A REVIEW OF THE INTRAMURAL PROGRAM OF THE NATIONAL CANCER INSTITUTE

A Report by the Ad Hoc Working Group of the National Cancer Advisory Board

June 9, 1995

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Barbara K. Rimer, Dr.P.H.
Chair, National Cancer Advisory Board
Professor, Community and Family Medicine
Director, Cancer Prevention, Detection
and Control Research
Duke University Medical Center
Durham, North Carolina 27705

Dear Dr. Rimer:

On behalf of the Ad Hoc Working Group of the National Cancer Advisory Board, we are pleased to submit its report on the intramural research program of the National Cancer Institute. After seven months of fact-finding and deliberation, the Working Group is fully convinced that the intramural research program of the National Cancer Institute serves a vital national purpose. But many aspects of its operation could be improved. In this report, the Working Group identifies and analyzes some of the problems that limit the effectiveness of the intramural research program, and provides a series of recommendations by which these problems might be addressed. We offer this report for review and action by the National Cancer Advisory Board.

We and our colleagues on the Working Group are grateful for your unfailing support and encouragement throughout the course of our deliberations. In addition, we wish to acknowledge the invaluable assistance given to us by Drs. Marvin Kalt and Vincent Oliverio of the National Cancer Institute staff, and by our private consultant, Dr. Kathi Hanna. We were also fortunate to have had the opportunity to hear from nearly 50 members of the Institute staff through testimony delivered during the course of our discussions. Over 100 National Cancer Institute staff members communicated their thoughts to us through the mail.

We have all been privileged to serve the National Cancer Advisory Board and the National Cancer Institute in this manner, and we stand ready to answer any questions that may arise. We hope that our report will be of value to you, the National Cancer Advisory Board, and the incoming Director of the National Cancer Institute, in planning and setting priorities for the intramural research program.

Sincerely,

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National Cancer Advisory Board Ad Hoc Working Group
on the Intramural Research Program

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Executive Summary

In the past few years, concerns expressed by the Congress and other bodies regarding the quality, appropriateness, size, and cost of the intramural research program of the National Institutes of Health (NIH) have led to a series of programmatic and administrative reviews. Most recently, in April 1994, an External Advisory Committee of the Advisory Committee to the NIH Director submitted a review of the intramural research program and its relationship to the extramural research program. One of the External Advisory Committee's recommendations was that each institute undergo a review of its intramural programs, taking into consideration the unique aspects of its mission and organization.

The National Cancer Institute (NCI) was the first institute to undergo the recommended review. A Working Group of extramural scientists was appointed by the Directors of NIH and NCI to determine the extent to which the recommendations of the External Advisory Committee applied to NCI, to assess NCI's implementation of the External Advisory Committee, and to identify and evaluate issues that might be distinctive for the NCI intramural program. The Working Group was advisory to the National Cancer Advisory Board, and its formation was a joint activity of NCI and NIH.

The broad issues considered by the Working Group were quality control; morale of the scientific work force; nurturing of talent, especially that of younger scientists; the intellectual suitability and administrative efficiency of the organization within the intramural research program; and the effectiveness of strategic planning. More specific issues placed before the Working Group for consideration included:

- the size of the NCI intramural research program relative to its mission; the status of clinical research within the intramural program in terms of suitability, quality, cost-effectiveness, and prospects;
- the appropriateness, quality, and future of drug development activities;
- the status of AIDS research within the IRP, in terms of suitability, levels of funding, and effects on other programs in the intramural research program; and
- the quality and necessity of NCI programs at the Frederick Cancer Research and Development Center.

Recent attrition at the highest ranks of NCI management provides an opportunity to reconsider the current structure of NCI. In addition, the entire NIH is under a mandate to streamline its operations and reduce its full-time-equivalent employees. The Working Group was asked to consider these events as an opportunity to reconfigure various components of the NCI intramural research program, and to provide advice on where resources are being used wisely and unwisely.

The Working Group met seven times over an eight-month period between October 1994 and May 1995. It requested and received detailed data on budgets, planning, quality review, personnel and administrative practices, operations of the Frederick Cancer Research and Development Center, AIDS programs, training, drug development activities, and the status of NCI Clinical Center programs; heard testimony from a variety of intramural personnel, including scientists, the NCI Director and Acting Director, division directors, Clinical Center staff, and administrative staff; solicited comments in writing from the entire professional staff of the NCI intramural research program; and made site visits to the clinical and drug development programs at the Frederick Cancer Research and Development Center.

More than 60 recommendations are offered to improve the quality and efficiency of NCI's intramural research program. They appear in their entirety in the full report. The spirit and intent of these recommendations are summarized below.

Strategic Planning: NCI's procedures for strategic planning could be improved. Efforts should be made to formally solicit input from leading clinical and laboratory investigators within the intramural and extramural research programs to provide regular and systematic advice to the Director.

There seems to be a disproportionate investment in the intramural research program, and at least some of its individual programs appear to be poorly coordinated. NCI should reconsider its current budget to determine whether the 25 percent devoted to the intramural research program is appropriate.

Organization: The current organizational structure of the intramural research program is unnecessarily complex and redundant, and potentially disadvantageous to the extramural programs. In addition, burdensome administrative requirements appear to deter intramural scientists from their missions in basic and clinical research and technology transfer. There should be full separation of the intramural and extramural programs, consolidation of programs within the IRP, and measures taken to reduce administrative redundancies and inefficiencies.

Quality Assurance: The procedures used to evaluate the intramural research program and its scientists should be improved to encourage more objectivity and expertise on the part of reviewers, to reward excellence and initiative, and to improve the diversity and morale of intramural investigators. Oversight of budgets for investigators, laboratories, and branches should be strengthened.

Sustaining and Renewing Talent: The intramural research program has failed to recruit new talent vigorously, its policies for promotion of scientists have lacked rigor, and it has allowed the distribution of resources to become authoritarian. In order to fulfill its mission, the intramural research program must consistently seek to renew its intellectual capital. Its scientists should be provided the opportunity to work in a setting that encourages independence and rewards both creativity and excellence. Specific actions should be taken to sustain and renew talent in an open, equitable, and consistent manner. Leadership should be held accountable for failure to provide stewardship.

Clinical Research: Innovative clinical research, especially translational research, must be an essential part of the mission of the NCI intramural research program. In an effort to restore the clinical research in the intramural research program to preeminence: all intramural clinical research should be gathered under one division; translational research should be made preeminent; the review and monitoring of protocols should be made more rigorous; coordination between basic and clinical investigators should be encouraged; consolidations and mergers should be considered between NCI and the National Naval Medical Center; clinical training should be enhanced; and review of clinical investigators should be subject to the same equitable and rigorous peer review for promotion as laboratory investigators.

AIDS Research: The intramural and contract program in AIDS research is a large enterprise with limited central direction or control. This makes the NCI intramural program particularly vulnerable to any reduction in AIDS funding. Greater efforts must be made to coordinate AIDS research within the Institute and to undertake an expeditious and comprehensive review of all of its AIDS research for suitability and quality. This review should be done in cooperation with the Office of AIDS Research.

Drug Development Activities: The development of effective therapeutic agents is one of the most challenging and important pursuits in cancer research and should continue in NCI's intramural program. However, drug development programs and the investigators in them should receive more rigorous and periodic review, as should the contracts supporting them. Serious consideration should be given to how NCI's drug development programs could become core facilities for the entire NIH. Collaborative opportunities related to the drug screening program should be increased and accelerated within NIH and beyond.

Frederick Cancer Research and Development Center: NCI activities at Frederick are not well integrated, either among themselves or with other aspects of the intramural research program. For programmatic and budgetary reasons, it would be wise to reorganize and consolidate the Frederick programs. The facility should be a core facility, or "cost-effective center," for the entire NIH. All clinical and laboratory components of the Biological Response Modifiers Program should be moved to the Clinical Center. Noncontract operations should be moved to Bethesda. When feasible, the operations of the Applied Biosciences Laboratory program should also be moved to the Bethesda campus.

Implementation Plan: NCI should submit an implementation plan to the National Cancer Advisory Board at the time of the Board's May 1996 meeting. After May 1996 the Board should review the progress of the implementation plan annually until it deems review to be no longer necessary.

These recommendations reflect a consensus of the Working Group. Some of the recommendations are straightforward and require only will and energy to implement. Many echo recommendations made in previous reports that have gone unheeded. They are offered in a spirit of adventure and urgency and in full recognition of the vitality and importance of the mission of NCI. The report is submitted to the National Cancer Advisory Board for its consideration and action.

I. INTRODUCTION

Cancer is a challenge of immense dimensions. As a major cause of death and debility, it is a frightening prospect for the general public. As a disease with many causes and forms, it is a complex problem for research scientists. The National Cancer Institute (NCI) represents our best hope for conquering cancer. No other institution combines the sense of national purpose, the diversity of instruments, and the magnitude of resources required to meet the challenge of cancer.

Over the past decade, the hope embodied in NCI has begun to reach fruition. Research has produced a unifying understanding of the cancer cell that promises new and more effective approaches to prevention, detection, and treatment of the disease. Despite this success and promise, however, there is doubt that our nation will find the resolve to sustain the fight against cancer in the face of fiscal constraints that threaten to cripple all of the biomedical sciences. It seems a suitable time to review how well NCI has performed in the past and what might be done to improve its performance in the future. This report concerns an inquiry into one important arm of NCI, the intramural research program (IRP), based on the campus of the National Institutes of Health (NIH) in Bethesda, Maryland.

Genesis and Structure of NCI

Cancer has been a focus of federally funded research since the first allocation of $30,000 for that purpose was made in 1927. NCI was formally established in 1937 at the behest of President Franklin D. Roosevelt, and in 1947 was reorganized into its current configuration, with an intramural component geographically localized in Bethesda and a separately constituted extramural research program (ERP) that awards grants to scientists at universities and other research institutions. In 1972 NCI was elevated to bureau status within the Federal Government through the National Cancer Act (or the "War on Cancer," as it was styled by then President Richard Nixon). Today, with a budget of more than $2 billion, NCI is by far the largest of the 24 institutes, centers, and divisions within NIH, with nearly 2,100 full-time-equivalent employees.

As a result of the National Cancer Act, NCI is like no other institute within NIH. The NCI Director is appointed by the President, as are the President's Cancer Panel and the National Cancer Advisory Board (NCAB). The President's Cancer Panel provides general oversight for the National Cancer Program and directly advises the President on the status of the program. The NCAB oversees the review of grant applications and provides advice on all aspects of program and planning for cancer research, reporting to both the Secretary of Health and Human Services and the NCI Director. This statutory organizational structure has created a distinctive working relationship between the NCI Director and his advisory bodies, and has created a sometimes difficult structural relationship between the NCI Director and the NIH Director, who must respond, sometimes in parallel, to both executive and legislative oversight.

After several decades of expanding resources, NCI and its sister institutes now face the prospect of abrupt and severe fiscal constraints. As a result, the balance between the IRP and ERP of NCI has become uneasy. Now commanding nearly 25 percent of the total NCI budget (if contracts serving the IRP are included), the NCI IRP is the largest of its kind across NIH, in both absolute and relative size. The NCI intramural clinical program now expends $100 million annually and is the largest program of the NIH Clinical Center, responsible for 40 percent of all its costs. NCI is further distinguished by its extensive contract program ($200 million), much of it for support of IRP activities; its programs in drug development; and its organization into four research divisions (rather than one), each with responsibility for both extramural and intramural activities.

NCI must respond to legislative and executive mandates regarding the pursuit of its mission. The usual result has been a further expansion of that mission. Until recently the expansion was accommodated by steadily increasing resources. But with resources now increasingly constrained, the ability of NCI to be fully responsive to its various constituencies has been compromised, and this in turn has required that the mission and operation of NCI be examined. These are times for the scientific community to exert exceptional stewardship over the public funding of cancer research.

Mission of the Intramural Program of the National Cancer Insitute

The stated mission of NCI is to plan, conduct, and coordinate a national program involving (1) research on the

detection, diagnosis, cause, prevention, treatment, and palliation of cancers and on rehabilitation of the cancer patient, and (2) demonstration of the effectiveness of cancer control methods and techniques. Specifically, NCI—

- conducts and directs research performed in its intramural laboratories and through contracts;
- supports and coordinates research projects extramurally;
- supports training in fundamental and clinical science;
- supports construction of laboratories and related facilities;
- collaborates with voluntary organizations and other institutions engaged in cancer research, training, and control activities;
- collaborates with industry;
- collects and disseminates information on cancer incidence, outcome, and control; and
- consults with cancer research programs in other countries.

The NCI IRP has a multifaceted mission that reflects the diverse challenges posed by cancer. In general terms, the IRP should serve as a model cancer center, striving for integration of basic and clinical sciences. More particularly, the IRP serves the following purposes:

- It is a flagship for all the efforts of NCI. Located close to the Nation's capitol, it is a visible representation of the cancer program to policy makers, and an intellectual resource for advice to the Federal Government as well as to the leadership of NCI and the entire cancer program.
- It has relatively stable research funding, providing its scientists the opportunity, indeed the obligation, to take intellectual risks and "push the frontier" of feasible experimentation.
- It should conduct fundamental research of the highest quality, to produce an example to the entire community of cancer researchers, as well as an intellectual infrastructure for the other activities of the IRP.
- It should set an example in pioneering clinical research on cancer.
- It provides an exceptional setting in which to link fundamental research to the bedside, to conceive and test novel therapies, and to lead the way in what is now called "translational research."
- It must often devote a small but critical portion of its budget to "strike forces" that can react quickly to newly emerging challenges in the fight against cancer, particularly through epidemiologic studies.

Some aspects of the intramural mission, however, pose special problems. For example, the prominence of the IRP as the flagship of NCI can be a double-edged sword by detracting from the larger mission of NCI. Research mandated in response to political expediency diverts funds from other programs and monopolizes resources on behalf of legislative and executive mandates. The basic research in the IRP needs to be sufficiently catholic, yet it is sometimes faulted for being unduly duplicative of efforts in the ERP. The stability of funding, while intended to encourage risk taking, can result in complacency, inbreeding, intellectual isolation, and lack of vision.

The challenges faced by the IRP justify investment of ample resources. The questions before the Working Group were, How well have the resources been utilized, and how well has the mission been pursued? The answers become especially critical in light of the rapidly changing environment for extramural biomedical research, where resources are increasingly scarce and pressure is mounting to hold down medical costs, sometimes at the expense of research and training. In this context, the IRP becomes an even more precious resource.

Previous Reviews of the NIH IRP and NCI

The performance of the IRP has been evaluated several times and in several different ways in the recent past. Some of the challenges facing NCI are universal among institutes, such as downsizing, streamlining, and calls for aggressive performance review at all levels. Previous advisory groups have addressed these issues in response to administrative and legislative mandates over the past 25 years. These included a 1976 review of NIH by the President's Biomedical Research Panel, a 1988 report of the Institute of Medicine regarding the NIH intramural program, a 1992 report of the Task Force on the Intramural Research Program of the National Institutes of Health, a 1994 report of the Committee to Examine How the NCI Can Best Manage Hard Times, and the 1994 report of the External Advisory Committee on the Intramural Research Program.

At first glance, this might seem an excess of scrutiny. But a neutral observer might equally wonder whether the repeated calls for review reflect a continuing concern about performance and a lack of response to criticism and recommendations.

A number of the issues identified by the more recent deliberative bodies deserve mention, in particular because they prefigured many of the problems encountered by the present Working Group. The 1992 Task Force on the Intramural Research Program of the National Institutes of Health was appointed by then NIH Director Bernadine Healy to prepare a report concerning the scientific vitality, excellence, and eminence of the NIH IRP. The Task Force in its deliberations relied on the views of working intramural scientists and developed recommendations for improving the NIH IRP. Specifically, it recommended--

- the creation of permanent-faculty trans-NIH organizations that would participate in the decisionmaking of the institutes;
- the establishment of discipline-based postdoctoral fellowships administered through the faculties, a clearly defined tenure track policy, and funding for recruitment of tenure-track scientists from outside the IRP;
- the development of a uniform process for the review of research scientists and administrators; and
- the establishment of a central Administrative Policy Board to evaluate the impact of administrative decisions on the conduct of research.

In January of 1994 an internal NCI committee, composed of representatives of each scientific division and the Office of the Director, NCI, examined selected aspects of the NCI structure, staffing, and functioning. This committee's report, The NCI in Hard Times, identified issues NCI leadership should address, including:

- redundancy and overlap among divisions and between the intramural and extramural programs,
- ineffective use of staff,
- insufficient vision and planning,
- lack of effective linkages among programs, and
- the adverse influence of operational styles on the conduct of research.

Concern expressed by Congress and others regarding the quality, appropriateness, size, and cost of the NIH IRP led to the establishment of the External Advisory Committee (EAC) of the Advisory Committee to the Director, NIH. In particular, the Fiscal Year 1994 House Appropriations Committee Report mandated the Director of NIH "to review carefully the role, size, and cost of the intramural program and its relationship to the extramural research program," and indicated that NIH must put together a process "for allocating resources to and among its intramural programs based on a thoughtful analysis of these issues." To review the IRP, the NIH Director appointed the EAC, which completed its work in the spring of 1994.

In its many recommendations to the NIH Director, the EAC concluded that the problems plaguing the IRP, unless

addressed, may destine it to a mediocre future. The EAC identified seven areas of concern:

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

In addition to its evaluation of the IRP throughout NIH, the EAC recommended that each institute be subjected to an individual review along the lines established by the EAC. The present Working Group was formed in response to that recommendation. The NCI was chosen as the first institute to receive individual attention because it is the largest, and because a substantial turnover in leadership has been in process, providing an opportunity for revision and renewal.

In response to the EAC report, NIH has prepared an implementation plan addressing the review process for tenured scientists, a tenure track program, and changes in postdoctoral recruitment and training. In addition, progress has been made in removing some of the administrative impediments to research and enhancing the attractiveness of employment in the IRP through changes in the payscale and retirement options for senior investigators. The Working Group considered the implementation plan and used it as one point of departure for its deliberations. However, there are aspects of the NCI mission and organization that are unique and were not reviewed by the EAC. The Working Group has taken pains to identify and evaluate these distinctive issues.

Charge to the Working Group

The charge to the Working Group was to perform a review of the NCI IRP similar to that conducted by the EAC for the entire IRP of NIH. The Group was asked to determine the extent to which the recommendations of the EAC applied to NCI, to assess NCI's implementation of the EAC recommendations, and to identify and evaluate issues that might be distinctive for the NCI IRP. The Working Group was advisory to the National Cancer Advisory Board, and its formation was a joint activity of NCI and NIH.

The broad issues considered by the Working Group were quality control; morale of the scientific workforce; nurturing of talent, especially that of younger scientists; the intellectual suitability and administrative efficiency of the IRP as an organization; and the effectiveness of strategic planning. More specific issues placed before the Working Group for consideration included:

- the size of the NCI IRP relative to its mission;
- the organization and mission of the IRP versus NCI's extramural research program;
- the suitability of the current organization of the IRP into four divisions, each encompassing both intramural and extramural activities;
- the status of clinical research within the IRP in terms of suitability, quality, cost-effectiveness, and prospects;
- the appropriateness, quality, and future of drug development activities;
- the suitability, levels of funding, and effects of NCI AIDS research on other programs in the IRP;
- the quality and necessity of NCI programs at the Frederick facility; and

- the challenge of increasingly limited resources.

Recent attrition at the highest ranks of NCI management provides an opportunity to reconsider its current structure. In addition, the entire NIH is under a mandate to streamline its operations and reduce its number of full-time-equivalent employees. The Working Group was asked to consider these events as an opportunity to reconfigure various components of the NCI IRP and to provide advice on where resources are being used wisely and unwisely.

The Process of the Working Group

The Working Group met seven times over an eight-month period between October 1994 and May 1995. It requested and received detailed data on budgets, planning, quality review, personnel and administrative practices, operations of the Frederick Cancer Research and Development Center (FCRDC), AIDS programs, training, drug development activities, and the status of NCI Clinical Center programs; heard testimony from a variety of IRP personnel, including scientists, the NCI Director and Acting Director, division directors, Clinical Center staff, and administrative staff; solicited comments in writing from the entire professional staff of the NCI IRP; and made site visits to the clinical and drug development programs at FCRDC.

This report is organized around the issues addressed by the Working Group and reflects its consensus. Each section provides background information, describes the problems identified by the Working Group, and lists recommendations. The report is submitted to the NCAB for its consideration and action.

II. STRATEGIC PLANNING AT NCI

Long–range planning of how to deploy resources and people is essential to meeting the goals of the NCI IRP. Such planning first requires crystallization of a vision for the future of NCI. Within that vision a role for the IRP must then be defined and continuously revitalized. Furthermore, knowledge of discovery in fundamental and clinical science relevant to cancer must be communicated regularly to the central planning process so that the vision reflects new discoveries and examines the presumed power of prior discoveries.

NCI faces special challenges in its planning process: much of its annual budget is committed for years into the future and, thus, is not available for new initiatives; and new mandates place unanticipated demands on the budget. These factors make it imperative that NCI have a resourceful and well–informed leadership, with well–articulated mechanisms for strategic and tactical planning.

Currently the strategic planning process at NCI is coordinated by the Executive Committee, a group of senior administrators from the Director's Office, the Budget Office, the Office of Operations and Planning, and Division Planning and Budget Offices. Each year NCI convenes planning meetings to initiate and review the Bypass Budget, review division activities, and identify new scientific opportunities. In addition to the regular planning process, the Institute must mount responses to public health crises, address the concerns of numerous health advocacy groups, and answer to congressional mandates. All of these require a more ad hoc approach to resource allocation.

In concept the Boards of Scientific Counselors (BSCs) are also involved in planning. They are charged to perform an annual review of division budgets, approve conceptually all contracts and requests for applications for grants before they are solicited, provide advice to the division directors and scientific staff, and provide peer review of intramural laboratories. Ostensibly, the BSCs serve as the principal source of scientific advice to the respective NCI divisions. The BSCs are appointed from the extramural community and report to the division directors, not to the NCI Director or the Executive Committee as a whole.

At yet another level, the President's Cancer Panel provides oversight over the development and execution of the National Cancer Program, and the National Cancer Advisory Board is charged with review and approval of grants, and program, policy, and budget guidance.

Strengths of Strategic Planning in the IRP

Strategic planning as now conducted by NCI has its virtues. There is a formal and well– articulated planning process that relies on an active Executive Committee and regular retreats. In addition, the preparation of the Bypass Budget provides an annual opportunity for the review and revision of mission, tactics, strategy, and requirements for resources. Finally, NCI has indicated its willingness to improve planning by periodically initiating processes of self–inspection, the latest example of which is documented in the 1994 report *The NCI in Hard Times.*

Problems with Strategic Planning in the IRP

Despite the strengths of the current planning process, the Working Group concludes that NCI's procedures for strategic planning could be improved. There is reason to believe that too much of the planning is reactive rather than proactive. As a consequence, vision suffers, in particular as it applies to the IRP. In addition, insufficient attention to strategic planning along substantive (rather than administrative) lines has resulted in the formation of a number of programs that seem poorly coordinated, either within themselves or with other NCI programs.

It is the impression of the Working Group that much of the involvement of the BSCs in planning is pro forma, the budget is presented as a fait accompli, and there is insufficient use of BSC scientific and clinical expertise in major NCI decisionmaking. (See also Part IV, Quality Assurance in the IRP.) According to their own testimony, the BSCs have not been utilized consistently or effectively for planning purposes.

Many of the IRP scientists consulted by the Working Group expressed frustration and a sense of disenfranchisement, engendered by failure of the Institute to consult them sufficiently in its planning activities. Moreover, researchers in the

extramural community, the largest scientific constituency of NCI, have almost no input into the NCI planning process (outside of membership on BSCs or the National Cancer Advisory Board). The Working Group is concerned that lack of input from the extramural community impedes scientific advances and isolates intramural scientists from the broader community of scientists. Lack of input from the extramural community is particularly problematic, given that NCI division directors control both extramural and intramural budgets.

NCI planning efforts, therefore, lack direct and consistent participation by the leadership of NCI's major professional constituencies, (i.e. working laboratory scientists and clinical investigators). The Working Group believes that NCI must correct this deficiency to make the most effective use of resources, and to preserve the long term health of the intramural program.

Lack of a coordinated and rigorous planning process has allowed an imbalance to develop between the budgets of the IRP and the extramural research program (ERP). This imbalance, which has developed over time, has resulted in a maldistribution of resources between the two programs. In addition, the Working Group was concerned about the current practice of counting contracts that support intramural research as a separate budget item. Many of these funds are actually expended by the IRP and account for an additional 7 percent above the commonly used figure of 18 percent for the IRP budget. Because the funds are used in support of intramural research, they should be presented and reviewed as part of the IRP.

The IRP allocation for the entire NIH is 11.3 percent, an average of all 24 institutes, centers, and divisions across NIH (including NCI). This average was selected by the 1994 EAC as the level above which the IRP portion of the total NIH budget should not rise. In considering this EAC recommendation, the Working Group recognized that the clinical and epidemiologic responsibilities of the NCI IRP are costly and might warrant expenditures that would bring the NCI IRP average legitimately above the 11.3–percent recommended ceiling. Other than the high outlays for these activities, however, the Working Group was unable to find any evidence of strategic planning by which the relatively high commitment of NCI to the IRP has been reached. This lack of justification was cause for concern, not because the IRP was found to be wasteful or deliberately over funded, but because the Working Group believes that the funding of intramural research should be suitably proportioned in reference to the remainder of the National Cancer Program. To place nearly one quarter of the entire federal investment for cancer research in one site expects too much of a single research community and short changes the remainder of the scientific enterprise engaged in cancer research.

It should be noted that the Working Group reviewed the IRP in isolation and on its own merits, recognizing that any comparison to or prescription for advancing the cause of the ERP could be viewed as suspect. Nevertheless, the Working Group concluded that the current investment in the IRP might be excessive. Any savings achieved through better planning and streamlining in the IRP could be used by the NCI Director either to redress some of the inequities between the ERP and the IRP or ro revitalize the IRP through innovative measures.

Summary and Recommendations

The Working Group found that the procedures used by NCI for strategic planning could be improved. In particular, there has been too little consultation with active scientists about goals and deployment of resources. One major issue in strategic planning for NCI is the allocation of funds within the IRP and between the IRP and the ERP. There seems to be a disproportionate investment in the IRP, and at least some of its individual programs appear to be poorly coordinated. To remedy these problems, the Working Group makes the following recommendations.

1. NCI should create a standing committee, composed of leading clinical and laboratory investigators within the IRP, to provide consistent and systematic advice to the Director as part of its long-range planning process. This standing committee should be included in planning retreats and should be represented directly on the Executive Committee of NCI.

2. The NCI Director should also consult regularly on planning matters with a committee of leading basic scientists and clinical investigators from the extramural community. The Chairs of BSCs should be included in this group. Like the IRP advisory group, the extramural committee would contribute to planning, especially to the identification and prioritization of emerging areas of research.

3. In addition to meeting regularly with the NCI Director, these groups should meet annually with the appropriate basic and clinical research subcommittees of the NCAB. Both groups should prepare brief annual reports summarizing their recommendations. Such reports would provide useful documentation of the input received by the Executive Committee and establish benchmarks for judging the quality of the advice and its implementation.

4. The Working Group urges NCI to reconsider its current budget to determine whether the 25 percent devoted to the IRP is appropriate. The Working Group believes that the current investment is disproportionately high, considering the relative size of the effort in the IRP and the remainder of the National Cancer Program. The Working Group recognizes that the ceiling of 11.3 percent for the overall NIH intramural budget recommended by the EAC in 1994 need not strictly apply to NCI. Nevertheless, efforts to adjust the allocation for the NCI IRP from its current level seem advisable.

   A report on efforts to adjust the allocation should be part of the formal agenda at the annual program review by the NCAB. The NCI Director and the division directors should provide the Board with projections of intramural compared with extramural funding, and with the rationales on which these are based. In addition, the cost of research and development contracts that support intramural research should be acknowledged as part of intramural expenses.

III. ORGANIZATION OF THE IRP

The current organizational structure of the entire NCI is based on five divisions, the directors of which report to the NCI Director. These are the Division of Cancer Biology, Diagnosis, and Centers; Division of Cancer Etiology; Division of Cancer Prevention and Control; Division of Extramural Activities; and Division of Cancer Treatment. Each division includes three to five programs (with the exception of the Division of Extramural Activities, which has five branches). The programs are in turn divided into laboratories and branches, and these are further subdivided into sections. The IRP presently contains 57 laboratories and branches. All but the Division of Extramural Activities have both extramural and intramural programs.

In addition to the strictly intramural program, there are two additional major programs that serve the IRP in some way. First, there is a substantial body of so-called "in-house" activities, though they are formally extramural in nature. These comprise mainly contracts awarded to the Frederick Cancer Research and Development Center and, in particular, to the Applied Biosciences Laboratories at Frederick, a freestanding, government–owned, contractor–operated research facility. Second, there are a series of extramural contracts awarded to provide logistical support for the IRP.

Seven large administrative offices also report to the NCI Director. The Director is advised by the NCAB and the President's Cancer Panel.

Strengths of the Current Structure

The Working Group recognizes the justifications and strengths of this organization: it accommodates the relatively large size of NCI and its IRP, allows for intimate interactions between the extramural and intramural programs, is thematically comprehensive, and is responsive to legislative and executive mandates such as cancer epidemiology, prevention, and control.

Problems Raised by the Current Structure

Whatever the worth of the current organizational structure, its evolution has not been one of coherent planning. Thus, the Working Group was not surprised to find that the structure has engendered multiple difficulties. Six organizational issues were identified that, unless addressed, will restrict the IRP's ability to perform its mission. While organizational changes cannot fully remedy entrenched administrative behaviors, significant changes should be made to reduce redundancy, streamline operations, promote collaboration, and optimize productivity.

Evolution of an elaborate bureaucracy. The current organization of the NCI IRP has evolved into an elaborate bureaucratic structure that has led to significant redundancy in management, with four lines of authority leading to the top. Many intramural scientists find this redundancy unnecessary and wasteful. The inertia of the system hinders the development of new scientific initiatives, inhibits collaboration, and allows the survival of unproductive programs.

Intramural and extramural programs are supervised by the same individual within a division. At any given time the attention and possibly the loyalty of the division director might be focused on only one program because of dual responsibilities. Division directors readily concede that the current system lends itself to advocacy of the IRP among the leadership; and coping with the demands of the IRP is a ready distraction from the seemingly more remote issues of the ERP. Although the capacity exists to coordinate the activities of the extramural and intramural programs, the Working Group found little evidence of attempts in this direction and therefore little justification for overlapping administration. In addition, different skills and experiences are needed to manage the intramural program versus the extramural, further warranting their separation.

The multiple divisions do not favor collaborative effort. Some programs have evolved into a fragmented feudal structure that is not conducive to collaboration or cooperation when the opportunity arises. Organizational units within different divisions have no motivation to share or collaborate, leading to intellectual fractionation.

The current organization of laboratories and branches encourages redundancy. The substructure of the IRP

presently comprises 352 separate research groups, an appreciable number of which appear to be thematically redundant. At least 46 of these are sections that each house only a single FTE scientist. In contrast, some laboratories and branches are exceedingly large and only could be effective if most of the doctoral–level staff were acting with full independence. Similarly, the divisions are strikingly disproportionate in size. In particular, the Division of Cancer Prevention and Control has only a token intramural effort. These disproportions may not be inherently disadvantageous on intellectual grounds, but they do raise managerial issues of efficiency and efficacy.

In addition, the substructures of the divisions, and in particular the number and sizes of laboratories, branches, and sections have been determined as much by considerations of personnel as by strategic and tactical needs. Simply put, the easiest way to reward scientists in the IRP is to make them laboratory, branch, or section chiefs, even if that requires the creation of new organizational units. The Working Group recognizes that this feature, while not unique to NCI, has produced some particularly striking results in its IRP.

Top-down scientific management. The present organizational structure appears to impose top-down scientific management, which prevents ideas and suggestions for new directions from rising up from the ranks of young investigators, a common occurrence in extramural research laboratories (see also Part V, Stewardship Review and Tenure Policy in the IRP).

Administrative burdens impede research. It has long been a complaint of IRP scientists that administrative requirements impede, rather than facilitate, the efficient conduct of high–quality research. Often the individual responsible for administrative decisions that affect research programs has no experience as a scientist. IRP scientists report high levels of frustration about being "hamstrung" by overly bureaucratic personnel and procedures. The structure as it now exists has failed to cope with regulatory and administrative impediments to research and technology transfer. The general view is that at least some of these impediments are remediable, but that the fractionation of administrative effort among the multiple divisions has thwarted finding the remedies.

Summary and Recommendations

The Working Group believes that the current organizational structure of the IRP is unnecessarily complex and redundant, and potentially disadvantageous to the ERP. In addition, burdensome administrative requirements appear to deter IRP scientists from their missions in basic and clinical research and technology transfer. Therefore, the Working Group makes the following recommendations regarding the organization of the IRP (see organization chart).

1. The Working Group recommends full separation of the IRP and ERP.

2. The IRP and ERP should each have a single deputy director. There could be two additional deputy directors, corresponding to existing positions: a Deputy Director in the office of the NCI Director and a Deputy Director for Extramural Activities. All the deputy directors should report directly to the NCI Director.

3. There should be two divisions in the IRP: the Division of Cancer Etiology and Biology, and the Division of Cancer Prevention, Diagnosis, and Treatment. Each would have a single director. An Associate Director should oversee operations at Frederick. In adding the position of Deputy Director for Intramural Research (DDIR) and reducing the IRP to two divisions, the Working Group intends that the NCI DDIR and the two division directors would all sit on the NIH Board of Scientific Directors and the Executive Committee of NCI.

4. The ERP was formally beyond the purview of the Working Group. But having recommended that it become a fully separate entity, the Working Group suggests that it have four divisions, the Division of Cancer Etiology and Biology, the Division of Cancer Diagnosis and Treatment, the Division of Cancer Prevention and Control, and the Division of Cancer Centers and Training. The Working Group proposes that an advisory body similar to the BSC be constituted for the divisions of extramural research, but recognizes that such a recommendation is also beyond its purview.

5. The Working Group endorses the recommendation of the 1992 Task Force on the Intramural Research Program for the establishment of an Administrative Policy Board chaired by the DDIR of NIH. It also recommends that NCI establish its own standing committee of scientists to review administrative issues and report to the DDIR of

NCI. This committee should serve as a central advisory panel to evaluate the impact of administrative decisions on research and to advise the NCI administration on the impact of current regulations and requirements.

IV. QUALITY ASSURANCE IN THE IRP

No aspect of the NCI IRP is more important than quality assurance. The continued monitoring of research excellence is the only way possible to guarantee that performance remains at the cutting edge. In addition, quality assurance provides an objective basis for allocating division funds and stimulates recognition of meritorious programs, especially those of young investigators.

In its 1994 report the EAC reminded NIH that periodic peer review is crucial to the long–term excellence of all scientific institutions, including the IRP. The report stated, "The review process can be positive when it calls attention to deficiencies in time for them to be corrected. When improvement is not adequate, a review provides reliable justification for shifting resources from less productive to more productive scientists."

The EAC also recognized the importance that intramural scientists be judged on past achievements rather than future projects, as this distinguishes the intramural from the extramural program. This requires, however, that reviewers take into consideration the long-term nature of some of the intramural projects, thereby allowing adequate time to develop innovative programs of excellence. The Working Group strongly concurs with the principles as stated by the EAC and finds that they are entirely appropriate in considering processes of review in the NCI IRP. However, during the course of the Working Group's review of the NCI IRP, it encountered diffidence about, and even resistance to, both the recommendations of the EAC and the NIH Implementation Plan. Thus, the Working Group found it necessary to reconsider the issue of quality assurance within the NCI IRP.

Any consideration of quality control for the IRP must acknowledge its special circumstances: its mission to push the frontier of feasible experimentation; the commitment to retrospective rather than prospective review; the privilege of relatively secure funding for individual investigators; the need to be nimble in response to national need and legislative or executive mandates; and the need for team approaches in some aspects of the IRP effort.

Strengths of Current Processes for Quality Assurance

The current process for quality assurance within the IRP accommodates many of the special features listed above. First, there is a formal structure for the review of all the activities of the IRP. Second, there have been efforts to improve this structure and its performance in recent years, which could now be augmented by the Implementation Plan of the DDIR of NIH. Third, there is an attractive new tenure system, as recommended by the Implementation Plan and in response to the EAC. And fourth, the NCAB provides a device for ongoing oversight.

Problems with Quality Assurance in the IRP

Despite concerted efforts by NCI to assure quality in the IRP, the Working Group found cause for concern. The review of programmatic performance has not been sufficiently rigorous or objective. Many members and some chairs of BSCs do not believe that the Boards have been effective. Their charges are vague, their utilization varies from one division to another, and their deliberations are typically rushed, superficial, and rarely proactive.

The Working Group encountered the same adverse opinion of the site visits used to evaluate intramural research programs. The selection of site visitors has been subject to cronyism, and the reviews and recommendations produced through the process tend to be muted.

The review process has given inadequate attention to the budgets for research programs and individual scientists, in part for want of adequate data. This has led to a lack of financial accountability on the part of investigators and NCI administrators and has increased the tendency of reviewers to conduct prospective, rather than retrospective reviews.

Lack of accountability and inadequate budget review has led to vast disparities in support provided individual investigators. The Working Group believes these disparities are not fully correlated with merit. The budgets for some laboratories within the IRP appear to have grown beyond any reasonable or effective level, yet do not seem to have been scrutinized for cost effectiveness. To dramatize this point, the Working Group notes that at least 55 of the individual investigators in the NCI IRP have line budgets of more than $1 million, and another 12 are just under that

amount. While investigators in the ERP are subject to exceptional budgetary surveillance when their funding rises above a set amount, the same accountability is not required in the IRP.

In addition, lack of accountability has led to the formation of some NCI research programs that have escaped the current system of peer review. These programs were described as extramurally based but intramurally administered. It is essential that peer review be performed consistently throughout the various units conducting research.

Finally, there has been no formal, consistent, and objective means of appeal for IRP scientists who have been the subject of adverse reviews. This deficiency, when combined with suspect site–review procedures, is particularly problematic.

Previous advisory committees as well as NCI staff have stressed the importance of the unique research opportunities afforded in the NIH IRP. Even a cursory review of NCI intramural programs, however, shows that relatively few are unique in concept or implementation. Most programs have counterparts in the extramural community, and many intramural programs cannot even be considered the best in their particular field of inquiry. The wisdom of retaining programs that are not unique, or at least outstanding compared with similar extramural programs, is questionable. To maintain state-of-the-art clinical and basic research at NCI, the programs must be periodically compared with the research that defines the "art," both inside and outside the IRP.

Summary and Recommendations

Stringent review of the NCI IRP is needed now, more than ever, because of the institutional "aging" typical of most large organizations, the acceleration of cancer research, and budget constraints. It was not evident to the Working Group that review of scientists and senior administrators within the IRP is uniformly objective or that there is sufficient distance between the BSCs and the scientific directors to ensure objectivity in review.

The Working Group recommends that the procedures used to evaluate the IRP and its scientists be improved to encourage more objectivity and expertise on the part of reviewers, to reward excellence and initiative, and to improve the diversity and morale of intramural investigators.

The Working Group recognizes the validity of retrospective review for the IRP. The excellence of the overall NCI program is built upon a variety of approaches to the management of research. Prospective and retrospective methods of evaluating research vary and encourage creativity in different ways. It is generally agreed that the overall performance of NCI is best served by retaining prospective review in the extramural program and retrospective review in the intramural program.

In order to ensure the best use of NCI funds, the Working Group believes that overall quality assurance needs to be improved. This requires changes in the way peer review is conducted for the IRP.

1. All research conducted by the IRP, whether in laboratories of intramural investigators or through extramural contracts serving intramural programs, should be subject to peer review administered by the DDIR.

2. Under the recommended revised organizational structure, there will be BSCs with oversight over intramural activities only. The BSCs should be substantively involved in the review of research in progress, budgets, setting of priorities and goals, and recruitment. These issues should be considered from the standpoint of individual investigators as well as the research programs of laboratories, branches, and divisions. To these ends, the BSCs should receive a clear written charge that specifies their responsibilities in detail, emphasizing the need for retrospective rather than prospective review and for oversight of budgets. The charge to the BSCs should be codified and standardized within the IRP.

3. Nominations to the BSCs should come from their sitting chairs, who may solicit recommendations from various sources. Nominations should then be discussed with the DDIR of NCI and the NCI Director, who has final appointment authority. Members should be appointed on the basis of their expertise and their ability to evaluate programs and personnel objectively. The BSC Chair should be selected by the DDIR of NCI and the NCI Director from past or current BSC membership.

4. Programs should be evaluated on the basis of past achievements, rather than future plans.

5. The Working Group believes that the use of site visits has not applied sufficient rigor in the evaluation of research in the IRP. Thus, the Working Group recommends abandoning the routine use of site visits for such evaluation. Instead, written progress reports from investigators under review should be submitted to extramural reviewers (perhaps two per investigator) chosen by the DDIR of NCI in consultation with the BSC chair. The reports should include all publications from the period under review, descriptions of published and unpublished progress, explanations for lack of progress, and full information on budgets. All tenure-track and tenured scientists in the IRP should be subject to such review at intervals of four years. The extramural reviewers would receive written instructions about the nature of the review (in particular, that it is deliberately retrospective) and would be asked to submit written evaluations of the research progress and the budget. The evaluations would be used by the BSC in making a final recommendation, which would be reached by discussion followed by a secret ballot.

6. Extramural reviewers and the BSC should be asked to consider the cost of research, including contractual fees. Reviewers should be provided with the exact cost of each project and its component parts, including the costs of contracts used in support of intramural research.

7. Written reviews could be supplemented by site visits when a BSC questions the judgment of the written reviews for an individual or when the BSC concludes that significant changes in existing budgets are appropriate.

8. Should an investigator feel that the review of his/her program was flawed, there should be a formal, uniform process for rebuttal and appeal available to address the investigator's concerns. A mechanism for rebuttal and appeal should be established and administered by the DDIR of NCI. It should not involve individuals in a supervisory position to the investigator.

9. It is the impression of the Working Group that budgets for some individual investigators in the IRP have become excessive. The Working Group suggests that the NCI Director consider whether investigator budgets above a predetermined amount should undergo special review, as is now the case in the ERP of NCI.

V. STEWARDSHIP REVIEW AND TENURE POLICY IN THE IRP

Quality in research requires more than rigorous review; it requires individual talent. It is vital that the NCI IRP sustain and regularly renew its scientific talent, through measures to encourage the creativity, independence, and welfare of its current staff, and through vigorous recruitment to fill vacancies.

Strengths of IRP Recruitment, Tenure, and Promotion Policies

There are reasons to believe that the NCI IRP could readily meet the objectives of rigorous recruitment and support of intellectual talent. First, the appointment to tenure track in the IRP offers attractive resources to young investigators. The IRP should be able to exploit this in the recruitment of new doctoral-level staff. Second, the leadership of the IRP has been subject to at least a modicum of surveillance over the stewardship of talent and resources. Third, there have been recent and laudable grass-root initiatives directed toward the encouragement of doctoral-level careers for women and minorities underrepresented in the sciences.

Problems in Recruitment and Stewardship

Despite areas of excellence, the Working Group found deficiencies in the recruitment and sustenance of individual scientists throughout the NCI IRP. Perhaps the most troubling finding was a broad dissatisfaction with the general ethos within the intramural community. Scientists reported a hierarchical approach to research that is both intimidating and limiting to the development of independent investigators. Examples of this were found among section, laboratory, and branch chiefs. While this problem is not universal, it appears to be alarmingly prevalent, and seems to have escaped remedy by the division directors. As a consequence, at least some scientists find their independence repressed, or at least discouraged, and creativity is secondary to the programmatic needs of superiors.

The Working Group recognizes that the mission of the IRP includes research that requires a team effort. But there is no substitute for the creativity of individual scientists in the long term, and some portions of the IRP seem to have lost sight of this principle. Arguments in support of the hierarchical approach to research within the IRP appear to be self-serving.

Similarly, the NCI IRP has used poor practice in recruiting new scientists. Like any other research organization, the IRP, in order to remain competitive and on the cutting edge, must constantly renew its store of intellect and ideas through aggressive, rigorous, and open recruitment of new talent. Although recommendations of the EAC regarding recruitment have already been implemented, the Working Group found evidence that all efforts are not being made to recruit young investigators with potential for independent research careers. Advertisements for tenure-track positions appear to be very narrow and designed to fulfill and sustain technical needs within existing programs. Vacancies at all levels have usually been filled by resident staff rather than through recruitment from the outside research community. This practice has led to an inbreeding of attitudes and failure to tap the full pool of biomedical talent available.

Once recruited, intramural scientists should be provided the opportunity to work in a setting that rewards excellence and creativity. The Working Group strongly endorses the new NIH-wide tenure policy which utilizes the judgment of senior NIH scientists rather than administrators. The system will have to be evaluated after some time, but the structure seems appropriate to meet previous concerns regarding arbitrariness, failure to recognize truly independent investigators, and the entrenchment of a reward system that favored those who followed the direction of laboratory chiefs rather than their own research paths.

The Working Group found little evidence of stewardship review at all levels of administration from laboratory chiefs to the Institute director. The current system permits dominance of laboratory chiefs in the scientific, budgetary, personnel, and operational issues faced by an independent investigator. This unchecked power allows laboratory chiefs to direct scientific operations toward their own line of research, thereby hindering the career development of independent investigators. There is little accountability required for administrative actions and too little attention paid to the role of laboratory chiefs in career development of junior faculty. Appointments to laboratory chief are rarely revoked. Individual investigators, particularly junior scientists, have limited opportunities to expand their research

portfolios and increase their resources beyond those allowed and approved by senior management.

The Working Group believes strongly that the independence of investigators can never be fully realized until all tenure-track and tenured junior faculty have independent annual budget authority and are given the opportunity to compete for additional funds to develop new ideas.

Despite recent efforts across the NIH IRP to improve tenure and stewardship review, the Working Group identified lingering concerns. In particular, the new tenure system has been greeted with resistance by some IRP supervisors. In addition, some IRP staff expressed concern that the new tenure system would not recognize the special difficulties that arise when research requires a team approach.

Finally, the NCI has historically paid inadequate attention to the barriers confronting women and underrepresented minorities in pursuing research careers within the IRP. Recent studies have shown that women and minorities generally enter the IRP at lower salary and that their career paths have a lower trajectory throughout their time in the IRP. Inequities at the lowest entry levels almost predestine an adverse outcome, for it is this early period in which the junior scientist must establish a track record, which will then justify additional resources and opportunities for advancement.

The Working group views these deficiencies in renewing and sustaining talent with great concern. They may represent the largest barrier to achieving and preserving excellence in the IRP.

Summary and Recommendations

The Working Group encountered within the IRP an environment that is not conducive to independence on the part of younger scientists. The Working Group also confirmed the EAC findings that the IRP has failed to recruit new talent vigorously and that its policies for promotion of scientists have lacked rigor. In order to fulfill its mission, the IRP must consistently seek to renew its intellectual capital. Its scientists should be provided the opportunity to work in a setting that encourages independence and rewards both creativity and excellence. To sustain and renew talent in the IRP, the Working Group recommends the following.

1. The role of the laboratory and branch chiefs should be defined more explicitly. The Working Group views them as comparable to department chairs in academic settings. In that light, they should encourage and facilitate the independent development of the scientists under their supervision.

2. Stewardship reviews of laboratory and branch chiefs and scientific directors should be conducted by extramural committees selected by the BSC Chair and the NCI DDIR. Reviews should consider each individual in terms of success in recruitment and mentoring, and in fostering the career development of independent investigators, the professional welfare of women and underrepresented minorities in the program, and the equitable allocation of funds. The reviews should be separate from any assessment of research performance and should seek the views of all individuals who are under the authority of the supervisor.

3. The Working Group recommends that laboratory and branch chiefs and scientific directors be appointed for renewable terms of five years. If a stewardship review is adverse, it should be repeated after one year. Two poor reviews would be cause for removal from the supervisory position.

4. The Working Group strongly supports the implementation of the new tenure system in the IRP and is confident that it will allow proper advancement of basic and clinical scientists.

5. Recruitment of excellent scientists at all levels of the IRP should be vigorously conducted, and competitions for positions should be fully open to scientists in the intramural and extramural communities. Primary consideration should be given to the abilities of the individual, rather than to fulfilling a particular need of the laboratory, branch, or section chief.

6. Independent investigators, tenure track and above, should receive fully specified budgets at the beginning of each fiscal year and should have full control over those budgets throughout the year. Any necessary rescissions over the course of a year should be accomplished in an equitable manner.

7. The Working Group believes that the NCI IRP should develop a cadre of talented young scientists who would establish their careers as independent investigators, but move on from the IRP to other institutions within three to five years. As a first effort, the Working Group suggests the establishment of an NCI Distinguished Fellows program, with awards made through a well-advertised national competition. The program would fund as many as 10 young investigators per year, with terms of no more than five years. Fellows would establish research groups of three to five individuals within select laboratories and branches. The program would be administered by the DDIR of NCI.

8. The Working Group recommends that NCI set aside approximately $3 million annually for an open grants competition within the IRP of NCI. An average of 30 three-year awards of $100,000 could be made for research above and beyond that already being conducted in accordance with the programs reviewed by the BSCs. Review of proposals could be conducted by a trans-NIH committee administered by the DDIR of NCI. The awards would be intended primarily for young investigators, but available to any tenure-track or tenured investigator.

   The funds should be used to develop new ideas and pilot programs with no programmatic specification. Funding should be considered supplemental to the investigator s programmatic research budget. It would become the responsibility of the investigator, with neither the competitively awarded funds nor the base funds available for reprogramming by the section or laboratory chief.

   Should the grants program prove successful, the NCI might consider making the competition available to all intramural NIH scientists conducting research relevant to cancer.

9. The Working Group recommends establishing a program targeted for recruitment of women and minorities at all levels, and endorses plans to include women and minority representatives on search committees for tenure-track and tenured scientists. Suitable examples for recruitment plans can be found in the measures required of extramural training grants.

10. The Working Group recommends developing programs of mentoring for women and minority scientists within the IRP.

11. The Working Group urges that the stewardship review of laboratory and branch chiefs and scientific directors address issues of recruitment and advancement of women and minority scientists. There have been laudable efforts to examine the welfare of minority and women scientists throughout NIH and NCI. These efforts have generated explicit recommendations regarding stewardship and stewardship review. The recommendations of those reports could be easily implemented through the review of stewardship recommended above.

12. An ombudsperson should be appointed by the DDIR of NCI to deal with career advancement (as well as other concerns of women and underrepresented minorities) and administrative issues.

VI. CLINICAL RESEARCH IN THE IRP

The IRP of NCI should provide a flagship for clinical research on cancer that leads the way in developing novel measures for the prevention, detection, and treatment of the disease. Moreover, increasing constraints of managed care on clinical research at academic medical centers may leave the NCI as one of the few institutions where this kind of research can be done. Yet this major resource for funded clinical research in the United States remains underutilized.

NCI studies in the NIH Clinical Center are an important component of the NCI intramural program. The Center serves as the site of innovative clinical research and as a training ground for clinical investigators. The participation of NCI in planning for a new Clinical Center is critical, as NCI is consistently the heaviest user of NIH clinical facilities. In 1994 NCI logged over 20,000 inpatient days and over 30,000 outpatient visits in the Clinical Center. Of the $220 million Clinical Center cost allocation in FY 1994, 42 percent was for NCI.

In reviewing the clinical programs of the NCI IRP, the Working Group evaluated the processes used to set priorities for clinical trials, train clinical investigators, accrue patients, and coordinate clinical investigation across the NCI IRP and with the extramural community. The Working Group also reviewed the need for IRP clinical research to be conducted at three separate sites: Bethesda, the Frederick Cancer Research and Development Center (FCRDC), and the National Navy Medical Center (NNMC).

Strengths of Clinical Research in the IRP

As part of its charge in 1994, the EAC reviewed clinical programs of the entire NIH and concluded that they are an essential, if not key, component of NIH intramural research programs. The Working Group recognizes that for NCI a crucial asset of the Clinical Center complex is the flexibility it offers to respond to new opportunities and needs by rapid redirection of resources. In addition, the existence of a high–caliber staff on-site, with expertise in clinical research, allows for the rapid implementation of new initiatives. The close proximity of laboratories to patient care facilities is an advantage and should be of considerable value in facilitating translational research because of enhanced interaction among basic and clinical scientists.

The Clinical Center, with its appropriate facilities and support staff, allows scientists to conduct long-term clinical studies of individual patients and large families that would be difficult, if not impossible, in the extramural community because of the lack of sufficient and long-term funding. The ability to see, evaluate, and treat patients who are not billed for services is conducive to their recruitment into studies. The Clinical Center also provides an excellent setting for the training of clinical investigators. In principle, the IRP is well positioned to fulfill its mission in clinical research. NCI plays a particularly determining role in the future health of the Clinical Center.

In addition, the Working Group acknowledges the advantages to the IRP of the interagency agreements with the Navy and the Uniformed Services University of Health Sciences. The combined NCI and Navy Medical Oncology Branch (NMOB) at NNMC offers the NCI intramural program a fully functioning hospital. The combined Navy and NCI Hematologic-Oncology Clinic administers to 1,600 new cases of cancer and 15,000 visits annually. The NCI and Navy are fully integrated with respect to training, protocol development, and patient care for medical oncology. Currently there are 26 clinical trials ongoing at the NCI-NMOB. In short, the NCI-NNMC agreement is a model of government interagency cooperation.

Problems in the Intramural Clinical Research Program

In the face of this attractive portfolio, there is widespread concern among the biomedical community that clinical research in the IRP is not thriving as it should. The Working Group shares this concern, sustained by reports of reduced patient enrollment, diminished luster of the training program, and a loss of regard among the research community at large.

Potential explanations for this decline include increased competition from cancer centers around the country; lack of innovation in IRP clinical protocols; decreased attention to patient needs and care; and an insufficient cadre of optimally trained clinical investigators to design and conduct research, especially in translational areas. A major failure

of the NCI IRP is that it has not achieved its potential in translational research, which should represent the predominant component of clinical research in the NCI IRP. Clinical research of all kinds in the IRP lacks a rigorous, centralized process for peer review. Amid a complex layer of review for clinical protocols, the Working Group could not perceive an assessment of scientific quality that was sufficiently removed from the sponsoring units to be considered objective. There is also a lack of prioritization and financial assessment of clinical/translational research in the IRP.

It is the view of the Working Group that current clinical research in the NCI IRP is, in large part, similar and duplicative of work going on in the extramural community. Allowing this situation to prevail fails to take advantage of the special characteristics of the NCI intramural clinical research program. There has been a general failure of collaboration and cooperation, both among clinical programs and between the clinical and basic research programs of the NCI IRP. Some, but not all of this failure can be attributed to a geographic dispersion of clinical/translational research off–site at the FCRDC. It is clear that the Biological Response Modifiers Program (BRMP) is entirely independent of the rest of the IRP clinical effort, and given the large financial resources devoted to this program, the NCI IRP is not well served by its geographic isolation.

There are deficits in the training of clinical investigators, mentorship for young investigators, tenure review, and salary scales. These difficulties are compounded by the frequent need for a team effort in the conduct of clinical and translational research. In addition, the availability and quality of subspecialty care for patients participating in clinical trials has been criticized.

Summary and Recommendatiuons

Innovative clinical research has been, and will continue to be, an essential part of the mission of the NCI IRP. Increasing constraints of managed care on clinical research at academic medical centers may leave the IRP as one of the few institutions where this kind of research can be done. In recent years this major resource for funding novel clinical research in the United States has been underutilized. In an effort to restore the clinical research in the IRP to preeminence, the Working Group recommends the following.

1. All intramural clinical research at NCI should be gathered under one division, the proposed Division of Cancer Prevention, Diagnosis, and Treatment. This should encourage interactions across disciplinary boundaries and facilitate strategic planning.

2. The IRP should establish a Protocol Review and Monitoring Committee similar to those required in NCI-designated cancer centers to provide more rigorous and uniform scientific review of proposed clinical trials and to set priorities for the trials.

3. Translational research should become predominant in the clinical program of the NCI IRP and should weigh heavily in the selection of the Division Director. There should be a major effort to recruit and train investigators in the IRP to perform clinical and translational research.

4. Activities that require interdependence between basic and clinical investigators should be encouraged. This should specifically include studies crossing programmatic and divisional boundaries.

5. The NCI IRP clinical research program should complement rather than duplicate the research programs of extramural cancer centers and NCI-sponsored clinical trials.

6. NCI would be well served by a Clinical Center with a smaller inpatient and larger outpatient facility. This consideration should be given great weight in planning future development of the Clinical Center.

7. The Working Group recommends that the NCI IRP explore whether the NCI and Navy Interagency Agreement could be expanded, so that more NCI IRP cancer patients who require inpatient care could be hospitalized in the National Naval Medical Center facility.

8. The Working Group recommends consolidation of the Medicine Branch, including the BRMP, and the NCI-Navy Medical Oncology Branch into one branch with one chief. This would address several current problems at

the Clinical Center, including a lack of house staff, poor quality and availability of specialty consultation, and insufficient exposure of medical oncology fellows to standard oncologic practice. Similar collaborations between NCI and the Navy should be considered for training programs in pediatrics and radiation therapy.

9. The clinical and related laboratory research effort of the BRMP should be relocated from Frederick to the Clinical Center. This consolidation would substantially benefit clinical research in the IRP. The production facility could remain at Frederick.

10. The Working Group endorses the clinical research training program recently proposed by the Director of the Clinical Center. By that means and others, the NCI should augment training in clinical research through its IRP.

11. NCI IRP clinical research staff should become knowledgeable of NCI-sponsored extramural clinical research activities.

12. Clinical investigators should be subject to the same equitable and rigorous peer review for promotion as laboratory investigators. The tenure review committee should recognize the differences in methodology, the different venues for publication, and the frequent requirement for a group effort in research that characterize clinical investigation.

VII. AIDS-RELATED ACTIVITIES OF THE IRP

Tumors such as Kaposi's sarcoma and lymphoma are common complications of infection with HIV, and the study of these clearly falls within the NCI mandate. In addition, HIV is a retrovirus—a type of virus most extensively studied for its ability to cause cancer. These circumstances have given NCI a particularly central role in AIDS research. The life cycle of HIV, and the cell biology and immunology of HIV infection are all natural areas for NCI involvement.

Funds appropriated for AIDS research within the IRP now constitute approximately 35 percent of the intramural budget. These include both monies directed to the IRP budget itself and expenditures for contracts at FCRDC. For example, 60 percent of the budget for drug screening by the Developmental Therapeutics Program at Frederick is allocated for AIDS research. Moreover, half of the other contracts supervised by the Developmental Therapeutics Program are for work on AIDS. All told, the IRP of NCI is now spending approximately $213 million on AIDS research annually.

Strengths of NCI Intramural AIDS Research

AIDS research in the IRP of NCI has a laudable history of wide-ranging responsiveness, innovation, and discovery. It is fair to say that, in the early days of the emerging challenge of AIDS, NCI led the way in the research response.

There is a strong rationale for NCI to continue with research on AIDS. First, the quest for remedies to infection with HIV represents a pressing national need that should be addressed by all suitable arms of the research community. Second, as noted above, certain tumors are prevalent in individuals infected with HIV, and these are clearly the province of NCI. Third, the IRP of NCI has historic involvement in AIDS research and brings special strengths to the study of the disease. These strengths include expertise in research on retroviruses in general and HIV in particular; the experience of NCI in drug development, and the commonality of structure that underlies some of the drugs useful against either cancer or AIDS; and the strong program in pediatric AIDS developed in the NCI IRP.

Problems in NCI's Intramural AIDS Program

Early in the AIDS epidemic, NCI had a special role because of its historic position in retrovirology and drug development. However, as the amount of money available for IRP AIDS research rose in subsequent years—and the money for IRP cancer studies declined—AIDS research has come to occupy a larger fraction of NCI IRP efforts. This raises the issue of whether the NCI IRP has become overly dependent on AIDS funding. It also conceals a disappointing decline in support for cancer research within the IRP.

The growth in AIDS funding within the IRP is, in part, attributable to increasingly liberal definitions of what research might be related to AIDS, and it has not been accompanied by effective coordination or strategic planning of the NCI AIDS effort. The failure to coordinate applies to both the IRP itself and interaction between NCI and the Office of AIDS Research (OAR).

The newly established OAR lacks clear jurisdiction over the AIDS budget of the NCI IRP. This is because the IRP budget is considered part of the "commitment base," that is, a portion of the budget which has been obligated and is not subject to negotiation. The OAR has no purview over this base, only over new or additional monies. Thus, only increases in the IRP budget would be considered by OAR, and then only in the year the increases were recommended, after which they become part of the commitment base. The OAR can only use its moral suasion to affect the directions of NCI IRP research in AIDS.

Although it might seem a useful recommendation for NCI to rethink its distribution of AIDS funds between the intramural and extramural programs, the purview of the extramural program is limited to HIV-related malignancies, whereas the IRP has no such limitation. Thus, the ability of NCI to redistribute AIDS funds is largely restricted to the IRP. Reprogramming of NCI IRP funds to the ERP would have to be done by OAR, through other institutes.

Summary and Recommendations

The NCI IRP and contract program in AIDS research is, in aggregate, a large enterprise with limited central direction or control. It has grown from a small number of appropriate activities into a substantial fraction of the NCI IRP. This makes the NCI IRP particularly vulnerable to any reduction in AIDS funding. The AIDS program also lacks a clear rationale, and some of its elements seem thematically inappropriate.

1. The NCI DDIR and DDER should be responsible for coordinating AIDS research within the Institute.

2. NCI should undertake an expeditious and comprehensive review of all of its AIDS research. This review should be done in cooperation with the Office of AIDS Research (OAR), which has the mandate to coordinate all NIH AIDS research. The review should focus on quality of programs; redundancy with activities in the ERP, the entirety of NIH, and industry; oversight and management of contract activities; and the future of the NCI IRP if AIDS funding were to decrease. Efforts should be made to redirect NCI funds, gradually and logically, while retaining truly meritorious research on AIDS.

3. The OAR director should have more influence over the use of AIDS research funds within the NCI IRP so that they can be seen as a considered part of the national effort. The Working Group believes that a significant reduction in the NCI IRP AIDS program may be in order, and that the released funds should be able to increase the pool available to extramural research on AIDS, even if that means putting the funds under control of a different institute. The NCI DDIR and DDER should work directly with the OAR Director to allocate and redirect funds as needed.

VIII. NCI AT THE FREDERICK CANCER RESEARCH AND DEVELOPMENT CENTER

The Frederick Cancer R&D Center (FCRDC) is a government-owned, contractor-operated facility located in Frederick, Maryland, approximately 37 miles from the NIH Bethesda campus. The genesis of the FCRDC had its origins in two actions by President Richard Nixon, exemplifying how executive and legislative mandates have influenced the National Cancer Program. President Nixon's executive decision to terminate federal research on reagents for biological warfare vacated a large laboratory facility at Fort Dietrich in Frederick, Maryland. His advocacy of the National Cancer Act provided both the resources and an implicit mandate for NCI to use that facility.

The FCRDC has grown to a point where it now consumes 25 percent of the IRP budget, or a total of approximately $140 million annually. There are three major components to the budget at Frederick: a large support contract, of roughly $95 million (recently recompeted and awarded to Science Applications International Corporation); a contract for the Applied Biosciences Laboratory (ABL)($14 million), which conducts fundamental research on cancer; and funds spent from the intramural budget proper for IRP laboratories located at Frederick. These funds together support a staff in excess of 2,000 of whom perhaps 350 are in the IRP proper. Thus, the FCRDC is a major entity within NCI and should be expected to enhance markedly the research of the IRP.

Strengths of the FCRDC

The FCRDC represents a substantial and complex satellite of the NCI IRP, some of whose components display considerable merit. Both fundamental and translational research are represented by excellent programs. The development of research at Frederick has been facilitated by the availability of ample research space, the productive use of contracts, and a relatively low–cost environment. Moreover, the site appears to have great potential as a core facility for all of NIH.

Problems in the FCRDC

Although the Working Group found evidence that excellent work was under way at the Frederick facility, a significant portion of the research does not appear to be well integrated among the various components of the FCRDC or with aspects of the NCI IRP in Bethesda. Greater opportunities at FCRDC for space expansion, hiring, and flexibility in operations have led to the growth of its programs, which are only loosely connected to the research program in Bethesda. Of necessity for its own activities, the FCRDC duplicates facilities maintained on the Bethesda campus. This diversion of funds is costly and fails to enrich the overall NCI IRP. Moreover, substantial new construction is now in progress, implying a long-term commitment to the site and discouraging thoughts of appreciably downsizing, or even closing, the facility.

The various components of the FCRDC do not comprise a coherent whole. They are not well integrated among themselves or with other aspects of the IRP of NCI. ABL itself is a successful research unit, intellectually self contained, productive, and well regarded. But it does not serve the IRP directly and appears to have little impact on it. A number of truly intramural laboratories are also situated in the Frederick facility. Their location at Frederick has no strategic purpose: it is simply a means by which to find more space, and many of the affected scientists now find themselves intellectually isolated from the main intramural program.

The BRMP represents one intramural entity that has thrived at Frederick. It has developed a self-contained unit, with both laboratory and clinical components. Its relatively remote location, however, deprives the IRP mainstream of what could be a strong positive influence on the tenor and quality of clinical and translational research. As one example, the Working Group notes that the BRMP presently makes little contribution to clinical training, even though this is one of the more vigorous elements in the intramural clinical program.

Elimination of these problems should be a major priority of NCI. Their resolution will require time and cannot be accomplished in one phase, given the present limitations of space on the Bethesda campus.

Summary and Recommendations

NCI activities at Frederick are not well integrated, either among themselves or with other aspects of the IRP. For programmatic and budgetary reasons, it would be wise to reorganize and consolidate the Frederick programs, as follows.

1. The Frederick facility should be a core facility, a "cost-effective center," for the entire NIH. The computer center, drug screening and development programs, and animal facilities at the Frederick center could serve many NIH needs.

2. The Working Group recommends that three components of the Frederick unit be moved to Bethesda, in the following order of priority.

    a) All clinical and laboratory components of the BRMP should be moved to the Clinical Center. The production facility could remain at Frederick. The Working Group repeats this recommendation here in order to emphasize that it was reached from two different vantage points. (See also Clinical Research in the IRP.)

    b) Return the remainder of the noncontract IRP operation to the Bethesda campus.

    c) When feasible, the operations of the ABL program should be moved to the Bethesda campus. Every effort should be made to retain current ABL operating practices. Relocation of ABL to Bethesda would dramatize the need to achieve parity in salary and benefits between federal workers and contract employees. The Working Group recognizes the difficulty of such a relocation, but believes it would be in the best interest of the NCI IRP over the long term.

IX. DRUG DEVELOPMENT IN THE IRP

The development of effective therapeutic agents remains one of the most challenging and important pursuits in cancer research. The NCI IRP has a long and meritorious history of research in drug development. Much of this activity takes place via in-house research programs and extramural contracts in the Division of Cancer Treatment's Developmental Therapeutics Program (DTP).

Strengths of Drug Development in the IRP

The facilities and programs for drug development and testing in the IRP have become an international resource, available to academic and commerical investigators alike. Examples include a distinctive screen for cancer therapeutics, a facility for the extraction and banking of natural products, and pioneering work on therapeutic agents for AIDS.

Problems in Intramural Drug Development Activities

A major problem identified by the Working Group is the fact that the resources of the drug development programs in the NCI IRP have been underutilized by both the intramural and extramural communities of NCI. Drug development activities are intellectually isolated, in part because most of the effort is based at Frederick and in part because of failure to reach out to a larger community of scientists. Perhaps as a result of this isolation, the program has not displayed much flexibility in its tactics and strategies. Failure to communicate with a broader community of scientists denies NCI its potential to serve as a national resource in drug development.

The Working Group also identified problems with accountability and review. Drug development programs appear to have less than adequate cost control, and extramural contracts administered by the DTP have escaped all but the most superficial review for mission, quality, and cost effectiveness.

Finally, the progam has only limited support from medicinal chemistry, a crippling flaw that should be corrected.

Summary and Recommendations

The development of effective therapeutic agents is one of the most challenging and important pursuits in cancer research. The justifications for NCI's historical involvement in drug development are numerous and persuasive, but have been challenged lately. Critics have questioned the relevance and appropriateness of the program, and the scientific credibility of some of its methods and approaches to drug discovery. The Working Group has reviewed the drug development activities of the NCI IRP and makes the following recommendations.

1. The Developmental Therapeutics Program at NCI should be continued.

2. Serious consideration should be given to how NCI's drug development programs could become core facilities for the entire NIH. Thus, its drug development capabilities could be made more broadly available for research on a variety of diseases. Why should this unique facility be supported in the future by NCI alone? For example, there has been a justifiable increase in the use of this resource for AIDS research, and this should be reflected in the way the facility is funded.

3. The responsible BSC should be instructed to review the viability, progress, direction, and orientation of NCI's intramural drug development programs. In particular, with the assistance of additional extramural experts, BSCs should explicitly review the overall mission of the Developmental Therapeutics Program at intervals of three years.

4. Standard review of individual investigators should proceed as elsewhere in the IRP.

5. Although concerns have been expressed about the applicability of the new tenure policy to investigators in drug development, the Working Group found no reason to believe that this policy will adversely affect scientists

working in drug development programs.

6. The extramural contracts administered by the IRP require full review carried out periodically and systematically. The reviews should be conducted by the appropriate BSC, assisted by scientists from the academic and industrial communities, and should examine the goals of accelerating and improving preclinical drug development and appraising resource allocation.

7. Collaborative opportunities related to the drug screening program should be increased and accelerated within NIH and beyond. There needs to be a considerable increase in communication and collaboration between scientists in the Developmental Therapeutics Program and those in the rest of the NCI IRP and ERP, especially with regard to the availability of the natural products collection and the screening capacity.

X. IMPLEMENTATION PLAN

In 1994 the EAC concluded its report by requesting a formal plan for implementation within on year.

Similarly, the Working Group recommends that NCI submit an implementation plan to the NCAB at the time of the Board's May 1996 meeting. After May 1996 the NCAB should review the progress of the implementation plan annually until it deems review to be no longer necessary.

XI. CONCLUSION

The Working Group has offered more than 60 recommendations designed to improve the quality and efficiency of the NCI IRP. Some of these recommendations are straightforward and require only will and energy to implement; many echo recommendations in previous reports that have gone unheeded. But, in the spirit of the IRP, other recommendations "push the frontier" of precedent, convention, habit, logistics, received wisdom, and perhaps even statute.

The Working Group offers all of these recommendations in the spirit of adventure and urgency. The NCI is a large and vital public resource, poised for change. All of those who care for the Institute should be willing to look at it from a new perspective, to see how it might be reshaped so as to better seize the day and meet the future. Recent progress in research has made the eventual conquest of cancer a realistic prospect. The best hope for realizing that prospect is NCI. This requires that we make the Institute the best that it can be.

APPENDIX A: List of Acronyms

ABL	Applied BioScience LaboratoriesAcquired Immunodeficiency Syndrome
AIDS	Acquired Immunodeficiency Syndrome
BRMP	Biological Respopnse Modifiers Program
BSC	Board of Scientific Counselors
DCBDC	Division of Cancer Biology, Diagnosis, and Centers
DCE	Division of Cancer Etiology
DCT	Division of Cancer Treatment
DDER	Deputy Director of Extramural Research
DDIR	Deputy Director for Intramural Research
DTP	Developmental Therapeutics Program
EAC	External Advisory Committee
ERP	Extramural Research Program
FTE	Full-time-equivalent
FCRDC	Frederick Cancer Research and Development Center
IRP	Intramural Research Program
NCAB	National Cancer Advisory Board

NCI	National Cancer Institute
NIH	National Institutes of Health
NNMC	National Naval Medical Center
OAR	Office of AIDS Research

APPENDIX B: Meeting Dates of the Working Group

October 27, 1994

December 6-7, 1994

February 15-16, 1995

March 8-10, 1995

April 11-13, 1995

May 1-2, 1995

APPENDIX C: List of Persons Appearing Before the Working Group

Carmen Allegra, M.D.
Chief
NCI-Navy Medical Oncology Branch
Clinical Oncology Program, DCT, NCI

Philip Amoruso
Director
Office of Administrative Management, NCI

Larry Arthur, Ph.D.
Director
AIDS Vaccine Program
Science Applications International Corporation, NCI-FCRDC

Susan Bates, M.D.
Senior Investigator
Molecular Therapeutics Section, Medicine Branch
Clinical Oncology Program, DCT, NCI

Clara Bloomfield, M.D.
Chairperson
Board of Scientific Counselors, DCT, NCI

Michael Boyd, M.D., Ph.D.
Chief
Laboratory of Drug Discovery Research and Development
DTP, DCT, NCI

Samuel Broder, M.D.
Director
NCI (retired)

Bruce Chabner, M.D.
Director
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Edward Chu, M.D.
Senior Investigator
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William Paul, M.D.
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Office of AIDS Research, NIH

Barry Pierce, M.D.
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Maxine Singer, Ph.D.
President
Carnegie Institution of Washington and
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Sandra Smith-Gill, Ph.D.
Women's Scientist Advisor
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Edward Sondik, Ph.D.
Acting Director
NCI (formerly Acting Deputy Director, NCI)

George Vande Woude, Ph.D.
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Harold Varmus, M.D.
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Robert Wittes, M.D.
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APPENDIX D: Data Collected and Site Visits

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April 27, 1995 - Developmental Therapeutics Program, Division of Cancer Treatment, NCI-FCRDC, Frederick, Maryland, and Building 37, NIH, Bethesda, Maryland.