harvard Medical School	$11,000,000	1988	1993
Johns Hopkins University	$7,150,000	1988	1996
Northwestern University	$5,890,000	1989	1993
Purdue University	$6,990,000	1988	1997
Stanford University	$12,613,550	1986	1997
The Whitehead Institute for Biomedical Research	$7,650,000	1988	1993
University of California, Los Angeles	$4,350,000	1988	1997
University of California, San Diego	$4,320,000	1988	1998
University of Colorado Health Sciences Center	$5,000,000	1991	1996
University of Miami	$6,270,000	1988	1999
University of Virginia	$6,100,000	1990	1996
Washington University in St. Louis	$12,100,000	1988	1994
Yale University	$12,100,000	1988	1997
Large - Investigator Initiated			
Princeton University	$4,500,000	1992	1997
The Scripps Research Institute	$5,000,000	1992	1996
The University of Michigan	$8,250,000	1989	1997
University of California, Berkeley	$8,500,000	1989	1994
University of Chicago	$9,219,223	1986	1992
University of Pennsylvania	$4,720,402	1988	1996
University of Rochester School of Medicine/Dentistry	$4,000,000	1991	1997
University of Washington	$7,500,000	1990	1997
Vanderbilt University	$5,500,000	1991	1996
Small - Infrastructure Development			
Carnegie Institute of Washington	$2,700,000	1988	1997
Carnegie-Mellon University	$1,925,000	1986	1992
Children's Memorial Medical Center	$1,000,000	1995	1997
Cincinnati Children's Hospital Medical Center	$3,500,000	1992	1996

continued

TABLE A Continued

Grant Recipient	Award Amount	Years of Funding	
		Beginning	Ending
Harvard University	$1,600,000	1995	1998
Harvard University, School of Public Health	$3,500,000	1991	1996
Massachusetts General Hospital	$3,000,000	1993	1997
New York University	$2,600,000	1991	1997
Public Health Research Institute	$2,500,000	1992	1996
Stanford University	$1,200,000	1995	1997
The Burnham Institute	$1,500,000	1992	1996
The Children's Hospital, Boston	$2,475,000	1988	1993
The Salk Institute for Biological Studies	$2,600,000	1994	1996
The University of Utah	$2,500,000	1993	1997
Thomas Jefferson University	$3,500,000	1990	1994
University of California, Santa Cruz	$2,500,000	1992	1999
University of Colorado, Boulder	$1,500,000	1995	1997
University of Massachusetts Medical Center	$1,500,000	1995	1997
University of North Carolina at Chapel Hill	$1,500,000	1995	1997
University of Oregon	$3,300,000	1988	1995
University of Texas-Houston Health Sciences Center	$1,000,000	1995	1997
University of Texas-Southwestern Medical Center	$2,280,000	1986	1992
University of Texas-Southwestern Medical Center	$1,045,000	1988	1994
University of Texas Medical Branch at Galveston	$1,000,000	1995	1996
University of Vermont	$2,300,000	1991	1999
Wisconsin University-Madison	$990,000	1988	1992
Small - Investigator Initiated			
Albert Einstein College of Medicine of Yeshiva Univ.	$2,310,000	1988	1995
Baylor College of Medicine	$1,400,000	1994	1999
Brandeis University	$3,200,000	1988	1996
Brown University	$1,300,000	1994	1998
Cornell University	$1,200,000	1995	1999
Dana Farber Cancer Institute	$1,500,000	1995	1997
Dartmouth Hitchcock Medical School	$1,500,000	1994	1997
Eleanor Roosevelt Institute for Cancer Research	$1,475,000	1988	1993
Georgetown University	$1,000,000	1995	1997
Johns Hopkins University	$1,300,000	1995	1997
Joslin Diabetes Center	$3,500,000	1993	1999
Kennedy Krieger Institute	$500,000	1995	1997

TABLE A Continued

Grant Recipient	Award Amount	Years of Funding	
		Beginning	Ending
Massachusetts Institute of Technology	$3,850,000	1991	1999
Memorial Sloan-Kettering	$2,700,000	1991	1994
Mount Sinai Medical Center	$3,000,000	1993	1997
Neurosciences Institute	$1,375,000	1988	1995
Oregan Health Sciences University	$1,300,000	1995	1997
Rice University	$1,200,000	1995	1997
Rush Presbyterian St. Lukes Medical Center	$1,000,000	1995	1998
Schepens Eye Research Institute	$1,000,000	1995	1997
SUNY-Buffalo	$1,000,000	1995	1997
Temple University	$2,500,000	1990	1996
Texas A&M University	$1,000,000	1995	1998
Tufts University	$2,000,000	1993	1996
University of Alabama at Birmingham	$1,500,000	1991	1995
University of California, Davis	$1,600,000	1995	2002
University of California, Irvine	$1,000,000	1995	1999
University of Florida	$1,600,000	1995	2000
University of Illinois Urbana Champagne	$3,000,000	1992	1998
University of Kentucky	$1,900,000	1995	1998
University of Maryland Biotechnology Institute	$1,000,000	1995	1997
University of Miami	$1,000,000	1995	1998
University of Pittsburgh	$1,000,000	1995	1997
University of Southern California	$1,800,000	1994	1998
University of Wisconsin-Madison	$3,000,000	1992	2003
Worchester Foundation	$1,000,000	1994	1997

establish the Program in Biomedical Science, which restructured research and graduate education in the School of Medicine. Although this award was originally classified as a General Organizational Grant by Markey Trustees, the committee saw in this award the genesis of the infrastructure development and concluded that for analytical purposes it should be considered a Research Program Grants award. This program subsequently received a site visit by the committee.

Although the PIBS program at UCSF was site visited by the committee and the committee considered it an exemplary program, technically it was not a Research Program Grants award. Consequently, data on the UCSF awards are not included in Appendix D. The Markey Trust awarded the first General Organizational Grant award to UCSF in 1988. In subsequent years, the Trustees changed the focus of General Organizational

Grants to training in translational research. For a more thorough assessment of General Organizational Grants in general and the PIBS program in particular, see Bridging the *Bed-Bench Gap: Contributions of the Markey Trust*, published by National Academies Press in 2004.

A third source of information came from analysis of the Lucille P. Markey Charitable Trust Records. As noted earlier, as the Trust was entering its final years, it arranged for all Trust documents to be archived at the Rockefeller Archive Center in Sleepy Hollow, New York. Following the conclusion of the Trust in 1997, all documents were transferred to the center, classified, and microfilmed. The archived Lucille P. Markey Charitable Trust Records currently consist of 153 reels of microfilm with approximately 800 frames on each reel. They are a rich source of information on all aspects of the Trust and will be made available to the public in 2007. The NRC staff searched the archive for information on the process used by the Trust to (1) define the rationale and focus of the Research Program Grants awards, (2) develop the solicitation process, (3) develop the mechanism and protocols for funding these awards, (4) establish the selection process for the awards, and (5) gain understanding of the decisions that led to the 18 supplemental grants.

LIMITATIONS OF THIS ASSESSMENT

Examination of these three data sources provided insights into the purpose of the awards, the processes of selecting grantees, and the impact of grant funds on researchers and recipient institutions. The committee realized that it was impossible to systematically collect data that would enable an assessment of individual programs. The committee had considered reviewing all publications that emerged from Markey funded projects; examining patents and licenses produced with Markey funding; and tabulating subsequent extramural funding that was produced by the Research Program Grants as one way to assess individual programs. However, the committee came to the conclusion that the data needed for such an assessment were inconsistent or missing or both—not only between programs, but also within them. For several additional reasons the committee's ability to conduct an evaluation was limited:

- The grantees, by design, were not homogeneous; rather they represented a broad spectrum of large and small universities, academic medical centers, and research institutes.
- There was no single, overriding principle that directed funding for Research Program Grants. Rather, the Trustees were directed by the guideline "for the purposes of supporting and encouraging basic medical research," and this guideline was broadly and variously interpreted.

- The focus of Research Program Grants changed over time from a few large awards to many smaller awards. Another part of the reason for this change was a conscious decision by Trustees to make a larger number of smaller awards to newly expanding programs in biomedical research. Another part of the reason for this change was pragmatic, based on the decreased availability of funding as the Trust neared completion.
- Grant applications were relatively short and were more conceptual than comprehensive. Consequently, goals, objectives, milestones, and activities were not stated in sufficient detail to be evaluated. . . .
- Systematic data were not collected on grantees' progress toward completing the goals and milestones specified in a grant. Although grantees were required to submit annual progress reports in order to receive subsequent-year funding, there was no specific format for these progress reports and they varied considerably in length and detail both longitudinally and across grantees.
- No comparison group of similar recipients of grants from other sources could be identified.

The committee concluded that neither the data nor the existing resources would permit a rigorous evaluation of the program. Unlike grant programs funded by NIH and NSF, the Markey Research Program Grants were not guided by a systematic, uniform solicitation on which proposals were based. In addition, the focus of the Research Program Grants was fluid—some grants were made to create or build programs, some were for research, and some were for infrastructure development— reflecting both the availability of funds and changes in the goals of the Trustees. Finally, the Trustees did not request data from the grantees that would permit the evaluation of Research Program Grants. Although the Trustees recognized the need for an assessment of the Trust's funding activities, the decision to conduct an assessment was made toward the end of the Trust's tenure. Ideally, program evaluation would have been built in from the very beginning of the program, with variables for measuring program outcomes identified and collected from its onset. In any case, the outcome of basic research is a very long term prospect and may not lend itself to easy assessment. Thus, intermediate or other variables, such as publication rates, new faculty and postdocs, or funding rates, might be used as proxies. Foundations or government agencies that wish to assess their funding programs will have to determine what kinds of information would be useful to guide future decisions about such funding schemes and build their evaluation around such measures.

The committee recognized that systematic collection of key variables would be essential to monitor grantees and assess the outcomes of grants

such as those awarded through the Research Program Grants. The committee considered a number of issues, including:

- Should there be a minimum data set (MDS) of variables collected from all grantees and, if so, what variables should be included in the MDS;
- How frequently should data be collected from grantees; and
- What mechanism should be used to collect these MDS data?

The committee found guidelines for these issues from the practices used by NIH and NSF for renewal or awards. Both agencies have established systematic reporting mechanisms for the renewal of grants. NSF uses the Annual Progress Report (through Fastlane) and NIH uses the Grant Progress Report (PHS 2590) to collect these interim data.

While the content of the two mechanisms differ in details, both agencies collect monitoring data in four areas:

- Detailed budget information, including costs for personnel (itemized for all staff employed on the project), consultants, equipment (itemized), supplies (itemized by category), travel, alterations/renovations, construction, other costs not elsewhere classified, and overhead.
- A listing of key personnel, their role on the project, and their annual effort;
- A narrative describing the project's progress including specific aims, studies and results, significance of findings, and plans for the coming year; and
- A listing of publications generated by the project.

The committee believes that these data elements could serve as the basis for establishing an MDS for annual progress reports grantees submit to funders. Both NIH and NSF utilize electronic transmittal of progress reports (NSF uses Fastlane and NIH uses SNAP, the Streamlined Noncompetitive Award Process). The committee recognizes the advantage of electronic transmittal, but believes that submission in a standardized protocol via the Internet would meet the needs of most philanthropic funders.

In addition, the committee recognizes that establishing an MDS in itself is not sufficient to assess the outcomes of programs like the Research Program Grants. This requires identification of the possible products of such programs and the more careful, in-depth, and systematic measurement of these outcomes by the evaluation team. Moreover, the committee recognizes that if the Markey Trustees had adopted an MDS and established goals and outcomes for grantees, its evaluation of the Research Program Grants would have been much more straightforward; although

the committee also recognizes that the implementation of the MDS and the identification, measurement, and collection of specific program products and outcomes will inevitably lead to greater bureaucratic requirements and less flexibility in program administration, characteristics identified as strengths of the Markey Trust's framework.

Outcomes of the Research Program Grants

The committee was able to arrive at some conclusions and offer observations about the success of the Research Program Grants program on several dimensions.

THE TRUST'S FUNDS WERE DISTRIBUTED IN ACCORDANCE WITH MRS. MARKEY'S WISHES

More than $325 million were distributed to 92 Research Program Grants recipients during an interval of only 10 years. This sum represented about three-fifths of the entire Markey estate. Funding for Research Program Grants was directed to basic biomedical research in accordance with Mrs. Markey's wishes; all funds were expended within 15 years of her death, and the Trust was terminated, as she had directed. The committee recognized that it was unable to assess either the scientific merit of the 92 Research Program Grants proposals or the outcomes of each grant. However, it was able to assess the expenditure of funds by grantees in relation to their original proposed uses of funds. The committee observed that in nearly every case, grantees spent the funds they received in accordance with the manner proposed.

THE SELECTION PROCESS USED BY THE MARKEY TRUST AND THE NATURE OF AWARDS MADE DIFFERED FROM THOSE OF THE NIH AND NSF

The selection process used by Markey Trustees was considerably different from that used by public funders of basic biomedical research. Rather than a peer-review system that is repeated on an annual basis, Markey Trustees solicited and invited elite and proven researchers to submit ideas for research proposals. Investigators whose proposals interested the Trustees were asked to revise and resubmit their proposals. For some investigators, this entailed multiple iterations to develop a proposal that fit the Trustee's criteria. In such cases, the Trust staff worked with potential grantees to fine-tune proposals. These criteria are detailed in the section "Selection of Research Program Grants" earlier in this report.

During its initial planning meetings and at the two think-tank meetings, the Trust established the grant mechanism as the vehicle for distribution of most of its fund. More than $325 million was given to an elite cadre of proven investigators with a high likelihood of success. Success can be measured by examining the characteristics of recipient investigators and institutions and comparing them with the criteria for funding mandated by the Trustees. Within this report, Appendix A provides descriptions of all Research Program Grants recipients. An additional approach to examining the success of the selection process is to examine the outcomes of the recipient investigators and institutions. It is possible in a very general way to say that Markey funds were used to support infrastructure, recruit faculty, support postdocs, and to fund research. The committee utilized analysis of progress reports to assess the outcomes of the Research Program Grants recipients. Finally, another approach to determining the excellence of awardees is to determine the amount of competition or the "success rate" of Research Program Grants applications, which is the probability of any individual applicant receiving an award. In addition, the Markey success rate can then be compared to that of other funders of basic biomedical research.

During its lifetime, the Trust received 792 proposals for Research Program Grants that were deemed of sufficient quality to be reviewed by the director for medical science and/or senior consultants. The success rate for Research Program Grants made by the Markey Trust was 12 percent. This was considerably lower that the 47 percent acceptance rate for research program projects (P01 awards) and the 27 percent of traditional research project grants (R01 awards) funded by the National Institutes of Health (NIH) during the same years (NIH, 2004). For the National Science Foundation (NSF), the success rate for grants in the Directorate of Biological Sciences during the interval ranged from 23 to 30 percent.

TABLE 1 Number of Research Grant Proposals Reviewed and Funded by the Markey Trust, Total Funding by Year, and Average Award Amount: 1985 to 1995

Fiscal Year	Applications Reviewed	Grants Awarded	Total Funding	Average Award Amount
1984	41	—	—	—
1985	202	0	—	—
1986	152	5	$38,037,773	$7,607,555
1987	47	0	—	—
1988	78	21	$105,120,402	$5,005,733
1989	77	3	$20,540,000	$6,846,667
1990	58	5	$27,100,000	$5,420,000
1991	32	12	$41,450,000	$3,454,167
1992	43	9	$29,500,000	$3,277,778
1993	10	5	$14,000,000	$2,800,000
1994	21	6	$9,100,000	$1,516,667
1995	31	26	$31,400,000	$1,207,692
Totals	792	92	$310,003,175	$3,437,486

SOURCES: Lucille P. Markey Charitable Trust, 1996. Lucille P. Markey Charitable Trust Records.

Table 1 shows the number of proposals reviewed and the number funded by the Markey Trust from 1985 to 1995. It is difficult to compare directly to NIH or NSF because they used a peer- review process and proposals were both reviewed and funded within the fiscal year of receipt. At NSF, for example, the median time for review of a grant application is about 6 months. For the Markey Trust, the lag between receipt of a proposal for review and its eventual funding was considerably longer. In many cases, the lag spanned several years.

NIH is the largest funder of biomedical research. Although there is no NIH funding mechanism that compares directly with Markey Research Program Grants, two similar mechanisms are traditional research projects and research program projects. During the 1985 to 1995 interval, NIH made 832 new research program project awards, each for about $800,000 per year. These research program projects, or P01, awards are made "for the support of a broadly based, multidisciplinary, often long-term research program, which has a specific major objective or a basic theme." They may involve relatively large groups of individuals under the direction of an established investigator or involve sharing of resources, includ-

ing clinical facilities. They are directed toward multiple problems having a central research focus. During the same interval, NIH funded 28,445 traditional research project, or R01, awards for about $180,000 per year. Table 2 shows the number of applications for P01 and R01 grants between 1985 and 1995, the number funded, and the average cost for the first year of funding.

Most Markey awards were made for a period of 5 years; but many of the awards made in 1994 and 1995 were for only 3 years. Because of the flexibility of the Markey award structure, many grantees were able to extend the period of performance up to an additional 3 years. The median length for the NIH competing research project awards was approximately 3.5 years (NIH, 2000). Thus, by extrapolation, the typical NIH research program project award was about $2,800,000, and the typical traditional R01 research project award was about $630,000 compared to $3,437,486 for the average Research Program Grants funded by the Markey Trust.

An additional difference between the Markey Trust and NIH was the focus and time frame for the selection process. The Markey Trustees and expert consultants were under no time constraints in their review of applicants. In many cases, the review process extended over many years and involved multiple revisions and resubmissions of an application. The focus of the Markey selection process was on the identification of a few outstanding applications that had a very high probability of achieving the project's goals. NIH, however, has less flexibility in funding and does not have the luxury of being able to establish interactive and iterative communications with an applicant.

The Directorate of Biological Sciences of NSF supports research to advance understanding of the underlying principles and mechanisms governing life. NSF does not fund basic biomedical research per se. Rather it funds research that ranges from the study of the structure and dynamics of biological molecules, such as proteins and nucleic acids, through cells, organs, and organisms, to studies of populations and ecosystems. In FY 2003, the Directorate of Biological Sciences awarded 1,448 grants with a median annual award size of $102,000. Table 3 shows the number of applications for NSF grants for the Directorate of Biological Sciences grants between 1985 and 1995, the number funded, and the median level of funding. The median length of these NSF awards was approximately 2.75 years (NSF, 2004), and by extrapolation, the median amount of the typical award was about $151,000.

In summary, the committee recognized that the Markey Trustees adopted a method of identification and selection of grantees that differed considerably from methods used by NIH and NSF. The approach adopted by the Trustees utilized an expert review rather than a peer- review approach to assess a proposal's merit. This approach provided dollars to

TABLE 2 Number of Research Grant Proposals Reviewed and Funded by NIH, Success Rate, and Average Annual Costs: 1985 to 1995

	NIH P01 Awards				NIH R01 Awards			
Fiscal Year	Number Reviewed	Number Awarded	Success Rate[a]	Average Cost[b]	Number Reviewed	Number Awarded	Success Rate[a]	Average Cost[b]
1985	214	76	35.5	$703,612	12721	3093	24.3	$124,286
1986	164	70	42.7	$709,287	12015	2821	23.5	$125,675
1987	200	94	47.0	$748,366	10525	2747	26.1	$145,827
1988	202	78	38.6	$876,216	11628	2545	21.9	$149,072
1989	186	66	35.5	$776,301	12203	2449	20.1	$169,682
1990	201	68	33.8	$783,349	12647	2217	17.5	$180,421
1991	218	80	36.7	$773,510	12041	2569	21.3	$193,754
1992	224	89	39.7	$850,039	12351	2555	20.7	$194,054
1993	218	74	33.9	$875,730	13971	2212	15.8	$198,789
1994	184	60	32.7	$946,895	15148	2755	18.2	$208,157
1995	268	77	28.8	$790,298	13923	2482	17.8	$223,078

[a]Success rates are the number of reviewed applications divided by the number funded, on a fiscal year basis.
[b]The cost is the sum of direct and indirect costs for the fiscal year, and not for the life of the project.

SOURCE: NIH Competing Applications by Type of Grant and Activity, available at http://grants1/nih/gov/grants/award/success/rpgbyacttype7002.htm

TABLE 3 Numbers of NSF Grants from the Directorate of Biological Sciences Reviewed and Funded, Success Rate, and Median Award Amount: 1985 to 1995

Year	Number Reviewed	Number Awarded	Success Rate	Median Annual Award[a]
1985	5459	1623	30	$50,000
1986	5520	1395	25	$50,000
1987	5254	1450	28	$51,685
1988	5959	1369	23	$53,222
1989	5319	1502	28	$52,373
1990	5881	1523	26	$50,000
1991	5670	1406	25	$57,167
1992	5147	1390	27	$59,242
1993	4863	1318	27	$56,667
1994	4677	1402	29	$63,083
1995	5216	1389	26	$61,803

[a]The median duration of awards wa about 2.75 years.

SOURCE: National Science Foundation. 2004. Funding Rate by State and Organization for Biological Sciences, available at http://delweb.bfa.nsf.gov/awdfr3/org.asp.

proven investigators and institutions that enabled them to take risks and innovate across disciplines and departments.

FUNDING OUTCOMES

Evaluating the outcomes of each of the 92 Research Program Grants is beyond the scope of this study. Nor are the data available to assess outcomes of the grants, for a number of reasons:

- For most awards, the level of funding originally requested was reduced by the Trustees to a more modest level, sometimes without changing the scope of the proposal. Because Research Program Grants were not renewed, Trustees tended to fund one-time expenses and leave funding of continuing operations to the host institution. Nevertheless, the sustainability of many of the programs, such as those at the University of Vermont, Baylor College of Medicine, and the Whitehead Institute, demonstrates the ongoing success of the programs.
- In many cases, moneys from the Markey Trust were commingled with funding from other sources. In such cases it was difficult, if not

impossible, to differentiate the outcomes attributable to Markey funding from those attributable to other funding.

- Research Program Grants were funded for 5 years. Moreover, owing to the flexibility of the Markey Trustees in administering Research Program Grants, many recipients were able to extend funding beyond the original dates. For some of these grantees, the original program goals and processes evolved and changed during the grant's tenure.
- Awards made by the Markey Trustees were not renewed because this was a limited-term trust. (However, some recipients received one-time supplements.) Consequently, the leverage generated by the renewal process was not available to enhance outcomes. Instead, the Markey Trust relied on leadership, faculty collegiality, and the identification of a productive scientific environment at host institutions to ensure positive outcomes.
- A small minority of grantees faced major obstacles or encountered major barriers to reaching their program goals. In most cases, this involved the inability to recruit or the unexpected loss of key personnel. In such cases, the grantee regrouped, reorganized, and targeted new areas of biomedical research. Unfortunately, in many cases, these changed plans were not documented and therefore the data are not available for evaluation.
- Finally, grantees were not required nor expected to conduct process and outcome evaluations. Consequently, they did not collect monitoring data that would aid in an evaluation.

Although the programs funded by Markey grants do not lend themselves to explicit evaluation of their outcomes, the committee believes that the grants were used by institutions and individuals in the way intended (i.e., to support the development of infrastructure, to recruit and provide start-up packages for faculty, to support training and research of graduate students, and to advance the biomedical sciences). The committee saw many examples of excellent science and outstanding programs in the site visits and interviews. In the committee's opinion these are worthy investments for other philanthropic organizations, but due to the structure and approach used here, there is little information to inform the specific guidelines for making grants. The committee, however, does want to note that investment in institutions with proven records and in an elite cadre of principal investigators is an appropriate approach by private funders to making grants.

A detailed listing of the minimal assessment of uses of grant funds is presented in Appendix D. In summary, the 92 Research Program Grants supported 1,744 persons: 150 faculty with full support; 502 faculty with partial support; 121 postdoctoral fellows with full support; 330

postdoctoral fellows with partial support; 471 graduate students and 11 undergraduate students; 112 technicians; and 47 investigators. Investigators included scientists in non-academic institutions, and scientists in academic institutions without academic rank. In addition, the 92 Research Program Grants provided $62,700,000 for major equipment purchases and $30,368,000 in construction and renovation costs. Finally, a number of recipients used Markey funding to support animal and other shared facilities.

One of the goals of the Research Program Grants was to fund projects that ordinarily would not be funded by NIH or NSF. The construction or renovation and major equipment costs were examples of funding sometimes not covered by NIH or NSF. Moreover, Markey funds were used to provide flexible dollars to support preliminary data or risky science often not supported by NIH or NSF.

Anecdotal evidence indicates that investigators often were able to commingle Markey funds with funding from other sources to achieve even greater goals. For example, at Cornell's Institute of Human Neuroscience, Markey funds were combined with those from other sources to make major equipment purchases. At Florida State University (FSU), Markey funds were combined with those from NIH, NSF, and the FSU Research Foundation to establish the Institute for Molecular Biophysics. At Carnegie Mellon University, Markey funds were commingled with funds from the University of Pittsburgh to establish the Pittsburgh Nuclear Magnetic Resonance Center for Biomedical Research. In addition, many of the scientists initially supported by Markey funding were able to obtain funding from other sources that enabled them to continue or expand their research agendas.

THERE WERE DIFFERENCES IN THE OUTCOMES FOR INFRASTRUCTURE DEVELOPMENT VS. INVESTIGATOR-INITIATED GRANTS AND FOR LARGE VS. SMALL AWARDS

As part of the assessment, the committee classified Research Program Grants as infrastructure development awards or investigator-initiated awards. In addition, the committee dichotomized awards as large—$4 million and or more in total funding—or small. The committee classified infrastructure development awards as those focused on the creation or major expansion of a department, center, or institute. Investigator-initiated awards were those that were oriented toward enhancing the research agendas of existing or newly hired scientists. The committee viewed investigator-initiated awards as being similar to R01 or P01 awards made by NIH.

Half of the awards made were for infrastructure development, and

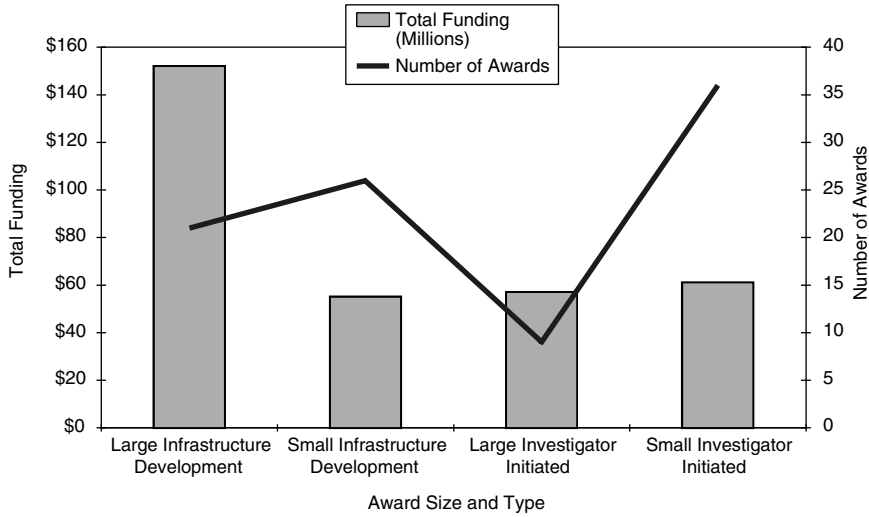

FIGURE 2 Number of research program grants awards and total funding by award size and type.
SOURCE: Lucille P. Markey Charitable Trust, 1996.

half funded investigator-initiated research. However, infrastructure development awards received more than $200 million in funding; considerably more than the $110 million awarded to investigator-initiated programs (see Figure 2).

Recipients of large awards were more likely to purchase major equipment and to use funds for construction and renovation. Of the 30 large awards recipients—21 infrastructure development and 9 investigator-initiated awards—over $62 million was used on equipment, construction, or renovation, an average of $2 million per award. Of the 62 of small awards recipients—26 infrastructure development and 36 investigator-initiated awards—$28 million was used on equipment, construction, and renovation. Almost all of these funds were used for equipment—an average of $450,000 per award.

Recipients of small awards tended to use Markey funding for human capital. The 62 small awards used Markey funds to support more than 1,000 persons, ranging from undergraduates to research professors. On average, the small-award recipients supported 8.6 persons for each mil-

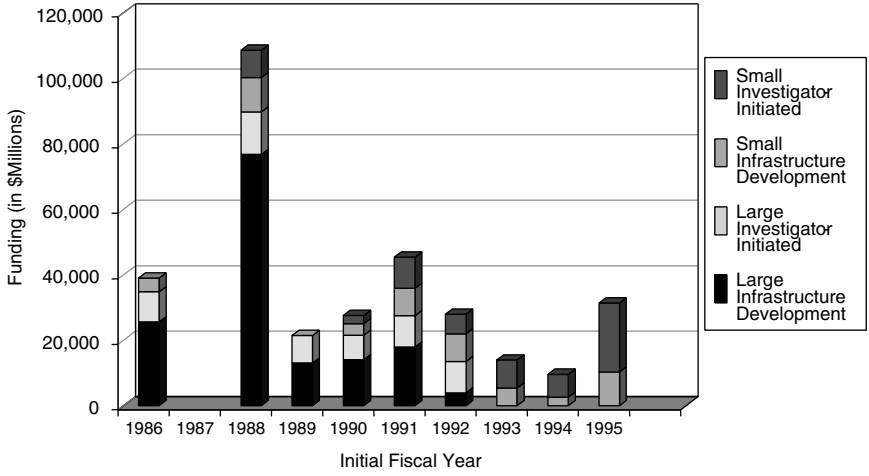

FIGURE 3 Funding of research program grants awards by size, type of award, and initial fiscal year.
SOURCE: Lucille P. Markey Charitable Trust, 1966.

lion dollars of Markey funds. The 30 large-award recipients supported more than 700 persons at all levels. On average, the large-award recipients supported 3.5 persons for each million dollars of Markey funds.

Figure 3 shows the changes in the distribution of Research Program Grants awards by size and type from the beginning to the final years of the Markey Trust. The figure clearly reflects the change in Trustee focus from large infrastructure development awards during the initial years of funding to small investigator-initiated awards during the final years of the Trust.

THE TRUST'S FLEXIBILITY IN THE ADMINISTRATION RESEARCH PROGRAM GRANTS WAS CITED MY MANY INVESTIGATORS AS EXTREMELY USEFUL

The Markey Trustees prided themselves on two aspects of the administration of the Trust. First, the Trustees were dedicated to minimizing costs associated with the Trust's administration; second, they wanted to maximize the flexibility by which funds were used by Research Program Grants recipients. The Trustees were less concerned with the processes and time lines adopted by the recipients to achieve the outcomes listed in the proposals; this was noted by recipients as a valuable attribute.

In addition, the Trustees were willing to allow principal investigators to carry funds forward if they could not be spent wisely in the current fiscal year. In some cases, protocols and personnel envisioned in the Research Program Grants proposals were not completed within the proposed funding period. Approximately 30 percent of the grantees requested no-cost time extensions, some for as long as 4 years. For some projects, this involved identifying and hiring key scientists. Usually the recipient could not commit to a new faculty slot until funding had been secured. In other cases, the recruiting and hiring process for new faculty lines took much longer than anticipated. A few recipients experienced the unexpected departure of key faculty at critical times and were forced to place the project on hold until replacement faculty could be identified and hired. Finally, for some infrastructure development awards, facility construction and renovation time lines took much longer than anticipated. For all of these examples, the Trust's authorization to carry funds forward and not lose them allowed the recipients to shepherd the funds until they could be spent wisely. One grant recipient wrote:

> One of the major reasons that the Markey funds have been so effective in supporting these successes has been the degree of flexibility that the Trust has provided for using these funds. Since the use of most other funding is tightly and narrowly restricted, *the Markey funds have been virtually the only source of flexible funding for our Institute, with which we can respond to new needs and, even more importantly, new opportunities.*

The flexibility of the Markey funds is not surprising. In an earlier study on the financing of biomedical research, Ginzberg and Dutka state (1989:91):

> On balance, foundation and private donor support for biomedical R&D is viewed by the respondents as providing more flexibility than government support. Specific attention is directed to less onerous reporting requirements, the ability to work with the donor in shaping the terms of the gift, and the speed of eliciting support when time is an important consideration.

Consequently, the committee believes that the policy of giving principal investigators flexibility in the use of funds contributed to the effective use of Markey funds. The committee recognizes that the "use-it-or-lose-it" approach of annual funding allocations can lead to less than optimal use of funds. The committee also recognizes that for large projects, such as infrastructure development projects, unexpected barriers to implementation can occur and that flexibility in funding can enable the recipient to develop strategies to overcome these barriers. Echoing these sentiments, another Research Program Grants recipient wrote:

> By being limited in time and focused in programmatic giving, it had a profound catalytic effect on American biomedical sciences related to problems of human disease. It will, of course, be more difficult to measure this than programs which have spent less of their resources and have used their resources to sustain themselves over many, many years. The Markey Trust was always lean and mean with minimal administrative staff and maximal flexibility. They had unique leadership in the persons of Dr. Robert Glaser and Mr. Louis Hector whose wisdom I have not seen equaled before or after. It is my impression that a great many charitable foundations spend a large proportion of their resources on program officers and staff; they inevitably become bureaucratized and they dole out funds in small amounts which have minimal impact. The Markey Trust used an opposite philosophy, giving relatively large sums that truly made a difference in a concentrated way with minimal bureaucratic micromanaging. This is, I think, a reflection not only of the trustees and of the excellent staff, but of the outstanding and enlightened leadership of Bob Glaser and Louis Hector.

THE MARKEY FUNDING ENABLED INVESTIGATORS AND INSTITUTIONS TO TAKE RISKS

The committee found notable examples of high-risk research funded by Markey that had substantial payoffs. For example, Dr. Eric Lander arrived at Whitehead as a Markey Fellow and then was appointed to the faculty. As a Markey Fellow, he could test and refine new concepts in gene mapping, gene sequencing, and bioinformatics. Today, he heads the largest academic genome center in the world. Through his work in functional genomics, he is building a new framework for deciphering the origins of complex human diseases such as cancer, diabetes, and heart disease. The Markey Trust helped lay the foundation for this progression by providing partial support for the Lander laboratory for 5 years. Lander has been the subsequent recipient of 11 NIH grants—1 research program project, 3 specialized center awards, 3 R01 awards, 1 scientific evaluation award, and 3 Cooperative Agreements.

In 1991, the molecular neurobiology group at Cold Spring Harbor Laboratory was initiated to study the molecular basis of learning and memory. The initial research focus employed learning and memory mutants of *Drosophila* to identify genes involved in these processes and determine how they affected behavior. The first big breakthrough came with the surprising and important discovery that *Drosophila* had long-term memory and that spaced learning trials were necessary to memorize learned tasks (as is true in humans). In succeeding years the group reported the identification of the transcription factor CREB as an essential

component of the memory process and the demonstrated enhanced memory by overexpressing a form of the CREB protein prior to learning. The initial success of this program led to its continued expansion. It now includes the molecular basis of long-term potentiation, synaptic plasticity, neuronal development, behavioral genetics, and computational neuroscience.

With the support of Markey funds, researchers in the Neurobiology Research Center at the University of Alabama at Birmingham identified new intracellular receptors for inositide polyphosphate for the regulation of intraneuronal calcium; a new synapse-specific protein molecule that is transiently expressed in certain developing dendritic spines in neurons; and the mechanisms of control of intracellular calcium and pH in modified glial cells in brain tumors. They also demonstrated the role of the brain's production of the gas nitric oxide in modulating the release of various chemical transmitters. Additional support and new equipment was procured for joint collaborative efforts for an electrochemical nitric oxide measuring system for investigators to pursue "risky" and novel experiments that might not have been possible with conventional research grant funds.

The committee notes with interest the inception of the Pioneer Awards by NIH in 2004. These awards fund high-risk, high-impact research, a component of the NIH portfolio that has been conspicuously absent. The Pioneer Awards give academic researchers $500,000 for five years to investigate unrestricted areas of biomedical research. NIH hopes that researcher's freedom to follow the science will lead to new breakthroughs (NIH, 2004b).

THE EXPERIENCE OF THE MARKEY TRUST MAY BE USEFUL TO OTHER FUNDERS OF BIOMEDICAL RESEARCH

The Research Program Grants comprised the largest category of Markey Trust awards. The Research Program Grants awards exhibited a number of characteristics that could be useful to other funders of biomedical research:

- Recipients were able to make major equipment purchases and to engage in construction or renovation projects to house new equipment and staff. These uses of funding are generally discouraged or prohibited by government funders such as NIH.
- Recipients were able to fund sizable start-up costs for promising scientists.

- Recipients were able to engage in high-risk research. In addition, Markey funding provided seed money to enable investigators to branch into new areas of inquiry for which they had no established track record.
- Recipients were able to use funds as a match for other funding, thereby increasing the total funding pool for the grant recipient.
- Interdisciplinary research in the biological sciences received support and grants to institutions facilitated the elimination of departmental barriers to such research.
- Awards were large enough to make a major impact on the recipient—to make quantum changes in the recipient's research agenda rather than incremental changes.
- Awards were based on merit and less so on competition. The Trustees and their scientific experts identified researchers and/or areas of biomedical research that had high expectations of success in the cutting-edge areas of biomedical science.
- A broad range of programs, subject areas, and emerging scientific topics received support. Rather than focus on any specific content areas, the Trust had no restrictions on content and focused instead on the contributions the work could make to basic biomedical research and on the qualifications of the researchers. The committee believes that the Research Program Grants funded many projects that would have fallen through the cracks of traditional funders.

Through the Research Program Grants, the Markey Trust created a program that identified scientists with promising ideas and models, providing them with substantial funding, and minimizing administrative barriers to maximize their potential to make quantum advances in biomedical research. The need still remains for funding basic biomedical research whose outcomes are neither ensured nor predictable. The Committee believes that the example of the Markey Trust can serve as a model for other funders of biomedical research.

The committee believes that the experience of the Markey Trust can serve as a model for other philanthropies that wish to consider a limited-term trust. The Markey Trust demonstrated that, with a relatively small administrative staff and the judicious use of expert consultants, a large sum of money can be distributed effectively to a large number of recipients in a short period of time. Because the Markey Trust was a limited-term trust, it never lost its funding focus and was able to fulfill its goal of awarding sums large enough to have a significant impact on the recipient institution. Other funders should view the Markey Trust as a case study to be considered and emulated.

The committee believes that the Research Program Grants made a

unique contribution to funding basic biomedical research. No other funder of biomedical research has filled the void left by the Markey Trust. The committee believes that future funders of biomedical research, both private and public, should consider funding mechanisms that provide support for infrastructure, purchase of equipment, funds for faculty recruitment, and support of graduate students—with the flexibility to follow new leads and change directions.

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Appendix A
Overview and Description
Lucille P. Markey Charitable Trust
Research Program Grants Awards

OVERVIEW AND DESCRIPTION
RESEARCH PROGRAM GRANTS

University of Texas, Southwestern Medical Center ($2,280,000 • 1986-1992). The grant provided support of the research program of Joseph Goldstein and Michael Brown in molecular genetics and genetic diseases. Research focused on understanding the control of transcription at the molecular level and the behavior of the receptor at the whole-animal level. Most funding was utilized for equipment and supplies to support pilot projects and to explore new areas of research (includes $1,155,000 in supplemental funding awarded in 1988 and $300,000 awarded in 1991).

Carnegie Mellon University ($1,925,000 • 1986-1991). The grant provided funds for research on spectroscopy in the biomedical sciences. Research was concentrated into two areas: (1) biomedical nuclear magnetic resonance (NMR) in collaboration with the organ transplant surgeons at the University Pittsburgh School of Medicine and (2) a program on X-ray crystallography of biological macromolecules. Funds were combined with the National Institutes of Health (NIH) and National Science Foundation (NSF) funds in support of the new NMR Center for Biomedical Research. In addition, some funding was applied to faculty and graduate student support. Chien Ho was the principal investigator (PI).

Stanford University ($12,613,550 • 1988-1996). The grant provided support for the Center for Molecular and Genetic Medicine and established

the Department of Developmental Biology. Research focused on examining how the complex multicellular structures of the adult organism result from the fertilized egg. Funding was equally divided among faculty salaries, equipment, and supplies, and other administrative costs. Lucy Shapiro was the PI.

California Institute of Technology ($12,500,000[1] • 1986-1997). The grant supported expansion of the Developmental Biology Center by attracting new faculty, upgrading instrumentation, and creating an intramural research funding program. About one-half of the grant was used to support internal grant programs—modest, multiyear innovative research—and one-third was used to support multiuser facilities and instrumentation. Leroy Hood and Eric Davidson were the PIs.

University of Chicago ($8,719,223[1] • 1986-1997). The grant supported an integrated program of research in neurosciences, emphasizing neurobiology and neuroimmunology. Funding was used to recruit new faculty and to renovate and equip laboratory space. Funds were equally divided among salaries, equipment, renovation, and a residual category of core support, supplies, and overhead. Samuel Hellman was the PI.

The Whitehead Institute for Biological Research ($7,150,000[2] • 1988-1996). The grant supported a program in developmental biology. Funding was used to support a number of young faculty and postgraduate students. Faculty were provided salary support and lab space with associated setup costs. About 20 percent of the grant was used for core renovations and equipment. David Baltimore was the PI, followed by Gerald Fink.

Washington University in St. Louis ($12,100,000 • 1988-1994). The grant established the Markey Center for the Study of Molecular Biology and Human Disease within the Department of Genetics. Four funding priorities were established: competitive research support, faculty recruitment, core research support, and equipment and instrumentation. The majority of funding was for faculty research support, with a significant amount of funding for equipment and core support. Daniel Hartl was PI, followed by Emil Unanue.

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[1]Includes supplemental funds of $500,000 made in recognition of outstanding progress by Markey-supported investigators addressing important problems in biomedical sciences awarded in FY 1996.

[2]Includes supplemental funds of $500,000 made in recognition of outstanding progress by Markey-supported investigators made in FY 1997.

Harvard Medical School ($11,000,000 • 1988-1993). The grant provided support to establish a program in molecular and cellular basis of development. The program resulted from the merging of several departments and received considerable intramural support. Funding was used for faculty salaries, technical and staff support, supplies, equipment, and facility renovation. Daniel Tosteson was the PI.

University of California, Los Angeles. ($4,350,000[2] • 1988-1997). The grant established the Lucille P. Markey Program in Cellular Biochemistry in the Department of Biological Chemistry. The program investigated the transport of proteins in cells and genetic regulation of the early development of higher organisms Funds were used for (1) faculty support; (2) stipends for graduate students and postdoctoral fellows; (3) renovation, equipment, and supplies; and (4) a series of symposia in cellular biology. Elizabeth Neufield was the PI.

Yale University ($12,100,000 • 1988-1997). The grant provided support for the program in molecular oncology at the Yale Center for Molecular Medicine, which became the Boyer Center. Funding was provided for faculty support, a clinical scholars program, supplies and services, core facility, equipment, and fellowships. Sherman Weissman and Vincent Marchesi were the co-PIs.

University of Oregon ($3,300,000 • 1988-1995). The grant provided funds to establish a Center for Macromolecular Assemblies in Cell Biology combining research in three-dimensional macromolecular structures utilizing crystallographic techniques, macromolecular thermodynamics, and macromolecular interactions. Markey funds were supplemented by those from NSF and NIH. In addition to major equipment purchases and lab support, funding was used for faculty support, recruiting, visits, seminar speakers, and support personnel. Brian Matthews was the PI.

University of Wisconsin ($990,000 • 1988-1992). The grant provided funding for support of studies of molecular biophysics and molecular genetics. Funding was used for the support of research associates, including several graduate students, working with principal investigators. The co-PIs were Barry Ganetzky, Julis Adler, and Ching Kung.

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University of Texas, Southwestern Medical Center ($1,045,000 • 1988-1994). The grant provided funding for a study on receptor G-protein systems by the Department of Pharmacology. The grant funded a number of postdoctoral fellows, supplemented faculty salaries, and was used for supplies. Alfred Gilman was the PI.

University of Pennsylvania ($4,220,402[1] • 1988-1997). The grant funded molecular genetic approaches to define the mechanisms and treatment of disease. This program was a joint project of the Schools of Medicine and Veterinary Medicine. Funding was used for salaries, supplies, equipment, renovation, and animal care or purchase. Mark Green and Donald Patterson were PIs. (Includes $370,402 in supplemental funding awarded in 1994.)

University of Miami ($6,770,000 • 1988-1998). The grant provided funds to enhance research efforts in the Department of Biochemistry and Molecular Biology. Initially, funding was used for the completion of shell laboratory space and for recruitment of a new department chairman. Because of recruiting difficulties the grant was put on hold until 1995 when a chair and five new faculty were recruited. Markey funds provided salary and start-up costs for these new faculty. Murray Deutscher was the PI. (Includes supplemental funding of $500,000 to support an endowed chair in biochemistry and microbiology.)

Brandeis University ($3,200,000[2]• 1988-1996). The grant supported the structural biology and biochemistry program and the mechanistic enzymology program. The research investigated the essential link between structural biology and biochemistry and determined the organization of the macromolecular assemblies that constitute living structures. The grant provided faculty support, graduate student stipends, and major equipment purchases. Gregory Petsko was the PI. (Includes $500,000 in supplemental funding awarded in 1990.)

University of California, San Diego ($4,320,000[2] • 1988-1998). The grant funded a project to support the study of cell growth and differentiation with an emphasis on the role of protein kinesis. Funding supported the

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[2]Includes supplemental funds of $500,000 made in recognition of outstanding progress by Markey-supported investigators made in FY 1997.

research of seven established professors in the Division of Endocrinology and Metabolism. The PI was Gordon Gill. (Includes $300,000 in supplemental funding awarded in 1994.)

Carnegie Institution of Washington ($2,700,000[2]• 1988-1997). The grant supported studies on the molecular basis of gene expression. It enabled interdisciplinary research in the Department of Embryology on what activates one set of genes in one cell and what keeps these same genes repressed in another specialized cell. Funds were used primarily for the support of established investigators, stipends for postdoctoral fellows, and for major equipment and supply purchases. Donald Brown was the PI.

Case Western Reserve University ($5,500,000 • 1988-1997). Funds supported the establishment of the Center for Developmental Genetics in the School of Medicine. The major emphasis of the center was the application of new techniques of molecular genetics to developmental biology. The center had three foci: studies on early embryogenesis in *Drosophila*, developmental neurobiology, and application of new molecular biology to understand developmental processes in the mouse. Funding was applied to faculty salaries, stipends for fellows, and major equipment. The PI was Huntington Willard.

The Children's Hospital, Boston ($2,475,000 • 1988-1993). The grant provided support for the Pulmonary Physiology Department and integrated pulmonary physiology with molecular biology and developmental biology. The mission of the lab was to study the transport defect in cystic fibrosis, the role of macrophages in inflammatory processes in the lung, errors in the synthesis of surfactant proteins, and the regulation of the pulmonary matrix. David Nathan was the PI.

University of Michigan ($8,250,000 • 1988-1997). The grant provided funding to increase understanding at the molecular level of neurotransmitters in the brain. The grant supported 10 research projects for individual faculty ranging from molecular biology of receptor signal transduction to behavioral genetics to regulation of nicotinic acetylcholine receptor expression and six core projects. The goal was to determine the manner in which proteins are inserted into membranes and the environ-

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ment and physiological effects of their activation. Sid Gilman and B. W. Agranoff were the PIs.

The Neurosciences Institute ($1,375,000 • 1988-1995). Funding supported the institute's theoretical neurobiology research program, whose goal was to understand how perception, memory, and other aspects of higher brain function are manifested as a result of elementary activity in the nervous system. The grant supported fellows in theoretical neuroscience, conferences, and summer programs. Research topics included visual perception and cortical mechanisms, mechanisms of synaptic modulation, and selective automata. The PI was Gerald Edelman.

Columbia University ($6,500,000 • 1988-1996). The grant supported the development of the Center for Molecular Toxicology and Nutrition. The center's coordinated investigation of the basic biological processes that underlie cancer, cardiovascular diseases, heritable genetic disease, and reproductive disorders. Research goals included (1) study of the cellular and molecular mechanisms of carcinogenesis due to chemicals; (2) reproductive and genetic toxicology; (3) study of nutritional factors linked to disease, especially atherosclerosis; and (4) molecular epidemiology. Funds were used for a major renovation and for salaries or stipends. Bernard Weisman was the PI.

Purdue University ($6,990,000[2] • 1988-1996). The grant supported the Center for Molecular Structure. The center utilized the university's supercomputer to determine the atomic structures of viruses and membrane proteins with the ultimate objective of identifying cell receptors involved in the binding of viruses and antibodies. Funding was used for expansion of the Purdue structural biology faculty, graduate student and postdoctoral support, equipment, and salary for a visiting senior scholar each year. Michael Rossman was the PI.

Eleanor Roosevelt Institute for Cancer Research ($1,475,000 • 1988-1993). The grant supported the study of somatic cell genetics and recombinant DNA and molecular understanding of human diseases and studies on mutagenesis, with emphasis on the mechanisms by which cyclic AMP (adenosine monophosphate) reverses malignant change in cells under certain conditions. Topics for studies included genome exposure theory,

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mutation, differentiation, gene mapping, and genetic biochemistry. The majority of funding was used for salaries. Theodore Puck was the PI. (Includes $100,000 in supplemental funding awarded in 1992.)

Albert Einstein College of Medicine ($2,310,000 • 1998-1995). The grant supported a program to study the role of membrane receptors in the control of cell growth and differentiation. The primary targets of research were the molecular basis of cell proliferation and differentiation initiated by hormone-receptor interaction; mechanisms of determination of specific cell types in differentiating systems; and the regulation of biosynthesis, processing, and release of growth factors and hormones. Laboratories were established for a number of scholars; support was provided for graduate students, fellows, and visiting faculty; and new faculty were recruited. Richard Stanley was the PI.

University of California, Berkeley ($8,500,000[2] • 1989-1997). The grant provided funding for the Fund for Innovation, a new kind of intramural innovation grant for faculty. Funds provided support for 12 faculty members to investigate molecular structure using recombinant DNA technology or other sophisticated approaches to define basic biological processes such as the transport of proteins, enzymes, and other macromolecules through membranes. The grant was housed in the Department of Biochemistry. The award combined two applications into a multidisciplinary award that bridged biology and engineering in a study of the structure and function of receptors. Jeremy Thorner and Daniel Koshland were the PIs.

Johns Hopkins University ($7,150,000 • 1989-1996). The grant provided funds to establish The Markey Center for Macromolecular Studies. The center, located within the School of Medicine, served as a focal point for research on structural biology of large molecules such as proteins and nucleic acids. The award enabled biophysicists, biochemists, molecular biologists, and computer experts to interrelate the structure and function of biological forms. In addition to salaries, the grant funded major equipment purchases and renovations. Jeremy Berg was the PI.

Northwestern University ($5,890,000[2] • 1989-1996). The grant created the Markey Program for Developmental Biology, an interdisciplinary pro-

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gram that bridged the three campuses of the university, housed in the medical school. The grant provided funds for extensive equipment and construction costs as well as faculty salaries for 10 new physician-scientists. In addition, Markey funds created and supported the Northwestern University Transgenic Facility and provided space for the Northwestern University Biotechnology Facility. Harry Beaty was the PI and Philip Iannaccone was program director. (Includes $$390,000 in supplemental funds awarded in 1989.)

Duke University ($8,00,000[1] • 1990-1997). The grant supported the reorganization of medical sciences at the medical center including the development of three new basic medical sciences departments—Cell Biology, Genetics, and Neurobiology. Funds were used for faculty salaries, support of research laboratories, major equipment purchases, and programmatic support of the new departments. Ralph Snyderman was the PI.

Thomas Jefferson University ($3,500,000 • 1990-1994). The grant supported the Jefferson Institute of Molecular Medicine. The grant covered the salaries of nine new tenured faculty; supported three core laboratories—a DNA repository, a DNA analysis laboratory, and a transgenic mouse laboratory; and supported the relocation of the institute into a new facility. Darwin Prockop was the PI.

University of Virginia ($6,100,000 • 1990-1996). The grant supported a research institute to investigate the molecular mechanisms of cellular signaling processes. The new institute incorporated an existing institute of molecular biology and some activities of the Biodynamic Institute. About half of the grant was used for faculty salaries and half to set up and equip the research facility. Robert Carey was the PI.

Temple University ($2,500,000 • 1990-1996). The grant supported the continued operation of the Fels Institute for Cancer Research and Molecular Biology. Funds covered partial support for 10 new junior faculty, supplies for these faculty, major equipment purchases, and support for postdocs and technicians. Research focused on molecular genetics, cell and developmental biology, immunology, and chemical carcinogenesis and molecular pharmacology. Carlo Croce was PI, followed by Premkumar Reddy.

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University of Washington ($7,500,000 • 1990-1997). The grant funded the Lucille P. Markey Molecular Medicine Center, which built on programs developed at the University of Washington School of Medicine and the Fred Hutchinson Cancer Research Center. Research was focused on gene therapy, developmental genetics and genetics of birth defects, and genetics of common disorders. Funding covered core facility costs including clinical, statistical, and laboratory staff; equipment; supplies; animals; and salary and start-up funds for new faculty. George Stamatoyannopolos was the PI.

University of Colorado Health Sciences Center ($5,000,000 • 1991-1996). The grant provided support for the School of Medicine program in the molecular biology of cell proliferation. Markey funds supported programs that focused on interdisciplinary investigation of the molecular basis of cell proliferation, and the control of cell division by the Departments of Biochemistry, Biophysics and Genetics, Microbiology and Immunology, Pharmacology and Medicine. Funding supported renovation of a core facility, salary and start-up costs for new faculty, and graduate and postdoctoral training. Charles McHenry was the PI.

New York University ($2,600,000 • 1990-1997). The grant provided salary and start-up support for four junior investigatorships to investigate the intersection of antigen processing and the control and signaling involved in the intracellular traffic of proteins. Two new faculty each from the Division of Immunology and the Department of Cell Biology collaborated in this study. Victor Nussenzweig was the PI.

Cold Spring Harbor Laboratory ($4,500,000[2] • 1991-1997). The grant provided support for the Neurosciences Center, dedicated to the study of the development and function of the nervous system, including processes of learning and memory, and how to attack diseases of the brain. Markey funding was commingled with funding from multiple foundations. Markey funding was dedicated to furnishing two floors of the center's research laboratory, providing salary support, and purchase of major scientific equipment. James Watson was the PI.

University of Vermont ($2,300,000[2] • 1990-1998). The grant supported the development of the Markey Center in Molecular Genetics housed within the Department of Microbiology and Molecular Genetics. Funding

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was equally divided for new faculty salary and start-up costs, major equipment purchases, and core facility operating costs. In addition, the award provided stipends for graduate students and postdoctoral fellows. Susan Wallace was the PI.

Massachusetts Institute of Technology ($3,850,000 • 1991-1999). The grant provided support for research in neurobiology. Funding supported both pre- and postdoctoral fellows, renovation of a confocal microscopy facility, purchase of consumable supplies, and meetings and seminars. Additional funding was used to provide "seed money" for individual research projects by MIT faculty. Emilio Bizzi was the PI.

Vanderbilt University ($5,000,000[1] • 1991-1997). This grant supported a program that investigated molecular mechanisms of growth regulation, including the processes that lead directly to the uncontrolled growth of cancer cells. Although researchers from several departments contributed their expertise, the three departments at the core of the research were biochemistry, medicine, and cell biology. Funding supported three new faculty, training for young scientists, and competitive funding for promising pilot programs. Stanley Cohen was the PI.

Memorial Sloan-Kettering Cancer Center ($2,700,000 • 1991-1994). The grant provided support for the cellular biochemistry and biophysics program. Research focused on (1) discovering the machinery that propagates and maintains the precise three-dimensional arrangement of organelles and biochemical processes in a cell, (2) determining the precise three-dimensional structure of this machinery using methods of X-ray crystallography and NMR spectroscopy, and (3) explaining these mechanisms of action in physical and chemical terms. Funding was used primarily for salary support for senior- and junior-level investigators and for equipment and supplies. Paul Marks was the PI.

University of Rochester School of Medicine and Dentistry ($4,000,000 • 1991-1997). The grant provided support for research conducted in the Neurosciences Institute. The research focused on (1) neural regulation of the immune system response, (2) neural transplantation and regeneration, and (3) brain aging and Alzheimer's disease. Funding provided sal-

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ary support for senior researchers, recruitment and start-up costs for new faculty, a program of pilot projects to promising young investigators, construction and renovation of laboratories in the Department of Neurobiology and Anatomy, graduate student stipends, and the support of a primate colony. David Felten was the PI.

University of Alabama at Birmingham ($1,500,000 • 1991-1995). The grant provided support for the interdisciplinary Neurobiology Research Center. The center's mission was to determine the fundamental processes by which brain molecules and cells develop in newborns to facilitate perception, movement, learning, and memory. The award provided salary and start-up costs for new faculty, salary support for lab technicians and stipends for graduate students and postdoctoral fellows, and equipment purchases. Michael Friedlander was the PI.

Fox Chase Cancer Center ($4,000,000 • 1991-1996). The grant provided support for the center's Molecular Oncology Program. The research focus was a multidisciplinary investigation of genes involved in cancer and other factors that transform normal human cells into cancer cells. Scientists and physicians teamed to develop ways to reverse this process at the molecular level, including studies of gene therapy. Funding supported core scientists, primarily junior investigators, for salary support, equipment and supplies, and start-up costs and provided stipends for postdoctoral fellows and graduate students. Alfred Knudson was the PI.

Florida State University ($4,500,000[2] • 1991-2000). The grant provided funds to develop a program in structural biology through the Institute of Molecular Biophysics. The program was an interdisciplinary blend of the Departments of Biophysics, Biochemistry, and Molecular Biology and investigated basic biomedical problems through the study of actions of macromolecules, including study of their three-dimensional structure. Funding included start-up costs for new facility, construction and capital equipment costs, stipends for graduate students, and support for research associates and assistants. Lee Makowski was the PI.

Harvard School of Public Health ($3,500,000[2] • 1991-1998). The grant provided support to the Laboratory of Toxicology within the School of Public Health to investigate the effect of toxic substances—environmental

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and otherwise—on various cells including bacterial and human cells. The grant funded salaries and start-up costs for new faculty, provided funding for competitive pilot projects, and supported an expanded training program for graduate students and postdocs. Armen Tashjian was the PI.

Cornell University Medical College ($4,000,000 • 1992-1997). The grant provided funds to establish the Institute of Human Neuroscience housed in the Biomedical Research Center. Within the center, laboratories investigated pediatric neuroscience, neurophysiology vision, cellular neuroscience, Alzheimer's research, multiple sclerosis research, and collaborative studies. Funding provided support and setup costs for the laboratories of several senior faculty, including salaries, stipends for graduate students and postdocs, and equipment and supplies. Fred Plum was the PI.

The Burnham Institute (La Jolla Cancer Research Foundation) ($1,500,000 • 1992-1996). The grant supported research in cell recognition studies in the Biophysics Resource Center focused on solving three-dimensional structures of cell adhesion peptides and the synthesis of cell type-specific carbohydrates. The award provided the purchase and on-site installation of an NMR spectroscope. Erkki Ruoslahti was the PI.

The Scripps Research Institute ($5,000,000 • 1992-1996). The grant supported the interdisciplinary application of genetics and molecular biology to advance understanding of the structure-function relationships of variously biologically important molecules. Research focused on the study of molecules responsible for cell-cell communication via chemical and electrical synapses, cell motility and cell division, regulation of the cell cycle, and transport from nucleus to cytoplasm. The award provided faculty salary, start-up support for new faculty, stipends for postdoctoral fellows and graduate students, and support for the purchase of major equipment. Norton Gilula was the PI.

University of Illinois at Urbana-Champaign ($3,000,000 • 1992-1998). The grant provided funding at the Beckman Institute to establish a program in molecular biology of neural development and plasticity. Research focused on four key areas of developmental neurobiology: (1) the origins and character of the signals involved in neuronal cellular determination; (2) molecular-level migration of cells and neurons to their targets; (3) the recognition mechanism responsible for the precision of synaptic connections laid down during development; and (4) the molecular processes that give rise to alterations in the functional properties of nerve cells, particularly as related to plasticity, learning, and memory. Funding was used

primarily for salary and start-up costs for new faculty, postdoctoral fellow and graduate student stipends, and major equipment. Theodore Brown was PI until 1992, replaced by Jiri Jonas.

University of California, Santa Cruz ($2,500,000 • 1992-1999). The grant supported the development of the Center for Molecular Biology of RNA. A major function of the center was to encourage and support interaction among structural biologists, molecular geneticists, and biochemists and to promote understanding of how the structure of RNA influences its biological properties. Funding was used primarily for major equipment purchases, faculty start-up costs, and postdoctoral fellow stipends. Harry Noller was the PI.

Cincinnati Children's Hospital Medical Center ($3,500,000 • 1992-1996). The grant was used to develop the Center of Pediatric Molecular Genetics, at Children's Hospital Medical Center and the University of Cincinnati. The center established five objectives: (1) to elucidate the molecular and pathogenesis of human inherited diseases and gene-influenced illnesses; (2) to develop new and improved methods for their detection; (3) to introduce and evaluate gene-based therapeutic strategies for the treatment of human diseases; (4) to provide the highest quality medical genetics care to affected families and patients; and (5) to educate and train physicians, geneticists, genetic counselors, and other allied health providers in the area of molecular and human genetics. Funding was used for faculty recruitment, salary, and start-up costs and for stipends for postdoctoral fellows and graduate students. Gregory Gabowski was the PI.

Public Health Research Institute ($2,500,000 • 1992-1996). The grant supported research on the molecular basis of pathogenesis through the Molecular Pathology Program. The program focused on development of critical core support facilities and resources including Biosafety Level 3 (BL-3) containment labs for handling highly infectious materials, undated and advanced computing, light and flourescence microscopy, and routine DNA and protein imaging systems. Funding was used for seed grants to investigators, instrumentation, and recruitment of new faculty. Abraham Pinter was the PI.

University of Wisconsin-Madison ($3,000,000 • 1992-2003). The grant supported research on the molecular basis of virus structure, replication, morphogenesis, host interaction, and pathogenicity in the Institute for Molecular Virology. A major focus of the grant was the development of a state-of-the-art molecular graphics laboratory. In addition to faculty sup-

port, the grant provided start-up costs for new faculty and stipends for graduate students and postdoctoral fellows. The PI was Roland Rueckert.

Princeton University ($4,500,000 • 1992-1997). The grant supported development of a program in structural cell biology within the Department of Biology. Research focused on exploring the relationship between the cell and its structure and assembly processes. Particular specialties of the program included cell biology, the cell membrane, the nucleus, and the transport of proteins in cells. Funding was used primarily for construction or renovation of shell laboratory space, the purchase of major equipment, start-up costs for new faculty, and stipends for graduate students and postgraduate fellows. Arnold Levine was the PI.

Massachusetts General Hospital ($3,000,000 • 1993-1997). The grant provided five-year support for the development of physician-scientists in oncology at the Cancer Center modeled after the NIH physician-scientist program. The research focused on multidrug resistance genes and the development of strategies for their activation; genetic changes involved in metastasis, with emphasis on the metastasis suppressor gene (NM23); and the use of monoclonal antibodies, cytokines, and antisense oligonucleotides as antitumor agents. Funding provided salary and start-up costs for faculty, stipends for graduate students and postdoctoral fellows, and equipment purchases. Kurt Isselbacher was the PI.

Mount Sinai Medical Center ($3,000,000 • 1993-1997). The grant provided support for a program in molecular biology, cell biology, and immunology. Research was targeted at three problem areas: (1) intricate patterns of nerve conductivity; (2) attempts to translate classical embryological concepts such as "induction" and "instructive interactions" into molecular terms; and (3) the relation of gene expression to spatial, positional, and temporal information in eukaryotic systems. Funds were for faculty salary and start-up costs and for graduate student stipends. The PI was Robert Lazzarini.

University of Utah ($2,500,000 • 1993-1997). The grant provided funding to establish the Center for Protein Biophysics. The center's research agenda investigated the structure, stability, and function of proteins. The center integrated the activities of structurally oriented scientists from the fields of biochemistry, biology, chemistry, and hematology-oncology. Funding was used primarily for the purchase of equipment for the center, salaries for technicians, and stipends for postdoctoral fellows and graduate students. Martin Rechsteiner was the PI.

Joslin Diabetes Center ($3,500,000 • 1993-1999). The grant provided initial support for research on the molecular basis of cellular communication and metabolic regulation. Markey funding led to the development of five new programs: (1) signal transduction and cellular regulation, (2) vascular cell biology, (3) cellular growth factors, (4) tissue-specific regulation of gene expression, and (5) molecular immunology. In addition, the grant established two core laboratories to support these programs—one for molecular instrumentation and a core animal facility. Funds were used for faculty salary and start-up costs, construction, major equipment purchases, and support of the core laboratories. Ronald Kahn was the PI.

Tufts University ($2,000,000 • 1993-1996). The grant provided support to the Departments of Physiology, Pathology, and Anatomy for research to determine the cellular targets of oncoproteins and growth factor receptors that mediate cell growth and transformation. Funds were directed primarily to support facilities needed for signal transduction research; to provide equipment and supply support for the Protein Chemistry, Baculovirus, and Molecular Biology Laboratories; and to support training of graduate students and postdoctoral fellows. Lewis Cantley was the PI.

Salk Institute for Biological Studies ($2,600,000[1] • 1994-1997). The grant provided support for a new Structural Biology Program. Funds were utilized for renovation of 5,000 square feet of space to accommodate the program and X-ray and computational equipment. Thomas Pollard was the PI.

Baylor College of Medicine ($1,400,000 • 1995-1999). The grant provided support for organization of an enhanced research and training program in developmental and tumor biology. Markey funds enabled the initiation of a new Developmental Biology Program. Funding was used for faculty salary and start-up costs and for graduate student stipends. Bert O'Malley was the PI.

University of Southern California ($1,800,000 • 1994-1998). The grant provided support for the University of Southern California Norris Institute for Genetic Medicine gene therapy program and founded the Lucille P. Markey Center for Gene Therapy. The goals of the center were to expand basic science strengths and develop new therapies in the molecular

[1]Includes supplemental funds of $500,000 made in recognition of outstanding progress by Markey-supported investigators addressing important problems in biomedical sciences awarded in FY 1996.

genetics of human disease, while providing new expertise in the areas of gene therapy and a research program to bridge the basic and clinical sciences. Funding was used for new faculty support. The PI was Larry Kedes.

Dartmouth Hitchcock Medical Center ($1,500,000 • 1994-1997). The grant provided funding to support a life sciences curriculum, particularly for the development of a multidisciplinary genetics program. Research focused on the genetics of fundamental model systems, such as yeast and *Drosophila*; the genetics of vertebrate systems, such as mice and zebrafish; the genetics of heritable diseases, such as cancer and heart disease; and the development of transgenic models. Funding supported salary and start-up costs for new faculty positions. The PI was Andrew Wallace.

Brown University School of Medicine ($1,300,000 • 1994-1998). The grant supported an interdisciplinary program to study the molecular and cell biology of disease. The grant funded new investigators, graduate and postgraduate training, opportunities for basic science training for medical students and residents, and equipment purchase. Agnes Kane and Arthur Landy were the PIs.

Worcester Foundation for Biomedical Research. ($1,000,000 • 1994-1997). The grant provided four-year support for a multidisciplinary program of molecular and genetic approaches to cell motility within the Cell Biology Group. Research focused on discovering novel approaches to controlling neoplasis, metasis, and a variety of diseases of the nervous system by understanding how cells move, divide and establish, and change their shapes. Funding provided investigator support. Thoru Pederson was the PI.

University of Colorado, Boulder ($1,500,000 • 1995-1997). The grant provided support to expand the Departments of Molecular, Cellular, and Developmental Biology and to create a Center for Mammalian Biology. The center focused on new research areas, particularly mammalian development, neurobiology, and other research relating to biology and health. Funding supported construction and renovation of the animal facility and salary and start-up costs for new faculty. Leslie Leinwand was the PI.

Dana-Farber Cancer Institute $1,500,000 • 1995-1997). The grant provided for a new Division of Human Cancer Genetics. The goal of the new division was to identify human genes that, when damaged or lost, play key roles in transforming normal cells into cancer cells. Funds were used

for faculty salaries and start-up costs, major equipment purchase, and support of the animal facility. David Nathan was the PI.

University of Massachusetts Medical Center ($1,500,000 • 1995-1997). The grant provided three-year support to the Program in Molecular Medicine for collaborative basic and clinical research programs. Research focused on (1) immunology and signal transduction, with an emphasis on mechanisms of tolerance applicable to the pathogenesis of autoimmune insulin-dependent diabetes mellitus and its correction by islet transplantation, and (2) virology and gene expression related to HIV infection. Funding supported four new faculty and shared equipment. Michael Czech was the PI.

University of Miami ($1,000,000 • 1995-1997). The grant provided four-year support for the study of neurotropic factors in spinal cord injury and repair. The research focused on tropic factors that have the capacity to influence neuronal health and regeneration in the spinal cord. Scott Whittemore was the PI.

University of North Carolina, Chapel Hill ($1,500,000 • 1995-1997). The grant provided support for a Program of Molecular Therapy for Human Diseases within the Gene Therapy Center. Research focused on designing virus vectors for inserting copies of a healthy gene to replace mutated or absent genes, ensuring compliance of experimental forms of treatment with the safety and efficacy requirements of the Food and Drug Administration, and testing new therapeutics in human trials at the medical center. Faculty salaries, gene therapy equipment, and fellowships were supported. Oliver Smithies was the PI.

University of Texas, Galveston ($1,000,000 • 1995-1996). The grant supported the Sealy Center's established (NMR) spectroscopy program in structural biology. Research employed emerging technology to increase understanding of diverse macromolecular systems and to improve strategies for drug design. Funding was used for faculty and staff salaries for the NMR spectroscopy center. Samuel Wilson was the PI.

Oregon Health Sciences University ($1,300,000 • 1995-1997). The grant provided support for studies of the genetic, cellular, and molecular basis of drug addiction conducted at the Vollum Institute. Research focused on investigation of the path from drug susceptibility behavior to the chromosomal location of a single "drug abuse gene" and to the electrophysiological and behavioral effects of mutating those genes in intact mice. Markey funds supported pilot projects and core facilities including: gene map-

ping and behavioral genetics, gene targeting, neuronal imaging, and molecular pharmacology. Richard Goodman was the PI.

Kennedy-Krieger Institute ($500,000 • 1995-1997). The grant provided support to determine the mechanisms by which central nervous system (CNS) capillaries develop and how they respond to injury for the purposes of defining how their growth and function might be regulated. The goal of the research was to demonstrate endothelial cell transplantation as a means of introducing genes for restoring normal CNS function. Funding provided faculty salaries, graduate student stipends, and equipment purchases. Gary Goldstein and John Laterra were the PIs.

University of California, Davis ($1,600,000 • 1995-2002). The grant provided support for the establishment of the Center for Comparative Medicine, a collaborative effort of faculty from the Schools of Veterinary Medicine and Medicine and the California Regional Primate Research Center. Research investigated the pathogenesis of persistent viral infections and chronic viral diseases. There were three areas of emphasis: transgenics and the optimization of gene transfer methodologies, development and evaluation of anti-retrovirus drugs, and studies of biological responses to antiviral immune responses. Funding was used for faculty salaries, postdoctoral fellow stipends, and core support. Frederick Murphy was the PI.

University of Florida ($1,600,000 • 1995-2000). The grant provided funding to establish the Markey Faculty Scholar Program in Neurobiological Research within the University of Florida Brain Institute. Funding supported five new faculty, designated as Markey Faculty Scholars, who facilitated new research collaborations with current basic and clinical University of Florida Brain Institute faculty and provided equipment for their research endeavors. William Luttge was the PI.

University of Pittsburgh ($1,000,000 • 1995-1997). The grant provided support for studies seeking ways to alter genetic information to treat a variety of life threatening diseases. The long-term objectives of the research were to alter genetic information within cells or virus vectors to correct major metabolic and immunologic deficiencies, to introduce a self-renewing source of potent therapeutic factors or cells, or to block the auctions of deleterious genes or gene products. Funds were used to enhance core facilities, provide laboratory space for new faculty, and provide seed money for innovative pilot studies. Ronald Haberman was the PI.

Harvard University ($1,600,000 • 1995-1998). The grant provided support to establish a combined Department of Biochemistry, Molecular Biology, and Developmental Biology. The research combined the conceptual and technical tools of genetics and cellular and molecular biology for approaching key problems of classical embryology—how different cell types arise during development and how those cells are arranged in tissues and organs. Funds provided a new vertebrate animal facility and provided seed money for pilot projects and collaborations. Jeremy Knowles was the PI.

University of California, Irvine ($1,000,000 • 1995-1999). The grant provided 4-year support for the UCI-Markey Initiative in Human Neurobiology. The research focused on brain plasticity and specifically on the study of mechanisms for modulating neuropsychaiatric disorders. Markey funds were used to provide stipends for postdoctoral fellows and for initial support for young investigators. The Co-PIs were Ian Lipkin and Carl Cotman.

Johns Hopkins University ($1,300,000 • 1995-1997). The grant provided 3-year support to develop a multidisciplinary research unit directed towards studies of the neural mechanisms in perception in the Zanvyl Krieger Mind/Brain Institute. The Markey award expanded the multidisciplinary activities in the areas of neuroanatomy, neurochemistry, experimental psychology, computational neurobiology, and cognitive neuroscience. Funds supported faculty investigators. The Co-PIs included Guy McKhann and Kenneth Johnson.

Georgetown University ($1,000,000 • 1995-1997). The grant provided support for the Center for Molecular and Human Genetics to promote research and training on the role of genetic elements in normal development and their altered role in the pathology of cardiac, cancer, developmental, and neurodegenerative disorders. Markey funds supported new faculty, laboratory equipment, and graduate training. John Griffith was the PI.

Cornell University ($1,200,000 • 1995-1999). The grant provided support for a program to provide rapid structural analysis of drug targets and their complexes with potential drug molecules utilizing fast charge-coupled device-based x-ray detectors. Additional research focused on the development of more powerful computer algorithms for the analysis of target macromolecules and computer-aided design of potential drug molecules. Funds were used for core personnel salaries and graduate training. The PI was Steven Ealick.

Children's Memorial Medical Center ($1,000,000 • 1995-1997). The grant provided 3-year support for a research program in human and molecular genetics in the Children's Memorial Institute for Education and Research (CIMER). Markey funds also facilitated a link with Northwestern University Medical School. The research focused on establishing a molecular biology and cytogenetics laboratory and established a postdoctoral training program. In addition to strengthening the equipment base at the Institute, the grant provided postdoctoral support in research genetics. Martin Myers was the PI.

Rice University ($1,200,000 • 1995-1997). The grant provided state-of-the-art instrumentation to enhance program development at the Institute of Biosciences and Bioengineering and the Keck Center for Computational Biology. The new equipment facilitated interdisciplinary collaboration in a series of projects involving: protein structure, design and determination of cellular function; atherosclerosis, cholesterol metabolism, thrombosis, and hemodynamics; tissue reconstruction by cell transplantation with biodegradable polymers; biotechnology; and neurobiology. Kathleen Matthews was the PI.

Rush-Presbyterian-St. Luke's Medical Center ($1,000,000 • 1995-1998). The grant supported studies on the cell and molecular biology of *hemopoiesis in vitro*. Research investigated processes that control and organize cell proliferation and differentiation, processes underlying such disparate phenomena as embryogenesis and maintenance of adult multicellular organisms in a health state. The investigators modified the stromal and the primitive progenitor cells so that cell production *in vitro* mimicked that which occurred *in vivo*. Harvey Preisler and Azra Raza were the Co-PIs.

Schepens Eye Research Institute ($1,000,000 • 1995-1997). The focus of this program was ocular immune privilege, the controlled expression of immunity and inflammation in the eye. The goal of the grant was to identify the unique molecular mechanisms by which the eye creates and sustains a local microenvironment that suppresses immunologic inflammation, and explains the phenomena of immune privilege. Funds provided salary support for a primary investigator, technicians, and the purchase of major equipment. J. Wayne Streilein was the PI.

Stanford University ($1,200,000 • 1995-1997). The grant supported interdisciplinary study of the ability of cells to turn on or turn off subsets of genes in precise temporal/spatial order in response to ever changing environmental challenges. The program focused on regulation at the mo-

lecular level of gene expression in the control of cellular and organismal development and cellular physiology. The grant provided funds for graduate stipends and postdoctoral fellows and for the purchase of major equipment. Patricia Jones was the PI.

State University of New York, Buffalo ($1,000,000 • 1995-1997). The grant supported a program in microbial pathogenesis. This program was a collaboration of 24 scientists with diverse research interests and numerous shared projects in molecular parasitology, sexually-transmitted diseases, vaccine development for pediatric infectious diseases, the molecular biology of tropical diseases, toxoplasmosis, and leishmaniasis. The funds provided salary and start-up costs for new faculty. John Hay, Philip LoVerde, and Bruce Hoims were the Co-PIs.

Texas A & M University ($1,000,000 • 1995-1998). The grant supported development of a program in structural analysis of cell signaling molecules within the Albert B. Alkek Institute of Biosciences and Technology in Houston. The program's mission focused on the study of molecular mechanisms of the cell signaling processes and the understanding of structural changes in the production of hormones, growth factors, cytokines, and cell behavior. Funds supported new faculty and the purchase of major equipment. Fuller Brazer and O. D. Butler were the Co-PIs.

University of Texas - Houston Health Science Center ($1,000,000 • 1995-1997). Funds supported the Center for the Neurobiology of Learning and Memory. The Center served as a unifying locus for the physiological study of learning and memory from one of four perspectives: (1) molecular mechanisms, (2) cellular integration, (3) modifications of neuronal structure, and (4) real-time neural network simulations. Funds supported major equipment purchases for the Center and start-up costs for new faculty. John Byrne was the PI.

University of Maryland Biotechnology Institute ($1,000,000 • 1995-1997). The grant provided 3-year support for studies of bioactive compounds for marine organisms living in extreme environments. The focus of the research was to determine the biochemical basis for their biological activity in order to facilitate drug design through molecular modeling and to enable their production through organic synthesis or expression in prokaryotic or eukaryotic cell culture systems. Funds supported core operational expenses, equipment, and graduate stipends. Rita Colwell was the PI.

University of Kentucky ($1,900,000 • 1995-1998). The grant provided 4-year support for immunotherapy and gene therapy programs at the Lucille P. Markey Cancer Center. Specific goals included (1) building expertise on the role of T-cells in the idiotypic network as a basis for critical investigation of anti-idiotype vaccines and (2) advancing gene cancer therapy by increasing tumor specificity in gene delivery through new techniques in the selective targeting of tumor cells. Funds provided faculty salary and start-up costs. Kenneth Foon was the PI.

Appendix B
Site Visit Reports
Lucille P. Markey Charitable Trust
Large Research Program Grant Awards

THE YALE UNIVERSITY SCHOOL OF MEDICINE
PROGRAM IN MOLECULAR ONCOLOGY
MARCH 2001

The site visit team had an informal dinner meeting with Vincent Marchesi, Director of the Boyer Center for Molecular Medicine, and Renee Dobos, Administrator of the Center. Dr. Marchesi briefly described the background of Markey funding for the Program in Molecular Oncology.

Background of Markey Funding

By the end of the 1980s, leaders at Yale had come to the realization that molecular biology was becoming the core of biomedical research and that Yale was falling behind other academic medical centers in its molecular biology research. Leon Rosenberg, then Dean of the School of Medicine, sought to remedy this by establishing the Boyer Center for Molecular Medicine. Boyer and the Howard Hughes Medical Institute had funded the Boyer Center building. The $12.1 million Markey funds were originally planned for developing the Program in Molecular Oncology, a part of the Boyer Center in July 1990. Markey funding was to be used for most of the equipment ($2.95 million) for the Program in Molecular Oncology and core facility needs and to fund individual investigators during their first five years.

The Program in Molecular Biology was to be built around six inte-

grated research programs, each headed by a principal investigator. Additionally, research training was to be an important part of all programs at the Boyer Center for Molecular Medicine and especially for the Program in Molecular Oncology. It was to have its own training director with responsibility for developing a cohesive program, and for integrating the Program's students with fellows of other programs in the center and other departments in the medical school.

An important goal of the Program was to have clinical fellows with an interest in cancer spend approximately one year learning advanced research techniques that will have later application in a clinical setting. The Markey funds were intended to support 10 predoctoral candidates and 10 postdoctoral fellows over the five-year term. In fact, 7 postdoctoral and 14 predoctoral fellows received support from Markey funding. However, staff at the Program in Molecular Biology were unable to provide data on the identities and current locations of these fellows. Site visit members were told that four young faculty were supported by Markey funds—Dr. Glazer, Dr. Stein, Dr. Xu, and Dr. Fearson.

It was hoped that the Program in Molecular Oncology would become the "molecular research arm" of the Yale Cancer Center. However, with the arrival of a new Director, the Yale Cancer Center also took on molecular oncology, which directly competed with the Boyer Center's Program. Therefore, the Program now has a new focus in development and space has been reallocated away from oncology.

The site visit team had the opportunity to meet with two young faculty who were recruited with Markey funds. Peter Glazer, who was the third faculty recruit into the Program was offered a large start-up package with equipment and supplies. This package allowed him to explore new directions in his research in developing gene-targeted drugs, research that he described as initially "risky" (his original NIH application was not funded) but which now has attracted external support. Although his clinical department paid his salary, Markey funds paid for 50% of his secretary and supported a postdoc for 12 months until an independent NRSA fellowship was obtained.

Tian Xu came to the Boyer Center from the University of California, Berkley, as a postdoctoral fellow in 1993. Although he was offered an HHMI fellowship at that time, the Boyer Center provided larger lab space and more equipment than most junior faculty received. Markey funds paid for five years of his salary, a postdoctoral student, and a lab technician. He became a Hughes Investigator in 1997. Similar to Dr. Glazer, Dr. Xu also believed that this support provided him with the opportunity to pursue more "risky" research. Dr. Xu is certainly a rising star. His science is extremely impressive so use of Markey funds in his recruitment was well worth the investment.

Sherman Weissman, Chair of the Boyer Center for Molecular Medicine, was at Yale before Markey funding. At the onset, the Program in Molecular Biology had decided to work with existing departments. For example, a committee of relevant individuals in medicine was formed to "find people and offer them to departments—a school-wide recruiting effort". This approach had never happened before at Yale. This goal of Program as being a "people incubator" led to the development of the Clinical Scholars program. The Clinical Scholars were to spend five or more years at the Boyer Center and then return to their departments. However, this approach did not work, because some departments were reluctant to have their brightest come to the Boyer Center. Also, problems with space meant that the Clinical Scholars, rather than having their own "module" and space, had to function more as postdocs. Dr. Weissman believed that the legacy of the Markey funding is the recruitment of outstanding young faculty and the provision of a start-up package that enables them to begin research in new and underdeveloped areas.

Markey money was used to support the development of several investigators: Dr. Stern (who returned to his department); Dr. Glazer, who received generous equipment and start-up funds, but also seems to be very well connected with the Cancer Center; Dr. Fearson, who was recruited to another institution, and Dr. Xu, who is now an HHMI Investigator. While the dollars were used well to catalyze an individual scientist's career development, it appears that they were not used to develop a coherent program of molecular oncology.

Conclusions

Other than support for a few young scientists, three of whom remain at Yale, the site visit team could find no evidence of a lasting legacy of Markey funds at the Boyer Center. It is very unfortunate that the plans for the $12.1 Markey funds did not develop into a thriving Program in Molecular Oncology. Moreover, the program's stated goal—"The money from the Markey Trust will provide the bulk of the financial support for each research program . . . and then phase out over time as grants from NIH and private agencies begin to phase in"—certainly was not fully achieved. The Markey Committee's assertions about what elements make a successful program seem to be absent from Yale. Below are several examples of critical factors contributing to the failure of the Program:

1. Unfortunately, after a new Director of the Yale Cancer Center began to emphasize a more molecular approach to his program, the Program in Molecular Oncology began to compete for distinguished faculty. Since the programmatic concept (a program that is staffed by faculty from

other departments) was foreign to traditions of Yale, the departments were reluctant to let their brightest and best faculty go to Boyer.

2. Yale's focus on the departmental structure of the institution inhibits its leadership from exploring new ways of training and collaboration with the Boyer Center. The Program in Molecular Biology did not fit into the overall vision for the institution. Almost immediately following the Markey award, Leon Rosenberg left Yale University to assume another position. Additionally, Dr. Fearson's departure from Yale left a gap in identifying potential collaborators for the junior faculty. While principal investigators often leave an institution after funding arrives, there is often vigorous, committed, and effective leadership in the wings. But along with other changes occurring at Yale (such as the arrival of a new Yale Cancer Center Director), the lack of leadership resulting from Rosenberg's, and Fearson's absence caused a lack of cohesion in the Program on Molecular Oncology. One lesson for future funders is the importance of program leadership and in having that leadership in place for the duration of the funding.

3. There appears to be a lack of interdisciplinary collaboration among researchers and faculty at the Center. The more successful programs that the Committee has visited have strong emphasis on collaboration and cooperation among not only the faculty, but also the students.

4. The Program in Molecular Oncology was able to build bridges to the clinical departments, but was unable to build similar bridges to the basic science departments. Basic science faculty retained their primary position, salary, and research identification with their basic science departments. They did not identify with the Program in Molecular Oncology.

5. Sherman Weissman's final comment was "it's a shame that the funds had to end". Even though the original goal of the Program in Medical Oncology was to create a program that would sustain itself indefinitely through succeeding NIH funding, the Program failed to thrive after the Markey funds ended.

The Markey Committee finds that private funders should consider program intent and goals in making awards, monitoring progress, and providing "assistance" to ensure program success. For example, could Yale's lack of "enthusiasm" or "commitment" to cross-department collaboration have been picked up at either a pre-award site visit or at the early stages of the program (e.g., a year after Rosenberg left)? The Committee is not suggesting heavy-handed "oversight" by a Foundation; however, it is nearly always the case that some number of projects/grants may not flourish as intended. In some cases, there may be nothing a sponsor can do, but in others, they may be able to help leverage some

change or at least circumstances that help a project get "back on track." Even at the very least, being more proactive about progress reports and record keeping seems to be not unreasonable.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO PROGRAM IN BIOMEDICAL SCIENCES MARCH 2001

The site visit team met with the university and program administrators during an informal dinner. During the course of discussion, the Vice Chancellor emphasized the importance of the leadership of University of California, San Francisco (UCSF) just prior to the Markey award. Because leaders such as Holly Smith, Bruce Alberts, and Mike Bishop had an unselfish approach to bringing the institution as a whole up to a higher standard, the foundation of collaboration was laid that enabled the Program in Biological Sciences (PIBS) to flourish. Those early leaders were willing to devote the substantial award wholly to the program with no or very little administrative costs. UCSF has been able to sustain PIBS after Markey funding ended because it has been institutionalized by the university leadership.

Background of Markey Funding

During the 20 years before the Markey award, UCSF had developed a distinguished faculty whose scholarship had gained international recognition. The renaissance was initiated largely in the Department of Biochemistry and Biophysics, but soon spread to other departments with recruitments often made in collaboration with the Department of Biochemistry. The collegial and altruistic example of this department greatly facilitated the rise of excellence of other departments at UCSF, which were soon populated with scientists who considered themselves citizens of the university and not of a single department. The prominence of the Biochemistry faculty made possible the creation of an outstanding graduate program in Biochemistry and Molecular Biology. Diversification led to the establishment of promising programs in cell Biology and Genetics, whose full potential required the establishment of PIBS. The remaining program in the initial PIBS consortium, Neuroscience, was sponsored by the Department of Physiology, and also benefited greatly from its proximity to and support from the Department of Biochemistry.

In 1987, UCSF applied to the Markey Charitable Trust for funds to form a unified program of research and graduate teaching that would unify biomedical research on the UCSF campus. The purpose was to foster and exploit unity and collaboration among the research faculty and

their scientific disciplines. Using Markey funds as a catalyst, UCSF hoped to establish new alliances for research, to diversify the faculty, and establish new programs for graduate and medical training and initiate new research programs to use recently developed technologies to address central problems in biology and medicine. PIBS has left a positive and permanent mark on the UCSF community. The impact of this award exceeds that of any other grant given to UCSF.

Thus in 1988, UCSF had several excellent graduate programs plus several additional programs of less distinction under the sponsorship of individual departments. These programs developed their own curricula, set their own standards for admissions and for the Ph.D., and had in most instances failed to develop adequate support mechanisms to support the initial years of graduate education. There were few mechanisms for communication between programs, particularly for graduate students. The Markey grant provided the impetus to develop a collaborative and interactive approach to graduate education and faculty recruitment that has continued to impact the UCSF campus.

This model for scientific development and graduate education made possible by Markey support has continued to influence UCSF. At the time of its formation, approximately 96 faculty participated in the graduate programs of PIBS. During the period of Markey support between 1988 and 1995, PIBS assumed the responsibility for graduate education previously divided among the basic science departments and created a collaboration with basic science and clinical departments for recruiting to UCSF outstanding young scientists. Using Markey support, PIBS collaborated with clinical and basic science departments in 21 successful recruitments, who have established creative research programs of international note.

Since the expiration of the Markey Grant, PIBS has retained its responsibilities for faculty recruitment, graduate education, and promotion of modern medical research. UCSF has been successful in continuing and expanding the support provided by this grant. Including the initial 21 recruitments, PIBS has now cosponsored 76 successful international searches for promising scientists, utilizing alternative sources of support. While the vast majority of the searches have sought assistant professors, PIBS has collaborated in the recruitment of directors for the Cancer Center and the Gladstone Institute in AIDS Research as well as the Chair of Pathology.

PIBS currently consists of seven graduate programs with shared governance and standards. The programs in Biochemistry and Molecular Biology, Cell Biology, Genetics, and Developmental Biology are closely aligned with a shared admissions process and largely overlapping curriculums. These programs cosponsor a single annual retreat and a common seminar series. Some of the individual programs have their own

journal clubs and retreats. The other graduate programs—Immunology, Neuroscience, Biophysics, and Chemistry and Chemical Biology—are much more loosely affiliated. Each program has its own admissions process, graduate curriculum, and seminar series.

PIBS is governed by an executive committee consisting of two members of each of its graduate programs. While this committee has responsibility for graduate education, its primary mission is to provide scientific leadership for the school. The PIBS executive committee is proactive in discussing the future of UCSF. All programs that are members of PIBS have agreed to a common governance including common and rigorous standards for participation by the faculty membership, periodic review of the faculty in each program, shared scrutiny of applicants for open positions, and common standards for graduate admissions and teaching. PIBS sponsors an annual retreat for each of its graduate programs, an orientation day for new students, a weekly faculty-student journal club, an annual course in the Practice of Science, and other activities.

Today PIBS has expanded by incorporating the Biophysics Graduate Program. To meet PIBS standards, this program conducted a rigorous internal review to ensure that only faculty who participated actively and maintained productive research programs retained membership. Recently, PIBS has sponsored a new graduate program in Chemistry and Chemical Biology. PIBS has a mission of sponsoring new programs and initiatives as opportunities arise in the medical sciences and will collaborate in the establishment of several major initiatives in the near future.

PIBS has also been expanded by successful applications from other professors at UCSF. The activities sponsored by PIBS have encouraged the participation and membership by faculty who were not initially involved in graduate education. A total of 223 faculty have been members of PIBS between 1988 and present. Of these, only 36 have left PIBS, either for retirement or to accept prominent positions elsewhere (e.g. President of the National Academy of Sciences, Director of the National Institutes of Heath, Dean of the Pharmacy School at Michigan, chairmanships of Cell Biology at Harvard and Neurology at Stanford). Notably, only 5 of the 76 scientists recruited by PIBS in international searches have accepted positions elsewhere. There are currently 185 active members of PIBS.

Meeting with Graduate Students and Post-Doctorates

The site visit team had an opportunity to meet with both graduate students and post-doctoral fellows in PIBS. It is interesting to note that many of the graduate students were not aware of PIBS when they applied to UCSF. However, most of the post-docs came to UCSF specifically because of PIBS. They may not have understood the exact structure of PIBS,

but they knew that UCSF had a unique program of collegiality and collaboration among different biomedical disciplines. So while PIBS may not be easily recognizable as a specific program, it is well known that biomedical research at UCSF will offer individuals more exposure across many departments.

Conclusions

The replication of a program like PIBS greatly depends upon the institutional leadership and culture. PIBS would probably not be successful in institutions that have strong departmental governance and entrenchment. However, with the right leadership, PIBS is a strong model for creating important collaborations across disciplines in both research and training. The Committee believes that there are three critical elements that must be present in order for a program such as PIBS to be successful:

1. An institutional vision from the top leadership is critically important in order to create and foster an atmosphere of collaboration and cooperation. Faculty collaboration among disciplines must be rewarded with prestige and funding. PIBS offers these rewards.
2. A collaborative relationship between basic science departments and the medical school must permeate down from the deans, to the faculty, and finally to the students. Students need to know that they are welcome to enter anyone's lab to ask questions or discuss problems or findings. All of the students that we talked with felt at ease talking with faculty from any of the PIBS disciplines.
3. The physical proximity of the labs to each other is very important in fostering informal discussions among disciplines. In fact, although the new building at Mission Bay will offer much needed space, many of the students (particularly those in neuroscience) are concerned about losing these informal, spontaneous meetings with colleagues in the medical school.

THE WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH MASSACHUSETTS INSTITUTE OF TECHNOLOGY PROGRAM IN BIOMEDICAL SCIENCES MARCH 2001

The site visit team had an informal dinner meeting with Gerald Fink, Director, Whitehead Institute; John Pratt, Associate Director, Whitehead Institute; and Eve Nichols, Director of Institutional Advancement. Whitehead representatives described the Whitehead Institute and Markey's role in developing the careers of young faculty and promising scientists.

Background of Markey Funding

The 1988 award from the Lucille P. Markey Charitable Trust to the Whitehead Institute for Biomedical Research played a vital role in the development of the Institute. Seed money provided by the Markey Trust and other funding sources helped the Institute launch talented men and women into careers at the forefront of biology. The award was used by the Institute to support both junior faculty members and participants in the Institute's Whitehead Fellows Program. The latter allows promising young scientists with exceptional research agendas to pursue independent research programs as an alternative to traditional post-doctoral positions. Every Whitehead Fellow who received Markey funds is now a prominent research scientist at a major university or research institute.

Whitehead recipients of Markey funds included Dr. Eric Lander, now director of the Whitehead Center for Genome Research, the largest contributor of DNA sequence to the public Human Genome Project; Dr. Peter Kim, recently named Executive Vice President for Research and Development of Merck Research Laboratories; Dr. Terry Orr-Weaver, a Member of the Board of the Genetics Society of America; Dr. Ruth Lehmann of New York University and Dr. David Page of the Whitehead Institute, both Investigators of the Howard Hughes Medical Institute; Dr. Paul Matsudaira, a leading researcher at the interface of biology and engineering; and Dr. Hazel Sive, a pioneer in the study of vertebrate development.

Seven of the eight junior faculty members supported by the Markey Trust at Whitehead became full Members of the Institute and received tenure in the Department of Biology at MIT. The eighth returned to Korea to head a new biomedical research institute. For the Whitehead faculty and Whitehead Fellows, seed money from the Markey Trust led the development of sophisticated research programs, which were subsequently supported by the NIH and other traditional funding sources.

In addition to advancing the careers of exceptional young scientists, the Markey Trust award had an important impact on the evolution of the Whitehead Institute as a whole. In 1993, Whitehead Director, Dr. Gerald Fink and the Whitehead Board of Directors established a strategic plan for the future of the Institute. This plan called for major science-driven investment in three key research areas: structural biology, transgenic science (animal models of human disease), and infectious disease. Two of the three initiatives, structural biology and transgenic science, emerged from research programs supported at least in part by Markey funds. The strategic plan led to the construction of a new research wing—completed in the spring of 1996—and to the expansion of research and teaching programs that helped alter the course of biomedical science throughout the research community.

The Markey Trust reinforced what is best about the Whitehead Institute—the ability to nurture outstanding young scientists in an environment that encourages creativity, collaboration, and technological innovation.

Meetings with Markey-Funded Faculty and Fellow

The site visit team had an opportunity to meet with four of the faculty who were funded by Markey: Paul Matsudaira, Terry Orr-Weaver, David Page, and Eric Lander. They also met with one of the Fellows, Bruce Tidor.

Paul Matsudaira, who researches the interface of biology and engineering, had just completed a post-doc in England when he arrived at Whitehead in 1985. His Markey funding began in 1988, which was used to enhance his PEW innovator award. He has a joint appointment with MIT, teaches two courses a year and works in the project lab about two hours a day. Markey funding has allowed him to focus on his research without having to manage other projects at the same time. He has made significant advances in microscopy and protein chemistry, and has identified elements of the molecular cytoskeleton that play a central role in cell function and structure. He has also created microelectromechanical devices to track biomolecular interactions and enhance the identification of human disease genes.

Terry Orr-Weaver was appointed as an assistant professor in 1987. Her six years of Markey support allowed her to start new projects in areas that were different from her original areas of research. She is researching how cells replicate their DNA (through the study of fruit flies), which has led to new information about two genes associated with cancer in humans. This research will help scientists understand the mechanisms responsible for this aberrant cell behavior and perhaps suggest new ways of blocking it. Her previous work, which focused on the mechanisms of chromosomal segregation in egg and sperm formation, was recognized in *Discover* magazine as one of the most important research achievements of 1995.

David Page is studying the importance and complexity of the Y chromosome. His laboratory was the first to clone an entire human chromosome—the Y chromosome—and will soon report the entire sequence of the Y. In addition, he has revealed the genetic basis of some types of male infertility.

Dr. Eric Lander arrived at Whitehead as a Markey Fellow and then was appointed to the faculty. This progression illustrates the critical role Markey funds played in the development of the Institute. Dr. Lander has a D. Phil. in Mathematics from Oxford University and spent five years

teaching at Harvard Business School. During his years at Harvard, he became interested in the applications of mathematics and new informatics technologies to biology. He began studying molecular biology and genetics, first at Harvard and then at MIT, where the Director of the Whitehead Institute invited him to join the Fellows Program. The Fellows Program enabled him to test and refine new concepts in gene mapping, gene sequencing, and bioinformatics. Today, he heads the largest academic genome center in the world. Through his work in functional genomics, he is building a new framework for deciphering the origins of complex human diseases such as cancer, diabetes, and heart disease. The Markey Trust helped lay the foundation for this progression by providing partial support for the Lander laboratory for five years.

Bruce Tidor was a Whitehead Fellow from 1990 to 1994 and is currently a member of the MIT faculty in the Department of Chemistry. The Fellows program is unique in that it offers the Fellows their own space and allows them to be the principal investigator for their research. The Markey funds enabled Whitehead to hire postdoctoral fellows for whom outside funding would be difficult.

Visit to Genome Lab

The site visit team had the opportunity to visit Eric Lander's genome laboratory, which is one of the national labs for the Human Genome Project. Over the last few years Dr. Lander's lab has developed methods and strategies applicable to high throughput genomic sequencing. The lab is a highly automated, scalable system that has all the necessary hardware and sofware to help in the worldwide effort to sequence the human genome.

He has developed and implemented fully automated systems for production sequencing as well as developed software for information management and sample processing and analysis. He is now focused on completing the vision of creating a high throughput system capable of providing the community with low cost, accurate sequence data.

Dr. Lander used $500,000 of Markey funding to progress from theoretical research to data-producing research, allowing his lab to produce markers and preliminary datat tha were used to garner NIH funds for the genomic lab. A concentrated "plug" of money was needed to get the lab started. It was not possible to get the NIH funding without preliminary data. Even though other funds were used to supplement the Markey award, Dr. Lander stated that, "Markey can take credit for building the genome center. This was high-risk research and money spread out does not allow for high-risk research." He further stated that his Markey fellowship was "a chance to behave more as a scientist than as a careerist,"

and that he had the freedom to explore his theoretical hypotheses without the risk of losing NIH funding.

Conclusions

The site visit team was very impressed with the Whitehead Institute. While the Markey funds certainly contributed to the success of this outstanding program, it is difficult to tease out Markey funds from the other sources of funding that were used to augment the Markey award. However, it is quite clear that both Markey funds and the other funds were used to create an atmosphere of cooperation and collaboration among the Institute's scientists.

The site team has identified four characteristics that appear to make the Whitehead Institute productive and effective.

1. Because Whitehead was conceived and built as a separate entity from MIT, its founders were able to create a research environment that did not bring with it some of the departmental "baggage" that traditional institutions may bring to a new program. In addition, the Markey award (along with other funding) was used for developing the institute as a whole and not just one area or department.

2. The Markey award (along with other funding) was used to fund new and promising researchers. These scientists were either undergoing a change in career directions or a change in research interest and probably would not have received adequate funding to make these changes without the Markey award. The funds were sufficiently generous so that these scientists were free to focus solely on their research projects without having to be burdened with conducting other research or administrative activities.

3. The physical layout and the vision of the Whitehead Institute encouraged collaboration and communication across disciplines. There are no barriers between labs and there are plenty of open spaces for informal discussions. The atmosphere of the Institute is one of openness.

4. The recruitment of faculty or fellows is very informal, which lends itself to greater flexibility and possibilities. Search committees are not constrained by institutional requirements, which might limit recruitment in some organizations.

Appendix C
Site Visit Reports, Telephone Interviews, and Letter Reports Lucille P. Markey Charitable Trust Small Research Program Grant Awards

BAYLOR UNIVERSITY SCHOOL OF MEDICINE
PROGRAM IN DEVELOPMENTAL AND TUMOR BIOLOGY
APRIL 2002

History and Background of Markey Funding

The request to Markey was to provide funding to help advance Baylor's effort to become one of the nation's pre-eminent biomedical research institutions. There was an extensive ongoing research effort in developmental biology and oncology, with emphasis on cell structure, oncogenes, growth factors, and tumor suppressor genes. Baylor now wanted to broaden graduate training to enable Ph.D. candidates to learn more about disease process in man. Specifically, the award was for $1.4 million to recruit two new senior faculty, two new junior faculty, and provide training stipends. Initial funding began in 1994 and continued until 1997.

Impact of Markey Funds

Markey funds were used to implement a new developmental biology program at Baylor College of Medicine, directed by Hugo Bellen. He has been able to recruit four developmental biologists: Kwang-Wook Choi from CalTech; Kathi Mahon from NIH; Anna Newman from CalTech; and Milan Jamrich, a senior scientist from Yale.

Perhaps the greatest impact of the $1.4 million Markey award was the leveraging of additional funding: a five-year training grant from NSF, which required matching funds for consideration; an NIH training grant; and a March of Dimes endowment of $5 million to support training and research. The Markey funds were the main stimulus to allow initiation of a new graduate program in Developmental Biology. From its beginning the program increased to 24 faculty and 16 graduate students at the end of Markey funding.

Markey funding has been used to continue support of graduate students. In addition, funding has been used to establish a series of lectures by distinguished guest speakers. Finally, Markey funds supported part of the salary of a program administrator who coordinated the daily activities of the program in developmental biology.

BRANDEIS UNIVERSITY
PROGRAM IN STRUCTURAL BIOCHEMISTRY
OCTOBER 2002

History and Background of Markey Funding

Brandeis proposed establishing a protein crystallography laboratory to complement existing facilities for x-ray diffraction, electron microscopy, and computer graphics. Funds were required for spectroscopy, protein sequencing, and peptide synthesis. A particular feature of the new initiative was the incorporation of a postdoctoral exchange program between the Brandeis Laboratory and the Laboratory of Molecular Biology at the University of Cambridge. In 1998 Brandeis was awarded $2 million over five years, including approximately $1 million in salaries for three investigators. Funds totaling $500,000 were sought for technical personnel for the first three years and approximately $500,000 for crystallographic equipment. Brandeis was awarded supplemental awards of $500,000 in both 1990 and 1996. The former was directed to the activities of the structural biology and biochemistry group under the direction of Laura Davis; the latter supported the research of Lizabeth Hedstrom, a professor of biochemistry.

Impact of Markey Funds

Gregory Petsko was the principal investigator of the Markey award. The award, and the supplements, was used to fund the research of a number of investigators. Principal among them are Hugh Huxley, Laura Davis, and Lizabeth Hedstrom.

Professor Hugh Huxley's research focused on the use of x-ray syn-

chrotron radiation to study changes in actin and myosin filament structure during tension development in muscle. Results of his work were reported at a number of international scientific meetings, including the symposium on actin structure sponsored by the United States, Australia, and Japan. Dr. Huxley also participated in a workshop on fibrous protein structure in Austria. Markey funds supported his participation at both of these meetings. Markey funds were used to support the modernization of the Rosentiel Center's instrument shop and significant improvements in its computer network. In addition, the grant allowed the University to acquire an Orbital Sciences scanner, which was installed in the center's electron microscope facility.

Dr. Davis's laboratory is devoted to the study of the transport at the cell nucleus. Access to and from the cell nucleus is governed by a large gate-like structure called the nuclear pore complex. The nuclear pore complex regulates entry and exit of protein and RNA over time. This regulation is crucial for turning specific genes on and off, and for controlling the time at which cells divide. Her laboratory is examining how the nuclear pore complex recognizes transport substrates and the mechanism by which transport can be regulated.

Dr. Hedstrom investigated the mechanism of enzyme action. Her studies focus on three enzyme symptoms: trypsin, streptokinase/plasminogen, and inosine monophosphate dehydrogenase (MPDH). This research seeks to understand the structural basis of enzyme specifity. She has addressed the problem of identifying the structural features, which determine substrates specificity in the trypsin family of serine proteases. Another project underway focuses on structure-function styles of zymogen activation. The goal of this project is to use site-directed mutagens to analyze the conformation change that occurs when trypsinogen is active and inactive conformations of trypsinogen and trypsin are assessed on order to define the forces that govern protein conformational stability.

BROWN UNIVERSITY
PROGRAM IN MOLECULAR AND CELL BIOLOGY
OCTOBER 2002

History and Background of Markey Funding

In 1990 Brown began developing a program focused on Molecular and Cell Biology of Disease. In 1991, new faculty in Cell Biology, Pathology, and Molecular Genetics were added along with a graduate program in pathobiology, thus creating the Division of Biology and Medicine. This new Division is intended to facilitate interdisciplinary collaboration. Additionally, Brown increased the participation of faculty members from the

clinical departments (all based in the medical school's seven hospitals) in new investigative initiatives. The goal of the new program was to enhance opportunities to help translate findings of basic research to the care of patients.

In 1992 Brown submitted a proposal to the Markey Trust for: (1) support for graduate students, M.D./Ph.D. students, and postdoctoral fellows; and (2) funding for new faculty positions as well as for equipment and renovation. In 1994 Brown was awarded $1.3 million for over five years. Subsequently, funds were extended through 2001 to support the molecular and cell biology of disease program. Agnes Kane was the principal investigator.

Impact of Markey Funds

The Markey grant helped the Division of Biology and Medicine to undergo at least 27 new research initiatives from cytokine networks in viral infections, to differential DNA replication in insect chromosomes, to studies on the mechanism of ribosomal translocation during protein synthesis. These new research initiatives attracted additional funding for 14 principal investigators.

Overall the Markey grant supported 66 predoctoral students, 15 M.D./Ph.D. students, and 17 postdoctoral fellows who engaged in research in this program. Stipends and tuition were provided for an additional three M.D./Ph.D. students. In addition, Markey funding enabled faculty to renew nine grants and to prepare proposals that resulted in the funding of five new grants.

A Fuji Phosphorimager was purchased with Markey funds and has been extensively used by faculty in the Division of Biology and Medicine, especially by Drs. Dahlberg, Gerbi, Hawrot, Hendrickson, Landy, Wessel, and Zarat. In addition, a Zeiss LSM410 confocal microscope was added to the core facilities. Drs. Bearer, Rioult, Wessel, Marshall, and Kane are the major users of this new equipment. They are working on collaborative research projects on emphysema, pulmonary hypertension, and breast cancer.

This grant provided infrastructure support, which allowed the individual departments to co-exist without competition—all facilities are shared. Equally important, the Markey funds have provided seed money for renewal of NIH research grants for Drs. Dahlberg, Gerbi, Henderson, Landy, Mowry, Sedivy, Wessel, Wyche, and Zaret. Funding of new NIH research grants has been awarded to Drs. Henderson, Sedviy, Wharton, and Wyche.

BURNHAM INSTITUTE
STRUCTURAL BIOLOGY PROGRAM
AUGUST 2002

History and Background of Markey Funding

Burnham requested funding for major equipment in support of its cell recognition studies and the establishment of a structural biology program. Burnham proposed to use Markey funds to set up laboratories for three scientists. This grant request marked a policy change for the Markey Trust because they had never before granted an award in which the majority of the funds were to be used to purchase equipment. However, because of the excellent reputation of the Institute and its leadership, the Trust decided that the policy change was warranted. In 1991 the Markey Trust awarded $1.5 million over five years. Erkki Ruoslahti was the principal investigator.

Impact of Markey Funds

The Markey funds were used to establish the Structural Biology Program. Instrumentation was purchased to provide the structural studies by x-ray crystallography, nuclear magnetic resonance (NMR), and computer graphics modeling. Funds were also used to provide laboratory setup costs and partial salary support to recruit new scientists to the program. Burnham was able to recruit four new scientists, all of whom were able to obtain federal funding for their salaries and research. The NMR laboratory is now established and functional and is a shared facility in order to support the operational costs and service contracts.

A 500 MHz spectrometer, manufactured by Varian, was installed in the newly developed NMR laboratory. Dr. Joseph Parello, relocated to La Jolla from the University of California, San Diego. His two postdocs—Francoise Roquet and Jean-Louis Baneres—joined with him in the new lab. They continued their structural studies of calcium-binding proteins (parvalbumins) and NMR analyses of fragments of the $\alpha_5\beta_1$ integrin that bind the RGD site in fibronectin. Nuria Assa-Munt, a new spectroscopist, has been recruited to the Structural Biology Program. She will initiate NMR analyses of the PU.1 transcription factor and additional studies of the molecular structures of other DNA-binding proteins

It is important to note that although the overall level of funding that the Burnham Institute received was not large compared to funding received by other recipients, it represented 10 percent of the total revenue for 1991. The Burnham staff stressed that the Markey funding was crucial for three reasons. First, the funding came during a period when federal

funding had been severely reduced. Second, the Markey funding enabled the purchase of expensive equipment. Third, the Markey Trustees were flexible with the timing of the release of funds, allowing funds to be shepherded until they could be used efficiently.

CARNEGIE MELLON UNIVERSITY
DEPARTMENT OF BIOLOGICAL SCIENCES
SEPTEMBER 2000

History and Background of Markey Funding

In 1985 Carnegie Mellon submitted a proposal from the Department of Biological Sciences for two purposes: (1) to establish the Pittsburgh NMR Center for Biomedical Research, and (2) for an NMR spectrometer. Funds were also proposed for faculty development of both senior and junior scientists. Carnegie Mellon proposed to work in collaboration with the University of Pittsburgh and with additional funding support from the Richard King Mellon Foundation, the Commonwealth of Pennsylvania, and NIH. The principal investigator was Chien Ho.

Impact of Markey Funds

The Department received $1.925 million in September 1985. Funding was primarily used in infrastructure development and to provide support and start-up costs for investigators.

The NMR Center was established and supported by a major grant from the National Center for Research Resources as a national biomedical facility on the application of magnetic resonance imaging and spectroscopy to biomedical sciences. It has become a major center on the application of MRI and MRS to biomedical sciences using animal models. They have developed novel MRI/MRS techniques and methodologies and have applied them to biomedical problems. During the past 15 years, the Center has also obtained grant funds from shared instrument grant programs of NSF and NIH to purchase new NMR instruments.

In the area of infrastructure development, the Markey funding (commingled with other funding) was used to purchase a high-field NMR spectrometer. This spectrometer has led to additional extramural funding and the development of a specialized program in structural biology that investigates the structural determinations of biological macromolecules. In the 10 years since the Markey awards were made, 3 M.D./Ph.D. students, 8 graduate students, and 12 postdoctoral fellows received degrees or engaged in substantial research using Markey funded equipment. In

addition, many undergraduates, graduate students, and postdocs have used this equipment as an ongoing part of their research activities.

In the area of faculty development, the Markey award was used to provide salary support and start-up costs for four new faculty members in the Department of Biological Sciences. These include Drs. Koretsky, Pollock, Lopez, and Minden (who was also a Markey Scholar).

The NMR Center remains a major center of the application of MRI/MRS to the biological sciences using animal models. In addition to the four faculty, the Center supports between six and eight graduate students each year.

COLD SPRING HARBOR LABORATORY PROGRAM IN DEVELOPMENTAL NEUROBIOLOGY IN THE NEUROSCIENCE CENTER OCTOBER 2001

History and Background of Markey Funding

During the tenure of James D. Watson, who was the director of Cold Spring Harbor Laboratory from 1968 until 1994, the programs of Cold Spring Harbor grew and prospered. Dr. Watson was an excellent recruiter of top-notch scientists and an effective fund-raiser. He renovated and expanded old facilities and began a major effort to create a Neuroscience Center, encompassing both research and education facilities accommodating a major initiative in the neurosciences. In 1990 the Lucille P. Markey Charitable Trust awarded Cold Spring Harbor $4.0 million, the largest of four Markey awards. In 1986 they received $150,000 to support advanced courses for neuroscientists during the summer. Also in 1986 Cold Spring Harbor received $863,500 from Markey Trust, which was seed money to begin a program in structural biology. They recruited two structural biologists and three crystallographers (and their respective equipment) with this grant. The $4.0 million grant was used as part of the capital campaign to begin the neuroscience program, including construction of a new facility. Finally, in 1996 the Markey Trust awarded an additional $500,000 for imaging equipment in the neuroscience program.

In 1994 Bruce Stillman became the Director of Cold Spring Harbor Laboratory. He has since used some of the Markey grant money to pursue behavioral genetics. He has investigated DNA replication, chromatin assembly, biochemistry, yeast genetics, cancer, and the cell cycle. This area of study is somewhat controversial, and many advised against starting such a program. But Tim Tully was recruited to Cold Spring Harbor to begin the behavioral genetics program by studying fruit flies. The Markey grant enabled Dr. Tully to create mutant fruit flies to study memory and

behavior, which led to a whole new pathway in memory research and the development of investigative drugs that can stimulate memory.

Impact of Markey Funds

According to Dr. Stillman, the greatest impact of the Markey funds was to enable Cold Spring Harbor to invest in good scientists early in their careers and give them the needed boost to get their research underway. Cold Spring Harbor used Markey funds to help support the salaries and operating expenses of new scientists until they were able to obtain sufficient research grants to maintain their own research programs.

There are numerous examples at Cold Spring Harbor of scientists who successfully obtained funding from various institutes of the NIH. Dr. Hollis Cline received an award from the National Eye Institute, Dr. Roberto Malinow received an award from the National Institute of Neurological Disorders and Stroke, and Dr. Alcino Silva received an award from the National Institute of Aging's Neuroscience and Neuropsychology of Aging Program.

The current funding for the program of 11 faculty is $6.7 million (including all grants, post doctoral fellowships, gifts, and foundation funding). Since 1990, three buildings have been constructed totaling 53,000 sq. ft at a cost of $17.7 million (not adjusted for inflation). To date, the molecular neuroscience program has accumulated a total of $50.3 million in funding from 1991 to the present (excluding construction costs). One of the neuroscience faculty, Karel Svoboda, was selected as a Howard Hughes Medical Institute Assistant Investigator in the recent competition. Three faculty have received $1 million grants from the Harold Mathers Foundation and numerous NIH grants have been obtained by these faculty.

The current number of faculty, students, and postdoctoral fellows are:

	Faculty	Postdoctorals	Students
Total since 1991	14[a]	76	34
Current	11	39	14

[a]Includes faculty who have left for University positions (R. Davis, Baylor College of Medicine; H. Nawa, Niigata University, Japan; A. Silva, UCLA).

Dr. Stillman believes that the Markey Trust was the first to emphasize the investment into the scientist rather than an institution. He also believes that a limited trust such as Markey can have greater vision for

changes in direction by being able to award large grants that have huge impacts on institutions or programs.

CORNELL UNIVERSITY
PROGRAM FOR STRUCTURE-BASED DRUG DESIGN
SEPTEMBER 2000

History and Background of Markey Funding

In 1993 Cornell submitted a proposal, which was a revision of an earlier proposal, for $3.4 million to fund half of the salary of the Director of the Program for Structure-Based Drug Design, salaries for a Ph.D. program manager, postdoctoral trainees, and student assistants. Although the primary target of the project related to drug design, the technology is applicable to a multitude of biologic problems in molecular and cell biology. Cornell has one of the nation's best veterinary medicine programs where there are active research collaborations between the veterinarian school faculty and the faculty in the biological sciences. The proposed research involved eight faculty members, four in chemistry, three in biochemistry, and one in the biotechnology program.

Impact of Markey Funds

In 1994 the Markey Trust awarded Cornell $1.2 million, which were often combined with other funds to accomplish the program's goals. The Markey funds were used to partially support several major pieces of equipment, specifically a 600 MHz NMR spectrometer, and two X-ray detector systems and computers for the synchrotron beam lines at Cornell High Energy Synchrotron Source (CHESS). In the case of the NMR machine, about $160,000 of Markey funds were used to get a commitment from the Dean for another $300,000. These funds were used as matching funds to obtain about $700,000 from NSF, giving a total of more than $1 million for the purchase and operation of the NMR. In the case of the X-ray detectors, about $100,000 of Markey funds were combined with government funds and Keck Foundation funds to purchase two detectors at a total cost of about $800,000.

The greatest accomplishment of the Markey grant was building Cornell's presence in the field of structural biology. About 20 research papers also resulted. They were able to attract an NMR spectroscopist to the biochemistry department and to build infrastructure in X-ray crystallography. They trained several graduate students and postdoctoral fellows.

Personal Observations

Dr. Steven Ealick, Director of the Institute of Human Neuroscience, stated that the greatest benefit of the Markey program was to provide a flexible source of funding that often provided leverage for obtaining additional funds. He stated, "In my experience, most foundations want full ownership. The Markey funds were used to partially support several pieces of equipment."

ELEANOR ROOSEVELT INSTITUTE FOR CANCER RESEARCH STUDIES ON THE MOLECULAR GENETICS OF CELLULAR PHENOMENA SEPTEMBER 2001

History and Background of Markey Funding

Although the Eleanor Roosevelt Institute is an independent entity under its own Board of Trustees, it is housed in the Department of Biophysics at the University of Colorado Medical School, with Dr. Theodore Puck as its director. Staff hold appointments on the University of Colorado Health Sciences Center faculty. The Eleanor Roosevelt Institute is organized into six basic science divisions: (1) Genetic and Metabolic Regulation, (2) Cell Regulation, (3) DNA Structure and Function, (4) Chromosomal Mapping, (5) Immunogenetics, and 6) Cell Membranes. These research programs are multidisciplinary and there is "crossover participation" by the investigators.

In 1988 the Markey Trust funded Eleanor Roosevelt Institute $1,375,000 to support work on cyclic AMP and mutagenesis, to discover the basis of malignant change, and to seek ways in which to protect against such changes. Specifically, the Markey funds would be used for additional faculty members, both at the junior and senior levels; graduate student stipends, technical help, and equipment. In 1992, the Institute was awarded a supplemental award of $100,000.

Impact of Markey Funds

There were several scientific advances made possible with support from Markey, which are summarized below:

- Methods for measuring exposure of genes have been developed and applied to a variety of normal and pathologic cell systems, which have identified sites of genome exposure in the nucleus. These studies promise to provide new insight for a variety of diseases and particularly cancer.

- The use of cyclic AMP for treatment of specific cancers.
- For the prevention of cancer, development of a simple, rapid procedure that is capable of rapid detection of mutation sources in a fashion that is more than 200 times more sensitive than standard methodology.
- Development of human gene mapping—especially chromosome 21, which has resulted in the identification of specific genes whose mutation can lead to ALS. These mapping studies have resulted in new approaches that promise the possibility of improved diagnosis, treatment, and prevention of many diseases.
- Creation of microdissection libraries from many regions of the genome that are shared throughout the world. Thus, the contribution from Markey's grant support has been useful both for the Institute's research and for many other laboratories engaged in genome analysis and positional cloning of disease-related genes.
- A theoretical formulation proposing a new function of lipoproteins in cell metabolism.

Scientists supported by the Markey grant have been appointed to key positions in the Cancer Center of U. Colorado School of Medicine and have been asked to advise this medical school about its future development in medical genetics. Trainees from Eleanor Roosevelt Institute laboratories have been appointed to professorships in distinguished universities throughout the world.

FLORIDA STATE UNIVERSITY
PROGRAM IN STRUCTURAL BIOLOGY
APRIL 2002

History and Background of Markey Funding

In 1988, Florida State University submitted a proposal to Markey to initiate a program in structural biology. The proposal included start-up funds for eight new faculty, capital equipment for ongoing research and for a new x-ray crystallography unit, initial support for research assistants, and construction funds to add 12,000 square feet of new research space. The new program, under the direction of Lee Makowski, was to have its administrative base in the Institute for Molecular Biophysics, which would change its name to the Institute of Molecular Biophysics and Structural Biology. The focus of the research was to be: x-ray crystallography and electron microscopy, nuclear magnetic resonance spectroscopy, laser spectroscopy, computational biochemistry, molecular endocrinology/neurobiology, and enzymology/protein chemistry. Ross Ellington is the current director of the Institute. In 1991, the Trustees

awarded Florida State $4 million for the structural biology program. In 1996, the program was given a supplementary award of $500,000.

Impact of Markey Funds

Most of the Markey funding was used for building renovation and start-up costs for the new Institute. Nine new faculty were hired and provided with set-up space and equipment. The molecular biophysics Ph.D. program was expanded. New facilities were created including X-ray crystallography, eukaryotic cell culture laboratory, physical biochemistry and molecular modeling.

A major success of the new initiative was the acquisition of an NSF training grant for $1.47 million over five years. That grant provided support for nine graduate students, six undergraduates, and two post-docs for a period of five years.

Markey funds were used to aid in the renovation of the electron microscopy facility, including a "clean room", and the purchase of two electron microscopes (in which Markey funds were combined with funding from other sources). According to its director, Florida State has developed one of the premier electron microscopes facilities in the world.

The structural biology 500 MHz NMR spectrometer was acquired, in part, with Markey funds and is maintained with Markey funding. This enables faculty from the structural biology program supported by Markey funds almost exclusive use of the NMR.

Finally, the supplemental grant was used to upgrade the Institute of Molecular Biophysics building which was literally falling down. Of special concern was fungal contamination resulting from badly designed and outdated air handling systems. Markey funds were used to replace the cooling system.

According to the director, the award of that grant marked the turning point in the growth and development of the Structural Biology Program. On January 9, 1997, Florida State University conferred an honorary degree to Louis Hector, Chair of the Markey Trust, in recognition of his management of the Trust, through which he provided a great service to basic biomedical research.

FOX CHASE CANCER CENTER
PROGRAM IN MOLECULAR ONCOLOGY
SEPTEMBER 2000

History and Background of Markey Funding

In January 1988 the Fox Chase Cancer Center submitted a proposal to the Markey Trust for funds to establish a new program in molecular oncology. The program was to be a multi-disciplinary effort, involving both M.D.s and Ph.D.s focusing on molecular and genetic changes in the cancer cell. Basic scientists were to work adjacent to clinical investigators in a new facility just being completed. The request from Markey was to be used in conjunction with other sources of funding, for a grand total of $15 million. The largest component of the Markey proposal is for new scientists, primarily junior investigators, for supplies and equipment.

Impact of Markey Funds

The Markey Trust awarded Fox Chase $4.0 million in early 1991. With these funds and funds provided by other donors, the Molecular Oncology Group grew from 2 members to 14 people, most of whom are now senior scientists either at Fox Chase or at other prestigious institutions. The Fox Chase Cancer Center has three divisions: (1) basic science, (2) medical science, and (3) population science. There are representatives from the Molecular Oncology working group in each of the divisions—four in basic science, eight in medical science, and two in the population science division. Of these 14, 3 are M.D.s, 4 are M.D./Ph.D.s, and 7 are Ph.D.s. The program is thriving and has grown from one working group to the current three.

Most of the funding has been directed to the support of 10 investigators. They work in laboratories that are relatively small (5 to 10 people), which is intentional so that junior scientists can acquire much needed research experience. In addition 4 graduate students and 37 postdoctoral fellows have been funded.

HARVARD UNIVERSITY
DEPARTMENT OF MOLECULAR AND CELLULAR BIOLOGY
SEPTEMBER 2000

History and Background of Markey Funding

Harvard's combined departments of Biochemistry and Molecular Biology, and Cellular and Developmental Biology submitted a two part

proposal for a total of $3 million to the Trust to subsidize the animal facility and for seed grants to enable junior scientists to pursue projects that have promise of opening new, major opportunities for which external grant support can then be expected from NIH. This is a concept similar to the Markey Research Program Grants at Caltech, University of California, San Francisco, and Washington University. Jeremy Knowles was the principal investigator for the Markey award.

Impact of Markey Funds

The Trust awarded Harvard $1.6 million in 1994. Half of the award ($800,000) was obligated to the Department for two purposes. The first was to help launch a Center for Imaging in Molecular and Cellular Biology, particularly through support for the purchase of a confocal microscope and related hardware. The Center offers access to the confocal microscope and an array of accessory hardware for high quality imaging and computer workstations for image analysis, modeling, and prepublication work. In 1998, the Department decided to use Markey funding to upgrade the Center's computer and printing capabilities. Finally, part of the grant was also used as a partial funding to purchase a luminescence deconvolution microscope to be housed in the Center for Imaging. This powerful instrument operates using faint signals or live samples and provides three dimensional enhanced images. Through the Markey Faculty Exploratory Research Program, 15 awards of $32 thousand each were made between 1995 and 1997. These awards supported exploratory research and involved collaboration across disciplines.

The second half of the award was used to support the animal facility of the Faculty of Arts and Sciences, which was critical to the research in vertebrate development conducted by Andrew McMahon and Elizabeth Robertson. Their research required significant numbers of mice.

OREGON HEALTH SCIENCES UNIVERSITY VOLLUM INSTITUTE FOR ADVANCED BIOMEDICAL RESEARCH MAY 2002

History and Background of Markey Funding

The Vollum Institute of the Oregon Health Sciences University was made possible by a gift of $23 million from Mr. and Mrs. Howard Vollum. In addition, a $20 million grant from the federal government was an important component of the basic funding for the Institute.

The Institute, a freestanding structure dedicated in 1986, is classified as a special research unit of Oregon Health Sciences University. It is located in the center of the medical campus and is connected to two other research buildings. The building was designed to accommodate 24 scientists. Its director reports to the president of the University, and although staff hold faculty appointments in the various academic departments, they have no formal teaching responsibilities except in respect to graduate students working in the Institute.

The Institute's work really began in 1990, when Dr. Richard Goodman became the director. The previous director had died and the Institute was disorganized and under-funded. Although the $23 million gift was intended for the Vollum Institute, there appears to be some confusion as to who controls the money. Dr. Goodman is concerned that Vollum is not wholly supported or respected by the University. There is some tension between the University leadership and the Institute director.

The request to the Markey Trust from the Institute's director was for the support of fundamental genetic, cellular and molecular studies of the basis of drug addiction. This proposal was based upon the work of Dr. Susan Amara on dopamine. Eventually, Vollum developed a transgenic mouse facility. The original request was for $2.1 million and they received $1.3 million.

Using scientists with expertise in behavioral psychology, electrophysiology, genetics, pharmacology, and molecular biology, Dr. Goodman developed four core projects: genetic models; gene targeting; neuronal imaging; and molecular pharmacology. The Markey award was used to develop technology and methodology for transgenic animals.

Impact of Markey Funds

In 1994 the Vollum endowment was about $20 million. This generated about $1.7 million in income of which Vollum received about half. With an operating budget of about $3 or $4 million, most of which went to salaries; there was little or no discretionary funding available. Consequently, the Markey award of $1.3 million had a huge impact at the time it was awarded. The award allowed the Institute to offer start-up packages for faculty, upgrade existing equipment, and provide bridge money for faculty.

Dr. Goodman stated many times that a small grant (in this case $1.3 million) can have a huge impact on small institutions that are doing good research. In the case of Vollum, Markey funds provided the initial recruitment of new faculty with relatively small start-up packages of about $250 thousand. However, in exchange for the small start-up package, Dr. Goodman guaranteed that each of the new faculty would be awarded

their first RO1 NIH grant. So far, 100% of these faculty have had NIH grants awarded on the first try. This success has been accomplished through a process of cooperation with and mentoring by senior faculty at the Vollum Institute. This mentoring of junior faculty is one example of the collegiality in evidence at the Vollum Institute.

SALK INSTITUTE FOR BIOLOGICAL STUDIES PROGRAM IN STRUCTURAL BIOLOGY AUGUST 2002

History and Background of Markey Funding

The Salk Institute requested to develop their structural biology program. Of the total request, the majority of funding was to be used to renovate the space designated for the program's use, and the balance was to cover the cost of x-ray and computational equipment. The original proposal also included additional funds for the neurosciences program.

Markey awarded $2.1 million, with the understanding that high priority would be given to awarding a supplemental grant of $1.5 to $2.0 million for the neuroscience program. An additional grant of $500,000 was made in September 1996. Thomas Pollard was the principal investigator of the award.

Impact of Markey Funds

The $2.1 million award was used to establish an x-ray crystallography laboratory and provide support and set-up costs for two faculty members (Joel Noel and Senyon Choe). $1.1 million was used for space renovation, $450,000 for start-up equipment, and $500,000 for program costs. The additional $500,000 award was used for shared instrumentation. This grant also provided significant leverage for obtaining funding from other sources to recruit additional faculty and their start-up costs. The timing of the initial grant was very important to Salk because without the promise of the new laboratory, Dr. Choe could not be recruited. He is undertaking one of the great outstanding challenges in structural biology, the determination of the atomic structure of an ion channel.

Joel Noel is working on the structure of the tryosine phosphates. The packing of molecules in crystal structure provides important insights into the regulation of enzyme activity.

The three labs have a total of 2 staff scientists, 10 postdocs, 12 graduate students, and 4 research assistants. During the past seven years a number of students and postdoctoral fellows have finished their training and moved on to faculty positions at top institutions including UCSF,

University of Texas Southwestern Medical Center, and CNRS Genoble. Research topics include biophysical and structural studies of ion channels, membrane receptors, enzymes that synthesize natural products, cell cycle protein, actin binding proteins, and molecular motors. This work is being published in the peer-reviewed journal. Thanks to the Markey Trust the labs are very well equipped for state-of-the-art biophysical and cellular studies.

The Salk staff stressed the importance of Markey funding as support from federal agencies was not available to purchase expensive equipment and to renovate space in which to locate it. Without the Markey funding, the director declared, Salk would not have been able to establish its structural biology program.

UNIVERSITY OF ALABAMA AT BIRMINGHAM PROGRAM IN NEUROBIOLOGY APRIL 2002

History and Background of Markey Funding

In 1986, the University of Alabama in Birmingham requested funding for the development of an interdisciplinary research program in neurobiology, involving the Department of Physiology and Biophysics. The program was developed using alternative funding and, in 1989, the University sought five years of funding for two new faculty positions in neurobiology, electronic engineering, a computer programmer, a tissue culture coordinator, five postdoctoral fellows, and an administrative secretary. About 10 percent of funds were requested for renovation and a lesser amount for equipment costs. The program director is Michael Friedlander. In 1992, the University of Alabama at Birmingham received a 5-year award for $1.5 million.

Impact of Markey Funds

Dr. Friedlander believed that the most important impact of the Markey funding was the credibility given to the department. With a major grant from Civitan International, the University is one of the leading institutions in mental retardation and developmental disorders. The center was able to recruit five young cellular/molecular neurobiology faculty, who brought technological approaches not previously represented at the center. Three of these faculty were initially completely supported through Markey funds and two received partial support from Markey funding. The Markey funds also provided laboratories for faculty who have trained 15 graduate students and 15 postdoctoral fellows. In 1996,

partially as a result of the Markey award, the department evolved into a new Department of Neurobiology.

All of the faculty supported by Markey funds have received additional extramural support. The three faculty completely supported by Markey funding have collectively received a total of 5 awards for over $2 million. The faculty partially supported have collectively received 3 awards for over $1.5 million. Finally the entire group was awarded three awards for over $3.5 million. Consequently, over $7 million of additional extramural support has been made possible by the support of the Markey Trust.

Although difficult to recruit postdoctoral students to the University, the Neurobiology Research Center (and later the Department of Neurobiology) has proven to be an exception with many outstanding scientific achievements. With the support of the Markey funds, researchers at the center identified new intracellular receptors for inositide polyphosphate for the regulation of intraneuronal calcium; identified a new synapse specific protein molecule that is transiently expressed in certain developing dendritic spines in neurons; identified the mechanisms of control of intracellular calcium and pH in modified glial cells in brain tumors; and demonstrated the role of the brain's production of the gas, nitric oxide, in the modulation of release of various chemical transmitters. Additional support and new equipment was procured for joint collaborative efforts for an electrochemical nitric oxide measuring system for investigators to pursue "risky" and novel experiments that might not otherwise be possible if only conventional research grant funds were available.

UNIVERSITY OF CALIFORNIA, DAVIS CENTER FOR COMPARATIVE MEDICINE AUGUST 2002

History and Background of Markey Funding

One of the unique features of University of California, Davis is the active collaboration between the faculties of the Schools of Medicine and Veterinary Medicine and the California Regional Primate Research Center. One significant contribution resulting from this cooperative effort has been the development of experimental models of animal and human disease. T.L. Hullar, chancellor, the University of California, Davis, contacted the Markey Trust in 1989 to discuss the possibility of developing a Center for Chronic Viral Disease Research. The Center was to emphasize the interdisciplinary aspects of the schools of Medicine and Veterinary Medicine and the Regional Primate Center. The request was in the amount of

$4.5 million to enable investigators to study the action of antiviral drugs, biologic response modifiers, and gene transfer therapy.

In July 1993, Markey received a formal request for a grant, with further delineation of the investigative plan for the reconsidered amount of $2.35 million. One half of these funds were to be used for recruitment and salary costs for new scientists, postdoctoral trainees, and start-up costs.

The two schools (medicine and veterinary) were successful in obtaining funding for a new research building to house the program and a core group of faculty. Markey funds would be used to add three new scientists. Ultimately, the Markey Trust awarded a grant in the amount of $1.6 million.

Impact of Markey Funds

The University of California, Davis, Center for Comparative Medicine is a cooperative, interdisciplinary research center co-sponsored by the Schools of Medicine and Veterinary Medicine. The Center has three major, inter-related missions:

- Research—the research mission is to investigate host-agent interactions and develop intervention strategies for persistent infectious diseases common to humans and animals. Center faculty possess a range of complementary and interdisciplinary expertise that is leading to novel approaches for prevention and therapy of persistent infectious diseases.
- Integrative Biology—the faculty provide expertise beyond infectious disease models, including laboratory animal sciences and model development for the entire scientific community on campus. The University of California, Davis, Mouse Biology Program is administratively centered in the Center.
- Training—Interdisciplinary research programs provide a rich academic environment for scientific training. This environment is intended to attract and train high quality candidates to the disciplines of comparative medical research, infectious disease research, and laboratory animal sciences.

Of the $1,600,000 funds awarded by Markey, approximately $730,000 was used for discretionary funding for the Director (administrative support, technical support, recruitment of faculty, start-up expenses, etc.). Faculty support, such as up-front salaries, technical support, and equipment and supplies for bridging new faculty, totaled about $751,000. The overhead allotment was $118,520.

The Markey funds played a major role in developing the new Center.

The award became the base for leveraging other programmatic funding, and upon which the faculty associated with the Center attracts world-class research talent.

UNIVERSITY OF CALIFORNIA, SANTA CRUZ CENTER FOR THE MOLECULAR BIOLOGY OF RNA SEPTEMBER 2002

History and Background of Markey Funding

In 1988 University of California, Santa Cruz, requested funding to establish a Center for the Molecular Biology of RNA. Funds were to be used to recruit an additional structural biologist and an x-ray crystallographer interested in RNA structure. Additionally, funds were requested for equipment to support the crystallographer, salaries for postdoctoral fellows, several technicians, a computer programmer, a secretary, and for a major symposium on RNA structure and function.

Impact of Markey Funds

The Center for Molecular Biology of RNA, which received $2.5 million from the Markey Trust, was established in 1992 and has developed into a thriving research community with an international reputation for RNA research. The Center has grown from five to eight faculty, from the Departments of Biology, Chemistry & Biochemistry, and Computer Sciences. In addition to funding from individual grants to Center faculty, the Center itself obtained funding from the W.M. Keck Foundation and from the Agouron Institute.

Among the Center's accomplishments are hosting the first two international meetings on RNA Structure (1987 and 2000), which were widely acclaimed (reviews of the first meeting were published in *Nature* and *Cell*).

The Center attracted eight faculty, spanning the areas of RNA structure and function, including X-ray crystallography, biochemistry, genetics, cell biology, computational biology, and genomics. One member has been elected to the National Academy of Sciences and another has been appointed as an HHMI investigator.

In addition to the new faculty, 43 postdocs were brought into the program and many are university faculty at such institutions as Massachusetts Institute of Technology; Harvard Medical School; Johns Hopkins; University of California, San Diego; Iowa State; and the University of Illinois.

Forty-seven graduate students were brought into the program. Most

have gone on to do postdoctoral research at prestigious academic institutions, while others have taken positions in the biotechnology industry.

UNIVERSITY OF CALIFORNIA, SAN DIEGO CHARACTERIZATION OF MACROMOLECULES REGULATING GROWTH AND ONCOGENESIS SEPTEMBER 2000

History and Background of Markey Funding

In 1988, the University of California, San Diego requested funding to support a program involving biochemists, molecular biologists, crystallographers, and experts in site-directed mutagenesis and sophisticated computer graphic modeling to enhance understanding of cell growth and differentiation. The program was to focus on four regulatory proteins, and then broaden to other regulatory molecules. Of the funds requested, $550,000 was to be used to cover half the cost of completing laboratory space in a new building. Other expenditures proposed were: core equipment for the labs, salary support for faculty, pre-and-post doctoral stipends, technical staff, and laboratory supplies. Gordon Gill was the principal investigator.

Impact of Markey Funds

The University of California, San Diego, received $3.2 million from the Trust in 1988 through 1993. In 1994, the University received $500,000 in supplemental funds. The program was directed towards merging molecular and structural biology in an interactive program. Although this theme is widely accepted now, it was quite novel in the 1980s. The program consisted of eight investigators. The awarding of the Markey grant allowed the completion of shell space in the new Molecular and Cellular Medicine West Building into the Laboratory of Regulatory Biochemistry. Shared equipment relevant to the goals of the project was purchased and the Markey program became a paradigm of cooperation between the campus and the School of Medicine. It created interactions that have been strengthened and are ongoing. Although the program is no longer active, it has evolved and there are several sources of follow-up funding. One faculty member obtained NSF funding for the Center for Computational Crystallography at the San Diego Supercomputer Center. He and two other faculty members have garnered the cooperation of other institutions in the San Diego area including Scripps Research Institute, to create a center of biological computation at the San Diego Supercomputer Center. This is now the principal NSF-funded supercomputer center directed

towards biological sciences, the home of the previous Brookhaven-sited protein data banks, and a pioneer in bioinformatics, including those relevant to structural biology and genomics. Much of this research arose out of the initial funding from the Markey Trust. It also evolved from the scientific success of the program. Each of the active investigators have well-funded, active research laboratories that continue the themes of the program. Training grants and a Burroughs Wellcome-funded program have been built on the foundation provided by the Markey program.

Personal Observations

Gordon Gill stated that his overall impression was that the Markey Trust is a unique experiment in philanthropy.

> By being limited in time and focused in programmatic giving, it had a profound catalytic effect on American biomedical sciences related to problems of human disease. It will, of course, be more difficult to measure this than programs which have spent less of their resources and have used their resources to sustain themselves over many, many years. The Markey Trust was always lean and mean with minimal administrative staff and maximal flexibility. They had unique leadership in the persons of Dr. Robert Glaser and Mr. Louis Hector whose wisdom I have not seen equaled before or after. It is my impression that a great many charitable foundations spend a large proportion of their resources on program officers and staff; they inevitably become bureaucratized and they dole out funds in small amounts which have minimal impact. The Markey Trust used an opposite philosophy, giving relatively large sums that truly made a difference in a concentrated way with minimal bureaucratic micromanaging. This is, I think, a reflection not only of the trustees and of the excellent staff, but of the outstanding and enlightened leadership of Bob Glaser and Louis Hector.

UNIVERSITY OF COLORADO, BOULDER CENTER FOR MAMMALIAN BIOLOGY SEPTEMBER 2001

History and Background of Markey Funding

The University of Colorado, Boulder, requested funding for a new Center for Mammalian Biology within the Department of Molecular, Cellular, and Developmental Biology. The newly formed center would focus on the biology of mammals, including humans, with emphasis on developmental and neurobiology. Leslie Lienwand is the chair of the depart-

ment. The Department maintains active ties with the university's Health Sciences Center in Denver, to which Markey also made a grant for $5.0 million in 1990.

The 3-year Markey award of $1.5 million, made in 1994, was to provide laboratory space and equipment for six investigators, develop a mouse facility, and add a conference facility.

Impact of Markey Funds

The Department of Molecular, Cellular, and Developmental Biology is undergoing a doubling in size of faculty and research space. New construction began in 1995—prior to this no work was being done in mammalian research at Colorado. The Markey funds provided start-up packages, equipment, mouse eggs, etc. for the Center for Mammalian Biology and enabled Dr. Leinwand to hire five new faculty members. The new mouse facility was completed in 1996.

Dr. Leslie Leinwand became the chair of the Center. She was recruited from Albert Einstein College of Medicine, where she was the Director of the Cardiovascular Research Institute and a Professor of Microbiology and Immunology. In addition to Dr. Leinwand, five other faculty were recruited. The department has grown to 27 faculty with plans to recruit an additional 14. The Center has 10 graduate students and 11 postdoctoral fellows.

Recent accomplishments include:

- Development of a genetic mouse model for juvenile diabetes along with one for congenital deafness
- Development of conditional knock-outs of the mouse to study the central nervous systems and its response to injury
- Identification of new transcription factors that appear to function in heart and eye development
- Work on the genetics of antisocial behavior

The Center is running well and is growing. The Center was able to leverage Markey funds with The William Keck Foundation, which provided an additional $1.5 million to set up a transgenic mouse facility. Additionally, all of the faculty members are well funded through NIH, MS, March of Dimes, or Burroughs Wellcome.

UNIVERSITY OF OREGON
CENTER FOR MACROMOLECULAR ASSEMBLIES IN CELL BIOLOGY
JUNE 2001

Background of Markey Funding

The Markey award was used to establish a new Center for Macromolecular Assemblies in Cell Biology, which builds on three fields of research: three-dimensional macromolecular structures, utilizing crystallographic techniques; macromolecular thermodynamics; and macromolecular interactions. This new Center permits an integrated attack on a central, but poorly understood problem, the intra and intermolecular interactions between proteins, nucleic acids, lipids, and carbohydrates. Such understanding is essential to the rational design of drugs, the definition of the genetic basis of many disease states, including metabolic disorders as well as malignancy, and the ultimate preparation of effective biological agents in useful quantities.

At the time of the grant, the administrative responsibility of the Center was carried out by Dr. John Moseley, Vice President for Research, with an advisory board consisting of representatives from the biology, physics, and chemistry faculty. Brian Matthews was the Center director. The Markey $3.3 million award was a five-year award that began in 1988.

The grant allowed the Center to upgrade existing research programs through the acquisition of an x-ray area detector facility, computing, graphics and NMR equipment, spectrophotometer, calorimeter, CD spectrophotometer, and freeze-quench apparatus. The Center also recruited three faculty members during the course of the funding and has recruited five more since funding has ended. According to Dr. Matthews, the Markey award was spent as follows:

Major Equipment	40%
Recruiting New Faculty	36%
Core Facilities	12%
Individual Labs	12%

The Impact of Markey Funding

The Center for Macromolecular Biology is now firmly established at the University of Oregon. Of the initial faculty recruited for the Center, two have since left the institution. After their departure, the Center experienced a bit of a decline during the search for new faculty. However, during the last year, five new faculty members have been recruited. Addi-

tionally, NIH funding has increased to the point of sustainability for the Center.

The impact of the Markey award was also monitored in terms of the number of graduate students and postdocs who were funded. Throughout the Institute of Molecular biology, 40 graduate students and 40 postdocs directly benefited from the award; an additional 80 graduate students and 80 postdocs indirectly benefited from the Markey award.

Because of turnover in Center faculty, Markey funds were put on hold while the search for a replacement occurred. Consequently the last of the Markey funds were spent in 1996. The flexibility in disbursement of funds was crucial for the Center to be able to recruit the best replacement. In fact, this process took more than two years.

By its very nature, the Center is interdisciplinary and students within the program are free to work in any of the labs (although their degrees are departmental, their research experiences cross the disciplines of chemistry, physics, and biology).

Even though the University of Oregon is small (one of the smallest of the major public research universities), it enjoys an excellent reputation. Faculty members attribute the communal spirit and the continuity of good leadership to the success of the Center. Two of the Center faculty are HHMI investigators and one is a member of the National Academy of Sciences. Because the Markey award came at a time when NIH funding was at its lowest point, the Center Director emphasized that the award was one of the most important factors in allowing the Center to maintain, enhance, and expand its research program.

UNIVERSITY OF ROCHESTER
THE NEUROSCIENCES INSTITUTE
OCTOBER 2001

History and Background of Markey Funding

The Lucille P. Markey Charitable Trust awarded a 6-year grant of $4 million to the University of Rochester to help develop the Neurosciences Institute. In 1997, the strategic plan at the Institute decided to commit extensive resources to three major research initiatives in faculty hiring and strengthening of facilities: (1) Aging and development, (2) Cancer biology, and (3) Immunology and vaccine development. The Institute director was David Felten.

The grant was used, in part, to recruit five new faculty, who all now have strong extramural funding, to support six investigators in pilot project research, and to support more senior investigators who wished to

change the fundamental direction of their research and needed support to come up to speed in a new area before submitting an R01 request.

Impact of Markey Funds

The Neurosciences Institute has established itself as one of the core strengths for the University's efforts for building research on aging. Because of this strength, the University's medical center added core support in the form of a transgenic facility, an imaging facility, and other key faculty to strengthen collaborations (particularly in translational research). The Institute has established focuses of collaborative research for additional opportunities to further attract NIH center or program project support, pharmaceutical support, foundation support, or venture capital support. They are also putting together a business plan for a new biotech company.

The Institute has developed a continuing research relationship with the National Institute on Aging in areas such as Alzheimer's diseases, Parkinson's disease gene therapy, neural-immune signaling and plasticity in aging, and neurotherapeutics. The four senior investigators hired with Markey funds—David Felton, Paul Coeman, Suzanne Haber, and Ira Shoulson—continue active research agendas. In addition, Markey funds were used to partially support an additional five investigators. These senior investigators continue to support the research efforts of many junior investigators and use a majority of their resources supporting projects that provide faculty development for these junior investigators to expand their research capacities and expand collaborative ties.

Finally, the Institute has supported six pilot research programs utilizing Markey funds. This support for younger investigators is based on the likelihood that it will contribute to the successful application of extramural support. Moreover, pilot support was provided to senior investigators who wished to fundamentally change the direction of their research and needed pilot support to come up to speed in a new area before submitting an RO1 proposal.

The faculty are encouraged to think in broader terms and programmatic efforts, to plan research activities as teams of collaborating investigators, and to explore non-traditional sources of support as well as standard NIH sources. The Chair has vigorously supported these efforts at the departmental level, and has recruited strong support for these interactions at the level of the Dean, the Vice President, Vice Provost for Health Affairs, and the President.

UNIVERSITY OF UTAH
CENTER FOR PROTEIN BIOPHYSICS
SEPTEMBER 2001

History and Background of Markey Funding

Martin Rechsteiner, of the department of biochemistry, requested funds in 1989 to establish a Center for Protein Biophysics. The proposed center would utilize the techniques of x-ray crystallography, nuclear magnetic resonance, and optical spectroscopy and be housed in the newly expanded basic science facilities of the medical school. Funds were to be used for two faculty members, graduate students, postdocs, major equipment, and remodeling of laboratory space.

Impact of Markey Funds

The Center received $2.5 million from the Markey Trust. Unfortunately, the Center is merely a shell at this time. The grant was significant in the history of the university because prior to Markey funding there was no structural biology. Equally important, the Markey funds were used to provide the salaries for support technicians, support that is generally unavailable from other extramural sources. The award provided 5-year support for both an x-ray technician and a peptide synthesis technician. In addition, the award provided 5-year support for graduate students and postdocs. Finally, the award was used for major equipment purchases and supplies.

The grant allowed recruitment of three structural biologists, two of whom are still on faculty. In addition, Markey funds supported the research of three established scientists. Finally, the Markey grant supported the research of 17 postdoctoral fellows and three graduate students. The university could not commit to the long-term support of the Center, but did pick up two positions for technicians (mid-level) to run the crystallography equipment.

Beginning in the mid 1980s, the level of extramural funding available from federal sources declined dramatically. Second tier schools were especially taxed by this decrease in federal funding. The Utah program in biochemistry was in desperate need of funding at the time of the Markey award and it enabled the program not only to retain talented faculty, but also to recruit new faculty.

UNIVERSITY OF VERMONT
THE MARKEY CENTER FOR MOLECULAR GENETICS
OCTOBER 2001

History and Background of Markey Funding

The University of Vermont, a small public university with a medical school, has created a joint department of microbiology to serve as a research center that serves both medicine and agriculture. Dr. Susan Wallace was recruited to direct the new center. In 1990, she submitted a request to the Lucille P. Markey Charitable Trust for a grant to study gene structure, function, and regulation. With considerable collaboration across disciplinary lines involving the Departments of Zoology, Botany, Biochemistry, Physiology/Biophysics, Cell Biology, and Pharmacology, the new joint program in microbiology explores fundamental processes by using plant cells.

In 1991, the Department of Microbiology and Molecular Genetics was awarded 5-year support for $1.8 million. In 1996, the Department received a supplementary award of $500,000. With the Markey funds, Dr. Wallace has established a core group of molecular biologists and microbiologists who provide a basic science hub for applied medical and agricultural research. The grant provided the start-up costs, equipment, and technical assistance for these faculty. She also purchased sequencers, scanners, and other analytic instrumentation and computers. Approximately one half of the $1.8 million went to faculty development, one-third to the core research facility and equipment, and the balance for operational support.

Impact of Markey Funds

The Markey award was used to develop a Department of Microbiology and Molecular Biology headed by the newly recruited Susan Wallace. When she arrived, faculty, staff, and students totaled about 20. The department now has a faculty of 29 professionals, between 30 and 35 graduate students enrolling each year, and between 40 and 50 undergraduate majors. The program is still growing. In fact, it now brings in annual extramural funding of about $5 million. For the decade of the 1990s, extramural funding exceeded $42 million.

Although the Markey funds were used in combination with other grants to develop the Center and its facilities, the impact of the Markey award appears to have been substantial. Not only is the Center name "The Markey Center for Molecular Genetics," but Dr. Wallace is quite enthusiastic about the equipment purchased and faculty recruited with

this grant. It is apparent that the University of Vermont nurtures the life sciences and invests in new and emerging technologies. Dr. Wallace believes that the lesson to be learned is that high quality teaching and research programs require investment and that the return on such investment is well worth the initial commitment. The Center is a lively research enterprise with enthusiasm and collegiality obvious even to untrained observers.

Appendix D

Outcome Measures for Research Program Grant Awardees

Grant Recipient	Award Number	Award Amount	Initial Year	Last Year	Faculty Full Support
Large - Infrastructure Development					
Stanford University	86-07	$12,613,550	1986	1997	9
California Institute of Technology[2]	86-08	$13,000,000	1986	1991	
The Whitehead Institute for Biomedical Research[1]	88-11	$7,650,000	1988	1993	
Washington University in St. Louis	88-12	$12,100,000	1988	1994	10
Harvard Medical School	88-13	$11,000,000	1988	1993	
University of California, Los Angeles[1]	88-15	$4,350,000	1998	1997	5
Yale University	88-16	$12,100,000	1988	1997	
University of Miami	88-22	$6,270,000	1988	1999	5
University of California, San Diego[1,7]	88-42	$4,320,000	1998	1998	
Case Western Reserve University	88-44	$5,500,000	1988	1997	
Columbia University	88-59	$6,500,000	1988	1996	
Purdue University[1]	88-60	$6,990,000	1998	1997	
Johns Hopkins University	89-09	$7,150,000	1998	1996	
Northwestern University[1,8]	89-28	$5,890,000	1989	1993	
Duke University[2]	90-08	$8,000,000	1990	1994	
University of Virginia	90-10	$6,100,000	1990	1996	6
University of Colorado Health Sciences Center	91-03	$5,000,000	1991	1996	
Cold Spring Harbor Laboratory[1]	91-05	$4,500,000	1991	1996	4
Fox Chase Cancer Center	91-26	$4,000,000	1991	1996	
Florida State University[1]	91-27	$4,500,000	1991	2000	4
Cornell University Medical College	92-08	$4,000,000	1992	1997	1
Total Large Infrastructue Development		$151,533,550			44
Large - Investigator Initiated					
University of Chicago[2]	86-10	$9,219,223	1986	1992	
University of Pennsylvania[2,6]	88-21	$4,720,402	1988	1996	
The University of Michigan	88-46	$8,250,000	1989	1997	
University of California, Berkeley[1]	89-08	$8,500,000	1989	1994	
University of Washington	90-12	$7,500,000	1990	1997	
Vanderbilt University[1]	91-16	$5,500,000	1991	1996	
University of Rochester School of Medicine/Dentistry	91-24	$4,000,000	1991	1997	5
The Scripps Research Institute	92-10	$5,000,000	1992	1996	4
Princeton University	92-25	$4,500,000	1992	1997	3
Total, Large Investigator Initiated		$57,189,625			12
Small - Infrastructure Development					
University of Texas - Southwestern Medical Center[6]	86-02	$2,280,000	1986	1992	
Carnegie-Mellon University	86-03	$1,925,000	1986	1992	2
University of Oregon	88-18	$3,300,000	1988	1995	
Wisconsin University - Madison	88-19	$990,000	1988	1992	

Faculty Partial Support	Postdoc Full support	Postdoc Partial Support	Graduate Students	Under-graduates	Tech-nicians	Invest-igators	Equipment	Construction/ Renovation
4			6				$3,330,991	$650,000
45								$4,200,000
8	3						$102,221	$571,500
17							$3,642,000	
24			12				$786,358	$3,500,000
		9	6				$1,033,788	
7	1						$2,350,000	
	8						$1,000,000	$1,382,000
8	4		4				$764,096	
15		6	4		2		$1,455,956	
5	5				4		$404,057	
13		8	17		7		$1,081,000	
6	3		3		2		$3,528,000	$1,125,000
			2	2	1		$241,101	$1,450,000
10	4						$2,493,000	$241,488
	1				6	4	$961,536	
14		4					$543,753	$925,457
1					1		$1,375,000	$2,000,000
		37	4			10		
3			8		1	1	$2,000,000	$800,000
8	2		9	6	10	1	$742,000	$122,000
188	31	64	75	8	34	16	$27,834,857	$16,967,445
19							$1,944,000	$3,480,000
15					4		$609,316	$306,899
11	7		4		2		$790,319	
7							$605,000	$2,000,000
12						5	$725,000	
10		8	4		4		$2,100,000	$600,000
25			20		3		$216,085	$900,000
7		25	5				$2,000,000	
		10	53				$815,000	$1,200,000
106	7	43	86		13	5	$9,804,720	$8,486,899
	3		2			2	$108,233	
2		1			1		$994,280	
3		40	40		4		$893,031	$75,989
		30			1	4	$73,363	

continued

Grant Recipient	Award Number	Award Amount	Initial Year	Last Year	Faculty Full Support
University of Texas - Southwestern Medical Center	88-20	$1,045,000	1988	1994	
Carnegie Institute of Washington[1]	88-43	$2,700,000	1988	1997	8
The Children's Hospital, Boston	88-45	$2,475,000	1988	1993	
Thomas Jefferson University	90-09	$3,500,000	1990	1994	
New York University	91-04	$2,600,000	1991	1997	4
University of Vermont[1]	91-06	$2,300,000	1991	1999	2
Harvard University, School of Public Health[1]	91-49	$3,500,000	1991	1996	3
The Burnham Institute	92-09	$1,500,000	1992	1996	1
University of California, Santa Cruz	92-21	$2,500,000	1992	1999	1
Cincinnati Children's Hospital Medical Center	92-22	$3,500,000	1992	1996	1
Public Health Research Institute	92-23	$2,500,000	1992	1996	2
Massachusetts General Hospital	93-01	$3,000,000	1993	1997	4
The University of Utah	93-03	$2,500,000	1993	1997	
The Salk Institute for Biological Studies[2]	94-13	$2,600,000	1994	1996	2
University of Colorado, Boulder	95-01	$1,500,000	1995	1997	
University of Massachusetts Medical Center	95-03	$1,500,000	1995	1997	2
University of North Carolina at Chapel Hill	95-05	$1,500,000	1995	1997	
University of Texas Medical Branch at Galveston	95-06	$1,000,000	1995	1996	
Harvard University	95-15	$1,600,000	1995	1998	
Children's Memorial Medical Center	95-22	$1,000,000	1995	1997	
Stanford University	95-26	$1,200,000	1995	1997	
University of Texas - Houston Health Sciences Center	95-29	$1,000,000	1995	1997	2
Total, Small Infrastructure Development		$55,015,000			34
Small - Investigator Initiated					
Brandeis University[1,5]	88-41	$3,200,000	1988	1996	6
Neurosciences Institute	88-48	$1,375,000	1988	1995	
Eleanor Roosevelt Institute for Cancer Research[3]	88-61	$1,475,000	1988	1993	
Albert Einstein College of Medicine of Yeshiva University	88-62	$2,310,000	1988	1995	
Temple University	90-11	$2,500,000	1990	1996	
Massachusetts Institute of Technology	91-07	$3,850,000	1991	1999	
Memorial Sloan - Kettering	91-17	$2,700,000	1991	1994	
University of Alabama at Birmingham	91-25	$1,500,000	1991	1995	3
University of Illinois Urbana Champagne	92-20	$3,000,000	1992	1998	4
University of Wisconsin - Madison	92-24	$3,000,000	1992	2003	3
Mount Sinai Medical Center	93-02	$3,000,000	1993	1997	9

Faculty Partial Support	Postdoc Full support	Post-doc Partial Support	Graduate Students	Under-graduates	Tech-nicians	Invest-igators	Equipment	Construction/ Renovation
	3						$135,000	
		6	4		2		$803,853	
4					4		$493,122	
9					2		$626,183	
		9	15	1			$290,000	
		6	4				$529,000	
4	6		6				$192,000	
	2					1	$1,024,815	
7		43	47		2		$1,270,000	
13	9		4		4	2	$100,000	
10							$253,000	
		4	4			3	$566,000	
6		17	3		2		$1,130,000	$200,000
							$959,000	$1,150,000
6							$76,000	$1,070,000
2					2		$667,000	
3			6				$550,000	
4					1		$1,340	
17					1		$317,000	$640,000
2							$600,000	
	3				2		$232,000	
1			3				$250,000	
93	26	156	138	1	28	12	$13,134,220	$3,135,989
3	2		5	2	1		$540,000	$100,000
		12						
3	1		5				$125,000	$150,000
6	2		4		1		$238,815	
6	1					4	$335,193	
12		16	12				$624,000	
7	18		10		1		$843,000	
2	5		2		4		$447,000	
	3		3		3		$521,000	
5	6		3		4	1	$185,000	
			5		3	6	$300,000	

continued

Grant Recipient	Award Number	Award Amount	Initial Year	Last Year	Faculty Full Support
Joslin Diabetes Center	93-04	$3,500,000	1993	1999	
Tufts University	93-05	$2,000,000	1993	1996	
Baylor College of Medicine	94-14	$1,400,000	1994	1999	4
Dartmouth Hitchcock Medical School	94-15	$1,500,000	1994	1997	3
University of Southern California	94-16	$1,800,000	1994	1998	4
Brown University	94-18	$1,300,000	1994	1998	
Worchester Foundation	94-19	$1,000,000	1994	1997	2
Dana Farber Cancer Institute	95-02	$1,500,000	1995	1997	2
University of Miami	95-04	$1,000,000	1995	1998	1
Oregan Health Sciences University	95-10	$1,300,000	1995	1997	
Kennedy Krieger Institute	95-11	$500,000	1995	1997	1
University of California - Davis	95-12	$1,600,000	1995	2002	3
University of Florida	95-13	$1,600,000	1995	2000	5
University of Pittsburgh	95-14	$1,000,000	1995	1997	
University of California - Irvine	95-18	$1,000,000	1995	1999	
Johns Hopkins University	95-19	$1,300,000	1995	1997	2
Georgetown University	95-20	$1,000,000	1995	1997	2
Cornell University	95-21	$1,200,000	1995	1999	
Rice University	95-23	$1,200,000	1995	1997	
Rush Presbyterian St. Lukes Medical Center	95-24	$1,000,000	1995	1998	
Schepens Eye Research Institute	95-25	$1,000,000	1995	1997	1
SUNY - Buffalo	95-27	$1,000,000	1995	1997	3
Texas A&M University	95-28	$1,000,000	1995	1998	2
University of Maryland Biotechnology Institute	95-31	$1,000,000	1995	1997	
University of Kentucky	95-32	$1,900,000	1995	1998	
Total, Small Investigator Initiatied		$61,510,000			60
Total, All Research Program Grants		$325,248,175			150

[1]Includes a $500,000 supplementary award made in FY 1996 in recognition of outstanding progress by Markey-supported investigators addressing important problems in biomedical science.

[2]Includes a $500,000 supplementary award in FY 1997 in recognition of outstanding progress by Markey-supported investigators.

[3]Includes a $100,000 supplement made in FY 1992.

Faculty Partial Support	Postdoc Full support	Post-doc Partial Support	Graduate Students	Under-graduates	Tech-nicians	Invest-igators	Equipment	Construction/ Renovation
11							$507,000	$300,000
6	9		12		3		$150,000	
			15				$78,000	
1					2		$586,000	$50,000
	2		2				$276,000	$200,000
9		17	83				$359,000	
	2		3				$130,000	$36,000
1							$391,000	$630,000
	1					1	$100,000	$170,000
6					3		$700,000	$11,000
	1	1			1		$70,000	
	2		1		1		$101,480	
3							$530,000	
12							$375,000	
7		14			1		$106,000	
					2		$350,000	$117,000
							$250,000	
5		1			3		$410,000	
							$1,200,000	
3			1		1	2	$88,000	
					2		$358,000	
							$2,000	
2	2				1		$150,000	
		6	6				$500,000	
5								$32,000
115	57	67	172	2	37	14	$11,926,488	$1,796,000
502	121	330	471	11	112	47	$62,700,285	$30,386,333

[4]Includes a $370,402 supplement made in FY 1994.

[5]Includes a $500,00 supplement awarded in FY 1990.

[6]Includes a $1,155,000 supplement made in FY 1998 and a $300,000 supplement in FY 1991.

[7]Includes a $300,000 supplement made in FY1994.

[8]Includes a $390,000 supplement made in FY 1998.

Appendix E
Biographies of Members of the Lucille P. Markey Charitable Trust Programs in Biomedical Sciences Committee

Enriqueta Bond, Ph.D., is President of the Burroughs-Wellcome Fund and will provide an important perspective on the committee as a leader in the philanthropic community. She is a former Executive Director of the Institute of Medicine of which she is also a member. Her research interests include genetics, molecular biology, and science policy. She has served on the IOM's Board on Health Sciences Policy and on the Committee to Study Incentives for Resource Sharing in the Biomedical Sciences. She holds a Ph.D. in biology.

William T. Butler, M.D., is Chancellor of Baylor College of Medicine where he is also Professor of Internal Medicine and Professor of Microbiology and Immunology. He served as the College's President and Chief Executive Officer from 1979 to 1996. Before joining the Baylor faculty in 1966, Dr. Butler served as the chief clinical associate in the Laboratory of Clinical Medicine at the National Institute of Allergy and Infectious Diseases at the NIH. He is on the boards of Browing-Ferris Industries, C. R. Bard, Inc., and Lyondell Petrochemical, where he is Chairman of the Board. Dr. Butler has done extensive research on the effects of corticosteroids and other drugs on the immune system and on the mechanism of rejection of organ transplants. He has authored numerous publications in the fields of immunology, infectious disease, and medical administration. Dr. Butler holds an M.D. (1958) from Western Reserve University and a B.A. (1954) from Oberlin College. Dr. Butler is a member of the Institute of Medicine.

Elaine K. Gallin, Ph.D., is the Program Director for Medical Research at The Doris Duke Charitable Foundation. Dr. Gallin's research involves the characterization of ion transport mechanisms in macrophages, leukocyte-endothelial cell interactions, and the effects of ionizing radiation of leukocyte function and vascular integrity. She received her B.S. from Cornell University, her M.S. from Hunter College, and her Ph.D. from City University, New York. She has held positions at the Uniformed Services University and Georgetown University Medical School, was a Congressional Fellow on the Public Policy Committee, and is a member of the Physiology Study Section at NIH.

Georgine Pion, Ph.D., is Research Associate Professor of Psychology and Human Development and Senior Fellow with the Vanderbilt Institute for Public Policy Studies at Vanderbilt University. She received her Ph.D. in social-environmental psychology from Claremont Graduate School in 1980 and did postdoctoral research training in the Division of Methodology and Evaluation Research at Northwestern University. She has served on committees involved in the evaluation of research and health professional training programs and gender differences in the career development of scientists for the National Research Council, the National Science Foundation, and the National Institute of Mental Health. Currently, she is involved in directing an evaluation of the neuroscience peer review process at NIH, evaluating the outcomes of new instructional strategies in biomedical engineering education, and assessing the outcomes of postdoctoral research training programs sponsored by the Burroughs Wellcome Fund and other foundations. She is an Associate of the National Academy of Sciences

Mary-Lou Pardue, Ph.D., is the Boris Magasanik Professor of Biology at the Massachusetts Institute of Technology and a member of the National Academy of Sciences. As a geneticist and cell biologist, she has studied eukaryotic chromosomes with emphasis on sequences involved in the structure and function of chromosomes as organelles. She served as president of both the Genetics Society of America and the American Society for Cell Biology and was Chair of the Institute of Medicine Committee on Understanding the Biology of Sex and Gender Difference. She received a Ph.D. from Yale University in 1970.

Lloyd Hollingsworth Smith, M.D., is Professor Emeritus of Medicine and a former Associate Dean of the School of Medicine at the University of California, San Francisco. His areas of expertise include biochemistry, endocrinology and metabolism, internal medicine, and medical genetics. His interests and capabilities also include medical center administration,

medical education, training of investigators, and medical research policy. Dr. Smith holds an M.D. (1948) from Harvard Medical School and a B.A. (1944) from Washington & Lee University. Dr. Smith is a past member of the Board of Overseers of Harvard University. He is a member of the Institute of Medicine. He has previously served on the Committee to Study Strategies to Strengthen the Scientific Excellence of the NIH Intramural Research Program.

Lee Sechrest, Ph.D., is Professor of Psychology at the University of Arizona. His primary interest is in development and improvement of methods for research and data analysis, particularly for research in field settings. He is also involved in program evaluation. Substantive areas include health and mental health services, clinical psychology, and personality. Additional areas of expertise include research methodology, measurement, program evaluation, quality assurance in service delivery, and quality of scientific information. He is interested and involved in matters having to do with the development of psychology as a responsible, science-based profession. Before coming to Arizona, he held faculty positions in Pennsylvania State University, Northwestern University, Florida State University, and the University of Michigan. He received his Ph.D. from the Ohio State University. Dr. Sechrest has served on five NRC study committees, including the Panel to Study Gender Differences in the Career Outcomes of Science and Engineering Ph.D.s.

Virginia Weldon, M.D., is retired Senior Vice President for Public Policy with the Monsanto Company. In this position she identifies public policy issues affecting the company and plans for and orchestrates Monsanto's approach to these issues. Prior to joining Monsanto in 1989, Dr. Weldon was Professor of Pediatrics and Associate Vice Chancellor for Medical Affairs at the Washington University School of Medicine. Dr. Weldon is on the Board of Directors of G.D. Searle & Company, The NutraSweet Company, and the Monsanto Fund. She holds an M.D. (1962) from the University of Buffalo and an A.B. (1957) from Smith College. She is a member of the Institute of Medicine and serves on the Report Review Committee of the National Research Council and Institute of Medicine.

James Wyngaarden, M.D., is Professor Emeritus at Duke University. At Duke, Dr. Wyngaarden served as Associate Vice Chancellor for Health Affairs, Chief of Staff and Physician-in-Chief at Duke University Hospital, and Frederic M. Hanes Professor and Chairman, Department of Medicine at the Duke University School of Medicine. From 1982 to 1989, Dr. Wyngaarden was Director, U.S. National Institutes of Health, and from 1989 to 1990 was Associate Director for Life Sciences, White House Office

of Science and Technology Policy. Dr. Wyngaarden holds an M.D. (1948) from the University of Michigan Medical School. He is a member of the National Academy of Sciences and the Institute of Medicine and is a former Foreign Secretary of NAS and IOM.