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Cancer March: Interim Report-Recommendations of The March Research Task Force

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INTERIM REPORT*

Recommendations of

THE MARCH – Research Task Force

Commissioned by

THE MARCH – Coming Together to Conquer Cancer

September 25-26, 1998

September, 1998

NOT FOR RELEASE OR DISTRIBUTION

* Final Report Pending

THE MARCH - RESEARCH TASK FORCE REPORT

REPORT OVERVIEW

- ❖ Background – A Report commissioned by The March to determine the status of cancer research and what would be required to accelerate progress and create a real “war” to conquer cancer – assuming availability of required resources. Over 165 leading basic and clinical scientists, executives, survivors and advocates from the leading academic cancer centers and private industry – working in 13 Subcommittees to develop recommendations that would cover the scope of cancer research from basic and clinical research to prevention and quality of life.
- ❖ **The news from this Task Force is in the numbers. Cancer is an “iceberg” that will surely become a major healthcare crisis in the next 10 – 20 years unless we attack the problem “head-on” right now.** The undeclared current and future cancer epidemic is neither fully appreciated nor understood by most of the Nation – including our congressional leaders.
- ❖ At current rates, cancer incidence will increase conservatively by nearly 30 % and deaths by over 25 % on an annual basis in the next 10 years, with a total healthcare financial burden of over \$ 200 billion annually. In 25 years these numbers, unchecked, will be even more staggering.
- ❖ **We must take action to change this future now** – if we continue with business as usual, funding cancer research at a level that employs 1 penny from every \$25.00 in taxes paid, we will change the not face of this looming epidemic significantly.
- ❖ The March Research Task Force believes that we can change the future. It is recommended that we **set a new course to conquer cancer - with a goal of funding cancer research at a level of \$ 10 billion per year in five years, beginning with a doubling of the current \$ 2.5 billion NCI budget to \$ 5.0 billion in 1999 and increase this budget by 20 % per year for the next four years.**
- ❖ The Research Task Force projects that if its’ recommendations are implemented and the resources are provided that **cancer incidence could be reduced by 20% in 10 years and 30% in 20 years, with deaths from cancer reduced from 25-40 % during the same period. – 150,000 – 225,000 lives each year.**
- ❖ Timing is critical. **We have unprecedented opportunities to make essential progress in all areas of cancer research now.** To that end, the Research Task Force recommended the following:
 - Increase funding for investigator-initiated basic, clinical and behavioral research – the bedrock of our international capability in biomedical research to continue the pace of discovery. **Increase the level of funding for investigator- initiated research to 45%.** Place increased emphasis on underfunded areas such as

clinical, behavioral and psychosocial research and address issues of research on cancer in minorities and underserved populations. Fund new research areas such as chemical-cellular biology. **Recommended five-year investment target - \$ 3.0 billion.**

- **Link discovery and commercialization of new cancer therapeutics** together through a public-private consortium that can validate new cancer targets and accelerate preclinical and clinical development. Provide incentives such as periods of exclusivity and tax credits to fully engage the private sector. **Five-year investment target - \$ 1.2 billion.**
- **Fund a major national initiative to accelerate the development of early detection technologies** for cancer, especially the use of markers for risk profiling, and develop public-private partnerships to commercialize these technologies. Educate the public and make these new technologies broadly available – especially to minority and medically-underserved populations. **Five-year investment target - \$ 1.3 billion.**
- **Double funding for cancer prevention, especially in areas such as diet and chemoprevention,** and establish “centers of excellence” established to support a proactive national initiative in cancer prevention. Fund or co-fund the large expensive clinical trials required to evaluate cancer prevention agents, so that the private sector can be engaged in the discovery and development of these agents.

As part of this national prevention program – **develop and implement a nationwide tobacco research and control initiative.** Five-year investment target for cancer prevention - \$ 1.5 billion.

- **Increase support for research in psychosocial and behavioral research to improve symptoms management and improve quality of life for cancer patients.** Place special emphasis on the development of **agents to manage pain in cancer patients and end of life symptoms management.** **Five-year investment target \$750 million.**
 - **We must support the research required to understand why cancer occurs in disproportionate rates in certain minority and medically underserved populations such as the poor and elderly. We must insure that new medicines and technologies are applied across all populations to reduce cancer incidence and mortality.**
- ❖ To build the infrastructure and develop the capabilities to translate the potential of recent discoveries into new products and technologies to cure and prevent cancer; we must address some key issues. It is critical that we develop a new culture to facilitate the synergy of basic and clinical scientists through “centers of excellence” for translational Research.” In parallel we must develop a new collaborative system to develop and commercialize new cancer therapeutics, preventives and early detection

technologies that optimizes the strengths of the private, academic and private sectors. To accomplish these goals, we ,must:

- **Provide incentives (tax credits, market exclusivity, patent extension) to increase the participation of the private sector as partners with the federal and academic sectors to create the public-private partnerships required to ultimately conquer cancer.**
- **Develop a comprehensive and responsive national cancer clinical trials system and increase the number of patients enrolled in approved clinical trials from the current 2% to 10% as quickly as possible. Create a training program for young clinical investigators and support the infrastructure required by the cancer centers to implement this program, along with new funds to support individual investigator initiated research to perform clinical trials research. Five-year investment target - \$ 705 million.**
- **Empower the National Cancer Institute to be a leader and a full partner in this new “war” to conquer cancer by increasing its flexibility and readiness. Remove administrative and policy constraints either through “reinvention” and/or application of a new model to allow the Agency to participate in and support the implementation of these recommendations.**

The message is – we can change the future but we must begin NOW.

EXECUTIVE SUMMARY

Background

Cancer is one of the most complex and tragic diseases that humankind has faced. It is also in a very real sense an “iceberg”, with most of the future devastation from the disease neither envisioned, appreciated, nor understood. Cancer has reached epidemic proportions in the United States, with an estimated 1,228,600 new cases and over 560,000 Americans lost in 1997 at an annual economic cost of over \$104 billion. If these rates continue, one quarter of our population will die from the disease. The effect of the changing demographics in America and our aging population will cause cancer rates to reach staggering proportions as early as 2010 with the incidence of cancer conservatively estimated to increase by 29% and deaths by 25% at an annual cost of over \$200 billion. It is even more sobering to realize that these statistics do not reflect the pain, suffering, emotional desolation and economic devastation that cancer inflicts on its victims, especially the minority and medically underserved populations such as the poor and elderly. **Although defeating cancer remains in every sense a daunting task, we can change the future. We now have unprecedented opportunities to achieve essential progress against cancer, but only if we move with real urgency to provide the necessary resources**

President Richard M. Nixon recognized that cancer would take an ever-increasing number of American lives, when in 1971 he signed into law the National Cancer Act, and declared a “war” – to eradicate cancer. This was a bold first step, unfortunately a “war” was never fully launched or funded in relation to the complexity, size and cost of the problem. We currently invest approximately \$2.5 billion per year in cancer research through the National Cancer Institute (NCI), which represents only 2% of the economic burden of the disease and translates to about 1 cent invested in research for each \$10.00 paid in taxes.

We could not have predicted in 1971 that solving the mystery of cancer would require that we literally “unravel” the basic secrets of normal life processes. Despite chronic underfunding, in the ensuing years our ever-increasing understanding of the fundamental differences between normal and cancer cells has finally given us the weapons we need to conquer cancer and many other diseases. It is an optimistic and hopeful time in cancer research.

This hope provided the energy for individuals from all walks of life to unite in a movement called “The March” – Coming Together to Conquer Cancer (hereafter The March). As part of The March, a group of experts that included basic and clinical scientists, behavioral and psychosocial researchers, cancer survivors and executives from academia, government, industry cancer research organizations and professional societies came together as “The March” Research Task Force to define what is essential and possible in all areas of cancer research.

The following recommendations are fully supportive of the National Cancer Institute's (NCI) Bypass Budget that delineates the needs and opportunities of the Nation's National Cancer Program. The Research Task Force recommendations represent broad research initiatives and actions needed to fully support an accelerated "war" to address the looming cancer crisis and ultimately to cure and prevent cancer for all Americans. The projected costs of these initiatives are estimates based on the status of current areas of cancer research and recommended levels of effort required.

Opportunities for Essential Progress

Basic Research. Most of our past investments in cancer research were utilized to build an incredibly powerful discovery resource, and the experts agree that we must accelerate our efforts to achieve the additional necessary breakthroughs required in basic research. For example, genetic changes in cancer, mechanisms by which cancer cells become immortal, pathways by which they signal and communicate and the process by which tumor cells spread all represent high potential pay-off areas that require increased support. The foundation of our unparalleled capability in basic biomedical and behavioral cancer research is the ideas that come from individual scientists. Unfortunately only 25% of approved grants are currently funded and many excellent ideas and investigators with great potential are lost. **We must increase this level to a minimum of 45% and fund more investigators and all areas of cancer research, especially in historically underfunded areas such as cancer prevention, behavior and psychosocial research. It is also critical that we attract young and minority investigators to cancer research and fund the most innovative ideas. The complexity of cancer and convergence of disciplines mean that the future belongs to teams of scientists working together to make discoveries and translate them into clinical applications. Therefore, current mechanisms to fund multidisciplinary research teams and "centers of excellence" (focused around the strengths of the Nation's cancer centers) to accelerate translational/clinical research must be expanded and new mechanisms developed as appropriate.**

Cancer Therapeutics. Basic research has provided us with a wealth of exceptional opportunities to develop new and better drugs to treat cancer successfully. . Drugs can now be more rationally designed and the process accelerated through the use of new technologies such as "combinatorial chemistry", computer modeling and "high-throughput screening". A new concept of chemical-cellular biology holds the promise of allowing us to convert our knowledge of biological molecules into cancer drugs that will be more effective in humans. There are hundreds of new compounds being studied in academic and private laboratories for application to the treatment of cancer, but new resources must be provided to realize these benefits for cancer patients. **There is currently an unprecedented necessity and real opportunity to link discovery to commercialization of new cancer therapeutics by forming a public-private consortium that can validate cancer targets and accelerate new cancer drugs through preclinical and clinical development. We must provide incentives, such as periods of exclusivity and tax credits, to fully leverage the strengths of the private sector, especially in the development of new cancer therapeutics. To fully**

implement this concept we must also empower and fund the NCI and other federal agencies and academic sectors to participate fully in this partnership.

Early Detection of Cancer. Imagine visiting your physician in the future and having your cancer risk determined from a single drop of blood. Our increased understanding of the genetic and other changes that occur in cancer cells has provided “signposts” or markers that will facilitate the development of risk profiles and screening tests to determine cancer risk. Once risk is determined, intervention strategies can rationally be used to prevent cancer. **Funding a national initiative to accelerate the development of these early detection technologies and developing public-private partnerships to make these tests widely available will save hundreds of thousands of lives each year.**

Cancer Prevention. Cancer is a preventable disease. Furthermore, cancer prevented is cancer we do not need to treat. Cancer prevention is multifaceted, ranging from research on behavior modification and diet control to chemoprevention and environmental exposures. For example, the potential causative role of the environment in many forms of cancer must be thoroughly studied. **Overall funding for cancer prevention research should be doubled and “centers of excellence” established to accelerate a proactive approach.** Chemoprevention research can be performed using the same public-private model that we will employ for developing cancer therapeutics, but we must be prepared to **pay for the large, expensive clinical trials required to engage the private sector** in developing chemopreventive agents for cancer.

Success in cancer prevention depends in large measure on the extent to which research can help people change destructive behaviors such as smoking and poor diets. To reduce cancer incidence and mortality from all tobacco related cancers, **we must develop and implement a major new nationwide tobacco research and control initiative.**

Improved Quality of Life. We can never forget the suffering that individuals face because of cancer, and through research, we can control the pain, fatigue, depression and nausea that so often destroy the quality of the lives of cancer patients. **With the necessary additional resources, we can understand and control the physical symptoms of cancer and the side effects of cancer therapies.** Psychosocial and behavior research related to cancer has not received adequate research attention in the past, but we have the opportunity to change this picture by **supporting important grants in these areas, training more scientists and addressing critical research issues such as controlling symptoms at the end of life.**

Minority and Medically Underserved Populations. To truly understand and impact the current and looming cancer epidemic, we must realize that the complexity of cancer goes beyond the multi-factorial nature of the disease and the mystery of the cancer cell. **We must support the research required to understand why cancer occurs in disproportionate rates in certain minority and medically underserved populations such as the poor and the elderly.** We must apply what we already know from previous research, such as breast, cervical and colorectal cancer screening technologies, to detect and treat cancer earlier in these populations. In addition, we must ensure that the

technologies and new medicines that derive from the discoveries and advances in clinical research detailed in these opportunities for progress are applied to all populations, so that rates of cancer incidence and mortality cannot only be reduced, but also equalized across all populations. Finally, we must support high quality registries to provide a basis for cancer control and assessment of our progress.

Necessary Actions

The results of past investments have produced a wealth of new opportunities to develop new medicines and technologies for translation to cancer patients, but to realize these gains we must take immediate actions to remove a few key barriers. In short, we must develop novel public-private partnerships, increase the participation of cancer patients in clinical trials, train the required cadre of clinical investigators and empower the NCI to spearhead a full national effort to accelerate progress to cure and prevent cancer.

A New Culture and a New “System”. We need to establish a new culture where “translational” research can flourish – centers of excellence that leverage the basic and clinical research strengths of our National cancer centers. We must also urgently develop a new system to translate laboratory discoveries into new products and technologies to cure and prevent cancer. This will require new models that optimize and speed this process. The current system is too slow and significantly underfunded to expedite laboratory discoveries into new drugs and technologies that will reduce the incidence and mortality of cancer. There is a real and immediate need to establish highly effective relationships and partnerships among the three sectors involved (government, academia and the private) with a special focus on leveraging the strengths of the private sector in our national effort to conquer cancer. To do this we need to **offer incentives such as increased periods of product exclusivity and federal tax credits, and take specific actions such as support for large, expensive prevention clinical trials.**

Reform and Expand Cancer Clinical Trials. Our clinical system for translating discoveries has not grown in accordance with need, and in fact the national Cooperative Groups that perform cancer clinical trials require a great deal more support. **An unacceptably low 2% of cancer patients are enrolled in clinical trials to test new agents. This number needs to be increased to 10%** through better public education, a simplified enrollment process and incentives for clinical cancer researchers to enroll cancer patients in trials. Brilliant young clinical investigators are pursuing careers elsewhere because of the lack of funds to insure training, research or ongoing career support. **A renewed national effort at an unprecedented scale must be made to attract and train these new clinician researchers and provide them the necessary resources to do their work.**

Empower the NCI. Finally, the implementation of the recommendations of the Research Task Force requires that the National Cancer Institute will have the increased resources, flexibility and authority required to plan, coordinate and implement the unified national initiative to cure and prevent cancer envisioned by the National Cancer Act. The NCI must be able to make rapid decisions, provide expeditious support for critical research

and our Nation's cancer centers and build the partnerships required to leverage discoveries into the clinic and, subsequently, into new products to cure and prevent cancer. **This required level of "readiness" means that the NCI must be freed of burdensome policy constraints and empowered in all respects. In fact, it should be considered as a potential national "reinvention laboratory" and/or empowered through the use of other models employed to meet similar goals.**

Return on Investment

We must immediately address the increasing burden of cancer that will hit America the hardest in the next 10-25 years as the population ages and the demographics of the country changes. The Research Task Force recommends that we initiate a National strategy – Cancer Reduction 2010-2025 – and incrementally increase our investment in all areas of cancer research. It is specifically recommended that we **increase our annual investment in cancer research to \$10 billion over the next 5 years. Implementation would begin in 1999 by doubling the current NCI budget to \$5.0 billion and increasing the budget by approximately 20% per year for the ensuing five years.**

The Research Task Force believes that if its recommendations (and those detailed in the Bypass Budget of the NCI) are implemented and the required resources are dedicated now, that required reductions in cancer incidence and mortality can be achieved. At current levels, it is anticipated that **cancer incidence could be reduced 20% in 10 years and as much as 30% annually in 20 years. This translates into 246,000 and 369,000 fewer cases of cancer annually in 10 years and in 20 years respectively. The Research Task Force also projects that deaths from cancer could be reduced from 25-40% over this same 20 year period, a savings of 150,000–225,000 lives each year in the United States and countless lives around the world from the recommended application of research discoveries and research-based initiatives such as tobacco control.**

Everyone working in cancer research feels the excitement and understands the possibilities offered by the vast number of extraordinary opportunities to make essential progress against cancer in all populations now. Through research we have cured several cancers such as testicular cancer, Hodgkin's disease, and certain types of leukemias, and we are hopeful that many more cancers can be cured in the next few years. The clear message from the members of the Research Task Force is - **don't let this moment pass; seize this opportunity to launch an inclusive, national, full-scale "war" to eradicate cancer for all Americans NOW.**

As a Nation, we know what this challenge means and how to meet it. We have done it before and we can do it again - to defeat cancer. We have supported the level of commitment it took to win World War II, put a man on the moon and triumph in the Gulf War. These campaigns required decisive commitment by our government and the American public, full engagement of our best research minds in the academic, government and private sectors, freedom to act by the federal sector, full participation and support from the private sector and dedication of the required resources. A full-scale, coordinated national effort to cure and prevent cancer will require no less.

THE MARCH RESEARCH TASK FORCE

The March – Coming Together to Conquer Cancer, hereafter “The March,” is an unprecedented grass-roots movement and historical national event dedicated to the conquest of cancer. The March unites cancer survivors, families, scientists and the public in an urgent campaign to place the prevention, treatment and cure of cancer at the top of research and health care priorities for every government official and American citizen.

The Research Task Force came together in support of The March to consider the wide range of diverse and related areas that comprise cancer research today. Their “charge” was to distinguish the essential needs and exceptional opportunities in basic and clinical research that are critical to addressing the current and looming crisis of cancer incidence, mortality and health care costs. The group focused on the identification of key barriers that must be removed if we are to reap the rewards of our past investments in basic research and accelerate progress against cancer now. Finally, each subcommittee gave serious consideration to particular research issues in minority and medically underserved populations and to underfunded areas of cancer research.

The Research Task Force consisted of approximately 180 leading scientists from the academic and private sectors and cancer survivors and advocates working together in 13 subcommittees. The focus of all of the groups was the same, - determine what it would take to expedite the conquest of cancer through research, if we were limited only by creative ideas and solutions – and if adequate resources were made available.

The following report details the exceptional opportunities and initiatives that **clearly justify a significant, immediate increase in our national investment in cancer research**. The Research Task Force recommendations capture an overall estimate of the breadth and depth of research and additional resources required to fully support an accelerated “war” to cure and prevent cancer for all Americans. These recommendations complement the National Cancer Institute (NCI) and its programs, specifically the annual Bypass Budget which delineates the needs of the NCI and recommends extraordinary opportunities for progress as a basis for its annual plan and budget request. The Research Task Force fully endorses the NCI Bypass budget.

INTRODUCTION

Cancer is a feared and deadly enemy. The current and future burden of cancer is staggering, both in terms of its human toll and economic impact. The American Cancer Society (ACS) estimates that in 1997 alone, 1,228,600 new cases of cancer were diagnosed and 564,800 Americans (1,500/day) died from their disease. To put cancer deaths in perspective, the number of our citizens that die each year from cancer exceeds the total number of Americans lost to all of the wars that we have fought in this century. The current economic burden of cancer is estimated at over \$104 billion per year, including medical costs, lost productivity and death.

As we look forward into the next century, at current rates, it is projected that one-half of men and one-third of women in America today will be diagnosed with cancer at sometime in their lifetime and **one-quarter of our population will die from cancer**. These statistics are extremely daunting in terms of increased health care costs, especially given the current managed care environment, and an estimated 40 million Americans under the age of 65 who have no health insurance.

The March is about ending the fatalism and apathy that cancer cannot be conquered. It is also about coming together as a nation to create a turning point in our long struggle to defeat cancer. **The March Research Task Force believes that cancer can be cured and ultimately prevented, and the time to wage a real “war” to achieve these goals is NOW.** Based on past success and future research opportunities, we can envision that patients with cancer will eventually be cured, or their disease will be treated as a chronic illness with good survival and quality of life, and that eventually many cancers will be prevented. Progress through cancer research will provide the weapons we need to realize this vision and win the numerous battles that must be fought to achieve the unified goal of The March - “No More Cancer.”

Thus, the Research Task Force turned its attention primarily to the extraordinary research opportunities to accelerate progress against cancer that have come directly from our past investments in cancer research – and they are numerous. The Task Force focused on: extraordinary basic and clinical research opportunities to expedite progress against cancer in all populations; improving the quality of life of cancer patients through psychosocial and behavioral research; building novel partnerships and engaging the private sector in all aspects of cancer research; and developing a “state-of-the-art” clinical trials system. The recommendations also highlight the real need to empower the major federal institution charged with leading our national effort to conquer cancer, the National Cancer Institute (NCI).

VISION OF A “WAR” TO CONQUER CANCER (1971-1998)

Recognizing the terrible specter and ever-increasing burden of cancer, President Richard M. Nixon declared a “War” against cancer in 1971, when he signed into law the National Cancer Act. This Act strengthened the National Cancer Institute (NCI), made the Director

of the NCI a presidential appointee, to be confirmed by the Senate, and created a budget process called the “Bypass Budget,” which goes directly to the President for transmittal to Congress. The Bypass Budget was created to provide a mechanism whereby the NCI Director could define the annual funding level needed to wage a full-scale “war” on cancer.

The National Cancer Act was a bold step, but unfortunately a “war” was never fully launched or funded in relation to the complexity, size and cost of the problem. We currently invest approximately \$2.5 billion per year in cancer research through the NCI. This investment represents only 2% of the current economic burden of the disease and translates to about 1 cent invested in research for each \$10.00 paid in taxes.

Despite the fact that our national commitment and resource allocations to create and sustain a “war” on cancer have never matched the magnitude and complexity of the problem, we have made astounding advances in cancer research with the programs funded through the NCI. During the past 25 years, and especially the past 10 years, our fundamental understanding of the basic molecular biology and genetics of cancer cells has virtually exploded, giving rise to an age of biology that will surely provide new opportunities to conquer cancer and many other diseases.

We have successfully cured some cancers, such as selected types of leukemia and testicular cancer in young people, and for the first time, the NCI reported in 1997 that overall the cancer death rates had fallen slightly between 1991 and 1995. This progress is also reflected in recent editions of the NCI Bypass Budget highlighting discoveries from basic research that provide us with unprecedented numbers of opportunities to develop new technologies and medicines to detect, treat and prevent cancer.

CANCER DEFINED

Research is unraveling the cloak of mystery and complexity around cancer. We now know that normal cells are programmed much like a computer through their genetic makeup (genes) to carry out specific functions, including when to divide. Normal cells become cancerous, or transformed, when abnormal changes occur in the genes to the extent that they no longer respond to normal control mechanisms and divide in an uncontrolled fashion. The genetic changes that lead ultimately to cancer can accumulate over a period of 10 years or more.

Cancer is not a single disease but a complex group of more than 100 different diseases. To add to this complexity, there are differences even within a specific type of cancer. For example, one type of breast cancer might have a set of three altered genes, while another type might have a different combination. Understanding all of the genes that can cause cancer, and how to type specific cancers to determine which genes are altered, is critical to designing new approaches to treatment and prevention.

One of the most devastating aspects of cancer cells is their capacity to spread to other organs and tissues within the body. This process of moving from the original site into other organs is called metastasis. While normal cells are programmed to remain fixed to perform their functions, changes in cancer cells allow them to move into organs and grow at the expense of normal cells. This ability to metastasize makes cancer extremely dangerous, as normal organs can be damaged to the point of being unable to perform normal functions and lead to the death of the patient. During the past few years we have made significant strides in understanding the basic biology of the metastatic process, and there are currently opportunities to design and develop new rational approaches to slow or stop the spread of cancer and eventually prevent it completely.

FUTURE BURDEN OF CANCER

Despite our increasing understanding of cancer, unless we act with urgency now, at current rates the human and economic cost to the United States is likely to become unmanageable within the current health care system in the next 10-20 years. For example, if current rates are used to calculate the incidence rate (number of people per 100,000 who develop cancer during a year) of cancer in 2010, the number of estimated new cases is expected to increase by 29% and the number of expected cancer deaths will increase by 25%. These projections are extremely conservative, as they do not account for changes in demographics and the increasing age of our population in 2010 and beyond. Using these conservative values, the projected economic burden due to the direct cost of medical treatment will increase to approximately \$65 billion per year and the “productivity” cost (lost economic productivity due to disability and death) will grow to over \$125 billion for a total expected economic burden approaching \$200 billion annually in 10 years.

Looking beyond 2010, cancer incidence and mortality in our aging U.S. population become even more staggering. Unless we act now to dramatically change current cancer incidence and death rates, we can expect over 2.0 million new cancer cases and 1.0 million deaths per year by 2025.

These estimates represent individuals that will suffer and die from cancer unless we do a great deal more now. Moreover, the brunt of these statistics will be borne disproportionately by those least able to bear it – minority and medically underserved populations such as the poor and elderly. **Launching a full-scale national effort to accelerate all of our efforts to cure and prevent cancer requires that we commit to a level of federal funding for cancer research that is several-fold higher than we are currently spending.** Unless we make this commitment now, we will be unable to significantly alter the inevitable increase in new cancer cases and deaths that will surely be a health care crisis of unimagined proportions.

STATUS OF CANCER RESEARCH: UNPRECEDENTED OPPORTUNITIES FOR PROGRESS

Fortunately this is a remarkable time for biomedical research and our national effort to eradicate cancer. Every day newspapers and television report new, exciting treatments and prevention approaches for cancer. Clearly it is a time for optimism. The NCI has spearheaded and supported new groundbreaking programs in all areas of cancer research, especially related to “unraveling” the intricate genetics and molecular biology of cancer cells. As a result of our past investments through the NCI, there are exceptional opportunities to make essential progress in basic and clinical cancer research. We can improve the survival of cancer patients and provide a better quality of life than experienced with earlier treatments. With an increased understanding of the process by which normal cells are transformed into cancer cells, we are truly on the brink of being able to prevent cancer, and our knowledge of the “signature” of cancer cells gives us enormous capability to detect cancer early.

The Research Task Force strongly endorses the four extraordinary investment opportunities delineated in the NCI Bypass Budget for FY 2000. These include broad, national programs to: identify and study all of the genes involved in human cancer, including the development of support and infrastructure to exploit these discoveries for all of our citizens; develop preclinical models of cancer so that cancer development can be studied and new prevention, detection and treatment strategies can be tested; pursue groundbreaking research in the imaging of tumors to significantly increase progress in early detection; and to utilize the molecular “signature” of cancer cells to detect tumors at their very earliest stages.

Research is a process, beginning with basic research, which produces discoveries that must be developed, “translated” and made available through the private sector for use in humans. This process requires the active participation of the government (NCI), academic and private sectors to move these discoveries into clinical applications. In the past, the preponderance of cancer research has focused by necessity on very basic questions to develop an understanding of cancer at the molecular level and we have been successful.

These past investments have produced a wealth of new opportunities to develop new medicines and technologies for translation to cancer patients, but **to realize these gains we must urgently develop a new culture. There is a real and immediate need to establish novel relationships and partnerships among the three sectors involved, with a special focus on significantly increasing the participation of the private sector in our national effort to conquer cancer. The NCI must be free to participate easily in these new partnerships, so we must do everything possible to relieve the Institute of bureaucratic constraints.**

The following recommendations of the Research Task Force are focused on real and immediate opportunities to accelerate progress against cancer; as well as the key barriers as must be removed to fully exploit these opportunities for current cancer patients,

families and the staggering number of our citizens who will yet fall victim to cancer in their lifetime.

OVERALL RECOMMENDATIONS

REDOUBLE OUR EFFORTS IN BASIC RESEARCH AND DISCOVERY

We Must Accelerate Progress in Basic Cancer Research (Discovery). Although we have achieved a significant basic understanding of cancer cells, there is a great deal left to do. Cancer remains, in every respect, an extremely complex disease – in fact, it is more than 100 different diseases.

Curing established cancer requires killing of tumor cells but not normal cells. We need to learn why and how cells decide to die, and specifically, how to induce preferential death of tumor cells. We have recently discovered that both normal and tumor cells have access to a mechanism called programmed cell death, and finding signals which preferentially induce switches to this program in different types of cancer cells is key to designing new therapies. We know that cancer cells are more genetically unstable than normal cells, and it is this quality that allows tumor cells to rapidly evade the normal growth mechanisms and resist response to drug treatment. We have only very recently begun to understand the cellular processes which underlie this ability to evade therapy. Clearly, more basic research is required to utilize this knowledge to discover new approaches to detect and prevent cancer.

Each cancer initially develops at a specific site in the body and from a specific cell. For example, this cell could be either a lung or colon cell and thus has a cell identity created through a developmental process as the adult body is formed from the fertilized egg. We know very little about this developmental process, which must be important in generating the character of tumors. Surprisingly, we also know very little about how the immune system restricts the generation of either very small early tumors or late-stage cancers. Cancers, like other parts of the body, must be perfused with blood to survive. The growth of the small blood vessels supplying such blood is called angiogenesis, and recent evidence suggests that blocking angiogenesis can block tumor growth. Hopefully this insight can be used to treat cancers. However, more basic science is needed to understand why the angiogenesis process of a tumor is different than that of a normal organ in the body such as a liver. It is this difference that must be exploited in cancer treatment.

Many tumors are restricted to one site in the body and can usually be successfully treated. However, cancer cells commonly acquire the ability to migrate throughout the body and metastasize to other sites rendering local treatment ineffective. We are only now beginning to understand the cellular processes responsible for cell migration and cell targeting to particular sites in the body. Obviously, further basic research is important in designing new treatments.

Modern chemistry has discovered powerful methods to generate and select specific inhibitors of cellular reactions. Such inhibitors can become “guides” to determine the role of that reaction in the biology of the cell. These inhibitors can also be important as pioneer drugs to test the role of the specific cellular reaction in the treatment of cancer. For example, does the pioneer drug preferentially induce the death of cancer cells? If the results were sufficiently positive, sophisticated chemotherapeutic and preventive drugs might be generated from the pioneer-lead drug. Thus, the future interaction of chemistry and the physical sciences with the basic science of cancer research is critical for rapid progress to better therapies and new preventive agents for cancer. This interface among chemistry, physics and molecular biology has given rise to a promising new concept and area of research called chemical-cellular biology.

Recommendations

- ❖ The “bedrock” of the unparalleled biomedical research capability of the United States is the ideas that come from individual scientists. The peer review system, organized and managed by the NCI, identifies the best of those ideas for support. Unfortunately, at current levels we are funding only 25% of the approved grants from these investigators who want to work in cancer research. Young investigators stand little chance of entering this system because of funding constraints, and there is a dearth of minority scientists across the spectrum of cancer research. **The Research Task Force recommends that we appropriate the money to fund a minimum of 45% of these approved grants.**
- ❖ The cure and prevention of cancer will require that scientists from all research disciplines work together in multi-disciplinary teams. **It is recommended that 50% of program project grants be funded** – especially in support of cancer prevention, the new emerging area of chemical-cellular biology, translational and psychosocial and behavioral research.
- ❖ We cannot predict where breakthroughs in science will come from, so we need to be able to move quickly, fund innovative ideas and attract scientists from areas such as physics, chemistry and the computer sciences to work on cancer. The NCI is leading the way in this regard. We should double current support for mechanisms that encourage innovation and recruitment of scientists from other disciplines and **utilize public-private partnerships to bring additional investments into these and other areas of basic cancer research.**

Five-Year Resource Target – \$3.0 Billion

ACCELERATE THE “TRANSLATION” OF IMPORTANT NEW LABORATORY DISCOVERIES

We Must Leverage Current Exceptional Opportunities in Clinical (Also Called Translational or Applied) Cancer Research. Advances in discovery research have

brought us to the most promising and exciting point in the 26-year history of what is commonly referred to as the National Cancer Program. We have unprecedented opportunities to develop new medicines and approaches to prevent, detect and treat cancer. Hundreds of new compounds are under active study in academic and private pharmaceutical laboratories for application to the treatment and prevention of cancer. Discoveries from molecular biology and genetics are providing entirely new approaches to detect cancer and profile the risk of cancer in high-risk and normal individuals. Findings from basic behavioral and psychosocial research could save thousands of lives and reduce suffering in cancer patients now. The fact is that we do not have nearly enough trained scientists and physicians, or the infrastructure and systems required to “translate” these discoveries into clinical applications.

We must act now to provide the resources required to leverage our past investments and create specific national initiatives to accelerate progress in the development of new cancer treatments; pursue novel strategies to detect cancer early; establish a national cancer prevention program; and fully support behavioral and psychosocial research to improve the quality of life of cancer patients. To create an environment in the academic sector where translational and clinical research will flourish requires that we bring basic and clinical scientists together from across key disciplines and diverse areas into “centers of excellence.” These centers would logically be located in our current cancer centers, and represent a new “translational research” culture that could focus on specific cancer sites and/or areas such as drug development.

To realize our goal of accelerated progress to conquer cancer, **it is critical that we act now to create a new overall national system for the “translation” of new discoveries that optimizes and maximizes collaboration and cooperation among academia, government and industry.** Building this new system also requires that we improve access to approved clinical trials and train the required clinical personnel. Lastly, we must fully empower the NCI to spearhead these efforts and act on behalf of the Nation.

Capitalize on Exceptional Opportunities in Cancer Therapeutics - Never have we understood the cancer cell and its myriad pathways as well as we do now. Although there is still a lot to do, through basic research we have developed a working understanding of areas such as the cell cycle, signaling pathways by which the cancer cell transmits information and how tumors make their own blood supply (angiogenesis). Every day we learn more about specific genetic changes in cancer cells, ways that we can detect them and how immune cells respond to these tumor cells. This knowledge has allowed us to develop vaccines and new agents to boost the immune system. Evidence is accumulating that many of the abnormal communication pathways in tumor cells provide rational targets for cancer treatment and prevention. In addition, there are new, exciting ways to rapidly make drugs that are based on our increased understanding of the fundamental biology of cancer cells. For example, computer modeling of specific molecular targets can aid drug discovery. Large numbers of new molecules can now be prepared through a process called “combinatorial chemistry.” We also can rapidly screen large numbers of molecules for activity using a process called “high-throughput screening.”

We need new cancer drugs that specifically kill tumor cells and spare normal cells to maximize the therapeutic effects and reduce damaging side effects. We can improve the scale, speed and effectiveness of the cancer drug discovery and development process through the creation of new partnerships – partnerships between chemists, biologists, clinicians and patients, and among academia government and industry. We need to fully leverage the strengths of the pharmaceutical and biotechnology industries as essential partners in the development of new anti-cancer drugs. They have extraordinary expertise and capabilities in all phases of drug discovery and development, especially the preclinical and clinical phases. We can thereby connect cancer drug discovery to preclinical and clinical development on a national basis and accelerate the process of getting new drugs into cancer patients.

Recommendations

- ❖ **Develop a public-private consortium (academia, NCI and pharmaceutical and biotechnology companies) to review molecules developed in the academic sector and/or proposed by the private sector as potential cancer therapeutics. The Consortium would prioritize and expedite the progress of the most promising candidates through the preclinical and clinical proof-of-concept developmental stages.**
- ❖ **Provide incentives for pharmaceutical and biotechnology companies** to engage in discovery of “lead” molecules for target validation and to perform Phase I and II clinical trials to test new cancer therapies. Incentives to perform Phase III trials for “orphan drugs” should be provided. Overall, incentives could include tax credits, patent extensions and/or market exclusivity.
- ❖ **Provide additional federal funding** for drug discovery and development through mechanisms such as the **National Cooperative Drug Discovery Groups and the new Rapid Access to Interventional Development** programs of the NCI.
- ❖ **Develop novel partnerships and new federal funding mechanisms to provide significant targeted support for key areas of therapeutics research**, especially the promising new field of chemical-cellular biology that will facilitate the conversion of knowledge about biological molecules into drugs that can be effectively used in humans.

Five-Year Resource Target - \$1.2 Billion

Early Detection of Cancer Will Save Lives – Early detection of cancer is our best hope for increased survival and cure of patients with cancer. Imagine in the future visiting your physician for an assessment of your risk for cancer, determined from a single drop of blood. This is no longer a dream – we now recognize many molecular “signposts” or markers that have evolved from our increased understanding of the genetics and abnormal functions of cancer cells. These markers have the power to predict who is at

risk for cancer early enough to intervene so cancer can be treated before it is out of control. These “signposts” will also allow us to follow the progression of cancer in patients to predict recurrence of cancer.

We have the sensitive tools available to develop these screening tests and implement intervention strategies to prevent cancer and/or reduce disease severity. We have opportunities to test for specific changes in genes that are altered in cancer, genes that affect an individual’s ability to break down cancer-causing chemicals, markers of damage related to smoking and environmental exposure and biochemical markers of deficiencies in key nutrients. As a result of the marriage of genetics and semi-conductor technology, “Chips” are being developed that will eventually allow testing for changes in a single gene, or hundreds of genes, and this field is moving rapidly.

To fully exploit these promising leads in early detection and risk profiling, we must test these markers in patients to determine which are most valuable in terms of their specificity, sensitivity and practicality of use. We also need to bring together scientists, clinicians and epidemiologists to test these markers in large clinical populations, especially large observational studies to identify gene-environment interactions.

To fully exploit this technology will require repositories of samples and data to support and accelerate progress in early detection. We must proceed with haste to implement a national program to realize the enormous value of early detection in cancer prevention and determining precisely when to initiate and terminate therapy. **Every effort should be made to apply these new screening approaches to minority and medically underserved populations that bear such a disproportionate share of the burden of cancer.** To proceed with early detection and risk profiling, we must insure through legislative action that this type of information is kept confidential and not used to deny insurance or otherwise discriminate. Lastly, realization of the promise of these powerful new tools for early detection of cancer requires that industry be engaged to commercialize the testing and make it widely available to everyone.

The NCI has proposed a program to expedite progress in this important area as one of its extraordinary opportunities (Signature of Cancer Cells) in the Bypass Budget for FY2000. The Research Task Force fully supports this initiative and recommends that we commit significant resources beyond the NCI request to accelerate the development of these early detection technologies.

Recommendations

- ❖ In keeping with the NCI Bypass Budget, **develop a major national initiative to accelerate progress in the translation of discoveries from basic research into new technologies for the early detection of cancer.** As part of this initiative, develop panels of markers to assess cancer risk, and facilitate early detection.
- ❖ **Determine the required research, resources, regulatory issues and partnerships required** to achieve a national program in risk-profiling and early detection in

individuals at high risk for cancer and in the overall population, and develop a system for implementation.

- ❖ **Provide incentives for the private sector** to commercialize technologies for marker development and risk profiling.
- ❖ Perform small mechanistic studies and larger confirmatory trials that focus on the development of exposure markers and the underlying biological mechanisms to **identify environmental agents that damage DNA and design protective agents based on these studies.**
- ❖ **In cooperation with the Centers for Disease Control (CDC) and other private and public organizations, implement a comprehensive national public education program on the value of screening and risk profiling in the early detection of cancer, with special emphasis on high risk and minority and medically underserved populations.**

Five-Year Resource Target - \$1.3 billion

Defeat Cancer Through Prevention – Our dream is the prevention of cancer in all Americans. Cancer prevention is multi-faceted, and a wide array of approaches must be undertaken now to reduce the cancer burden in both the short and long term. The major areas of prevention research that promise to have a significant impact on cancer incidence, and in certain instances mortality, include behavior modifications in tobacco, nutrition and diet, and chemoprevention. It is likely to be several years before we can fully understand and control all genetic and/or environmentally-induced genetic changes that cause cancer. In the meantime, many lives can be saved by dedicating significant additional resources to the needed basic and clinical prevention research in each of these areas.

The Research Task Force supports the need for a major national, comprehensive tobacco research and control initiative to reduce morbidity and mortality from all tobacco-related cancers. Although prevention of smoking in children and interventions designed to facilitate cessation of tobacco use in adults should be a major focus of this national program, studies on the impact of passive smoking, fetal effects and interactions of nicotine with other carcinogens should also be undertaken. Major emphasis in this research-based tobacco control initiative should be on reducing tobacco related cancers in medically underserved and minority populations.

It is estimated that one-third of cancer is related to poor nutrition and diet. Knowledge of the behavior of cancer cells at the molecular level offers significant opportunities to specifically study and monitor the effects of diet in the prevention of cancer. Specific nutrition research should be pursued in multi-disciplinary teams to develop testable, rationally designed nutrition approaches in clinical trials. In addition, we should apply what we know from prior research on the role of diet in cancer prevention to all populations.

Basic research has provided an encouraging picture for cancer prevention in the future. Knowledge of the changes in cellular pathways and specific genes that occur as cells progress from normal to cancerous states provide targets to develop new chemical agents for cancer prevention. As an example, in a recent study, intervention in women at high risk for breast cancer with a drug called tamoxifen resulted in a 45% reduction in breast cancer in treated patients.

Discoveries from basic research have shown that it is possible to protect DNA from damage by substances called free radicals and reactive oxygen species. Studies with agents such as vitamin E, selenium, certain vitamin A compounds and active substances from natural products such as green tea support the testing of these types of agents in clinical trials. The clinical trials required to test cancer prevention strategies and agents will be large and expensive, but we must allocate the funds to support these trials. Otherwise, years of research that establish a sound basis for cancer prevention will be lost.

Finally, there are unprecedented opportunities to apply the principles of therapeutic drug development to cancer prevention. All of the tools of chemistry and biology can be used for the rational design of new chemopreventive agents for intervention, initially in high-risk populations of patients and eventually in the general population. Pharmaceutical and biotechnology companies must be engaged in the development of new chemopreventive agents. The NCI must be empowered and funded to take the lead in designing and conducting these types of trials – and building the partnerships required to significantly engage the private sector in cancer prevention.

Recommendations

- ❖ As part of a national research and education initiative that addresses all aspects of cancer prevention, **develop and implement a major new tobacco-control initiative to reduce the incidence of all tobacco-related cancers** and educate the American public on sound prevention approaches. Ensure a focus in these efforts that targets minority and medically underserved populations (see also behavior research).
- ❖ **Double current funding for clinical and behavioral cancer prevention research** and support review processes and support mechanisms such as program project grants that reflect its multi-disciplinary nature.
- ❖ **Create several “cancer prevention centers of excellence,”** primarily through the current cancer centers, to bring scientists and clinicians together in an environment focused on cancer prevention **in areas such as nutrition, behavior and/or chemoprevention.**
- ❖ **Utilize a consortia approach similar to that proposed for cancer therapeutics to facilitate the discovery and preclinical and clinical development of new**

chemopreventive agents for cancer, providing incentives for pharmaceutical and biotechnology companies to enter the cancer chemoprevention field.

- ❖ **Support and/or co-support with industry the large and expensive clinical trials** required to test the efficacy and safety of new chemopreventive agents.

Five-Year Resource Target – \$1.5 billion

IMPROVE QUALITY OF LIFE FOR CANCER PATIENTS

We Must Address Exceptional Needs in Behavior and Psychosocial Research. In an era of unparalleled advances from prior investments in basic and clinical research, it is important to remember that cancer occurs in people; it is individuals, not just the cancer, who must be treated. We should also realize that, in order to effectively eradicate cancer, we must understand much more about human behavior. For example, research into understanding how to influence behavior relative to lifestyle choices is critical to reducing the incidence and death from lung and other cancers caused by smoking and poor diets.

In a period when we have, by necessity, focused a substantial proportion of our resources on understanding the biology and genetics of cancer, historically, behavior and psychosocial research have not been well supported. We must now increase support for research directly related to the psychosocial aspects of cancer, to improve the quality of life for the millions of Americans who must undergo treatment and ultimately live with cancer. By targeting more resources to support high-quality research in these areas, we can learn to deal with the major problems of pain, fatigue, depression, nausea, and other side effects of cancer therapy that makes cancer so horrific for its victims.

Research in basic behavior is needed to realize the potential of new strategies to treat and prevent cancer. Moreover, if we are to prevent cancer, we must convince people to adopt healthy lifestyles that include making changes in long-standing eating, smoking, and alcohol consumption habits as well as other behaviors. To develop effective techniques that will enable people to make these changes, we need an understanding of some basic principles of human behavior. We need to know what motivates people, what maintains behavioral change over time, what factors lead to addictive behaviors, and how learning affects the immune and nervous systems.

There is currently great need and opportunity to conduct research on the decision-making process by which patients and their physicians choose among cancer treatment alternatives. Each treatment has its own associated probability of success and effect on the quality of life of the patient. Research on the decision-making process by minority populations in areas such as treatment options is especially in need of increased emphasis. Members of these populations often seek medical attention late in the disease process. Research to determine the effects of cultural differences and economic factors in minority and medically underserved populations, relative to access, screening and cancer

treatment should be performed and the findings implemented to reduce the toll of cancer in these groups, where incidence and mortality rates of cancer are disproportionately high.

Tools are now available to understand and control the causes of the physical symptoms of cancer and its treatments, including clinical trials research. These symptoms include pain, fatigue, nausea, depression and difficulty breathing, many of which are especially pervasive at the end of life. Pain and fatigue in particular merit additional attention, since most cancer patients experience these debilitating side effects, yet few patients have them adequately controlled. Partnerships among the academic, government and pharmaceutical and biotechnology sectors must be established to pursue the development of new, rationally designed pain control agents, and a similar initiative is needed for fatigue. Significant new resources must also be invested in research to improve treatment and provide relief from these symptoms to cancer patients at the end of life. In order to make progress in these areas, investment in both basic and clinical biobehavioral research is needed, especially through multidisciplinary teams of investigators working together to reduce the suffering and distress caused by cancer and its treatment

Recommendations

- ❖ **Support the behavioral research required to reduce cancer incidence and death caused by tobacco use in children and adults.**
- ❖ **Increase support for basic behavioral and psychosocial research** to individual investigators through the current individual investigator grant mechanisms of the NCI and allocate a minimum of \$75 million per year to these critically important areas.
- ❖ Provide the NCI additional resources to provide incentives and participate in partnerships with the academia and private sectors to **engage in pain research and develop new agents to address the problem of pain in cancer patients** as part of the recommended therapeutics initiative.
- ❖ Use current grant mechanisms, such as program project grants, to **support national multi-disciplinary research initiatives to specifically understand and manage end-of-life symptoms and care in cancer patients.**
- ❖ **Study behavioral and psychosocial interventions** in patients through approved clinical trials. **Create a clinical trials program to study these interventions**, or perform these studies as part of the current National Cancer Cooperative Groups Program, to collect data from large groups of patients.
- ❖ **Create training programs in psychosocial and behavioral oncology research and practice** to address the increased demand for expertise in these areas and provide funding for five-year periods.

Five-Year Resource Target – \$750 million

NECESSARY ACTIONS TO REALIZE ESSENTIAL PROGRESS

CREATE A NEW “SYSTEM” OF PUBLIC-PRIVATE PARTNERSHIPS TO IMPLEMENT AND ACCELERATE THE NATIONAL CANCER PROGRAM

Academic institutions, government agencies and private industry all play critical yet distinct roles in cancer research. Together these sectors create a “system” of research that ranges from fundamental insight into the mechanisms that cause cancer to the translation of that knowledge into new products for the prevention, treatment and diagnosis of cancer. This tripartite system of cancer research has evolved over many years, resulting in large, highly complex and separate sectors that operate somewhat independently and are driven by different strategies. We now have a major opportunity and need to leverage the strengths of these sectors to accelerate our national goal to conquer cancer.

A fully responsive partnership, combining all of the strengths of academia, government and industry, is perhaps our greatest opportunity to leverage all of our national expertise to cure and prevent cancer. Unfortunately, the existing tripartite system has a number of weaknesses. Among them is the duplication of research, resulting from a system that is less than maximally efficient. Communication gaps and cultural differences also hinder the development of the truly optimum partnerships that are so desperately needed to accelerate progress against cancer. Individually, none of the three sectors can provide the breadth and depth of research, development and commercialization required to adequately advance discoveries from basic research to the introduction of new safe and effective medicines.

A national strategy based on the full participation and expertise of all three sectors in a full-scale effort to conquer cancer is required now. To create a new system of partnerships, we must identify and eliminate any existing barriers that stand in the way of achieving the synergy needed to achieve our goal.

The novel partnership model must become a major focus for everyone with the capabilities to accelerate progress against cancer – academia, the NCI and the nation’s cancer centers, and industry. These novel relationships should be designed to use the strengths of the three sectors at the various stages of the research process. These partnerships must also focus on increasing the efficiency and effectiveness of discovery, development and commercialization, while preserving intellectual property rights. The stated goal of these new high-performing partnerships will be to accelerate the application of the best discoveries into new strategies for the early detection, treatment and prevention of cancer.

Recommendations

- ❖ Private industry allocates its resources based on a risk-reward analysis to maximize value to its shareholders. To fully engage the private sector, we must be able to mitigate these risks. It is recommended that the following **incentives be provided to engage private companies in a unified national partnership to eradicate cancer:**

- Grant **extended periods of increased product exclusivity.**
- **Make government tax credits available to participating companies.**
- Provide **government funding and/or co-funding for the large prevention trials** that must be performed to develop new strategies for cancer prevention.

Five-Year Resource Target – \$1.5 billion

**DEVELOP A COMPREHENSIVE AND RESPONSIVE NATIONAL
CANCER CLINICAL TRIALS SYSTEM**

Realization of nearly all of the extraordinary opportunities to “translate” previous discoveries into safe and effective treatments depends on a highly effective and efficient national system of clinical trials. A clinical trial is the process by which a new anticancer drug, preventive agent or behavior or psychosocial intervention is tested for safety and effectiveness in patients. Drugs and chemopreventive agents proceed through preclinical development and, initially, into a Phase I clinical trial that primarily tests safety. If an agent is safe, and there is evidence that it is likely to be effective in treating cancer in humans, it is tested in Phase II and III clinical trials for efficacy and to optimize issues such as dosage and regimens of treatment. Studies may also be performed in Phase IV trials to address additional questions about the drug. If new drugs are shown to be an improvement over current therapy, they become the new standard of care.

Clinical trials to test new agents and approaches to treat and prevent cancer are performed primarily through an NCI-funded program called the National Cancer Cooperative Groups. These NCI-sponsored groups place approximately 20,000 cancer patients on clinical trials each year, which represents only 2% of patients diagnosed with cancer. These groups currently receive only 50-60% of the funds recommended by experts as needed to perform these studies

It is currently extremely cumbersome to place cancer patients on clinical trials through the Cooperative Groups. Each group has its own set of forms and definitions, creating barriers for physicians to place patients on studies in more than a single group. Moreover, it costs physicians approximately \$3,000-4,000 per patient, out of pocket, to enroll patients in clinical trials, and they are reimbursed between \$750 and \$1,500 per patient for this work. Contrast this to industry-sponsored clinical trials research, where per-patient payments average in the range of \$5,000. The Cooperative Groups are simply not efficient or cost-competitive with industry in conducting cancer clinical trials. The NCI is currently attempting to improve this situation, but a major increase in funding is required to enroll enough cancer patients to develop new, more effective agents to treat cancer.

We must fund the Cooperative Groups at a level that will allow them to deal with issues of research modernization, administrative efficiency, information exchange and reimbursement to physicians. In addition, we need to also focus on the development of partnerships with industry to perform clinical trials to test new cancer prevention and

treatment agents. Building a “state-of-the-art” national clinical trials system will allow studies to be completed much faster and enough patients can be enrolled to identify small but important differences. “What can be done to speed the pace of progress in cancer research?” This single activity – substantially increasing funding to the Cooperative Groups and building partnerships with the private sector – is an immediate answer. An aggressive increase in support of cancer clinical trials now will yield significant results in lives saved in years to come.

Recommendations

- ❖ **Accelerate the “translation” of new discoveries, including behavior and psychosocial findings, into possible treatments for cancer patients** and improve the statistical validity of trials. Increase the number of patients enrolled in approved clinical trials each year, from 2% to 10%.
- ❖ **Remove economic barriers to participation in clinical trials by requiring third party payers to cover routine patient care costs** for those enrolled in clinical trials. Coverage should be provided for routine patient care costs for patients in trials that are approved by government agencies, including the National Institutes of Health, the Food and Drug Administration, the Department of Defense, and the Veterans Administration, or private organizations, such as the American Cancer Society, with adequate peer review mechanisms.
- ❖ **Develop a national campaign to improve public awareness of the importance of clinical trials**, provide high-quality, up-to-date information to consumers and simplify the process for enrolling patients.
- ❖ **Double current funding to the Cooperative Groups just to meet present workloads.** Equalize case reimbursement to attract adequate research physician resources to implement this urgent national agenda to test potentially more effective treatments and preventive agents in cancer patients.
- ❖ **Optimize the infrastructure of the clinical trials cooperative groups** to reflect the modern approaches to information handling and analysis.

Five-Year Resource Target: Approximately \$600 million (The entire national cancer clinical trials program is currently funded at approximately \$140 million. The recommended level of investment is required to begin to move the number of patients enrolled in clinical trials toward 10%, and support needed information systems and infrastructure requirements).

TRAIN A CADRE OF CRITICALLY NEEDED CLINICIAN SCIENTISTS

The number of clinical researchers in oncology is diminishing, and fewer young people are entering this field at a critical time when there are literally hundreds of new compounds and strategies that must be evaluated. The current environment of managed care places tremendous pressure on clinical investigators to generate clinical income, and

senior clinical researchers face the same pressure. Few formal training programs are available to clinical investigators, and clinical trials often take several years to perform and analyze – raising the question of stable support for this long process. All of these forces have reduced the number of clinical investigators available to perform high-quality cancer research.. The NCI recently proposed a training program to respond to this critical need, but funds are not available to support this new effort.

We must act now or we will not have enough investigators to perform clinical cancer research. Investment is urgently needed to support a new training and research program for clinical research investigators, ideally at the nation's cancer centers. There may also be opportunities through public-private partnership to partially underwrite the costs of this program.

Recommendations

- ❖ **Fund the new NCI clinical training program and/or create a new programs for young clinical investigators** to provide competitive support for 5-year renewable terms (\$45 million) and approximately \$20 million to fund the mentors and infrastructure required for this program. (Support for a minimum of 15 investigators at each of 30 cancer centers is recommended.)
- ❖ Academic clinical investigators are promoted through the academic ranks, in part through the performance of peer-reviewed, investigator-initiated research. Although approximately 30% of investigator initiated research grants supported by the NCI have a clinical component, less than 1% of these grants are allocated for the support of clinical scientists to perform clinical trials research in patients. **It is recommended that a minimum of \$40 million of additional grant funds be allocated to specifically support clinical investigators to perform clinical trials research in cancer patients.**

Five-Year Resource Target: Approximately \$105 million

EMPOWER THE NATIONAL CANCER INSTITUTE AND FREE IT OF BUREAUCRACY

The implementation of the recommendations of the Research Task Force requires that the National Cancer Institute has the increased resources, flexibility and authority required to plan, coordinate and implement a unified national initiative to cure and prevent cancer. It is unlikely that the NCI will be able to respond as required under the current burdensome policy constraints. The NCI needs to be able to make rapid decisions, provide expeditious support for critical research and build the partnerships required to leverage discoveries into the clinic and, subsequently, into new products to cure and prevent cancer. This required level of “readiness” means that the NCI must be empowered to reprogram funds and carry over funds between fiscal years.

The NCI needs to be free to both allocate and accept funds to build novel partnerships and develop consortia with industry and academia. In this regard, the NCI could fund some of its requirements for infrastructure improvements if it were allowed to use

revenues from sources such as royalties from licensed patents for these purposes. The NCI also needs flexibility and freedom to develop and fund contracts efficiently and purchase services and materials to support the recommended national initiatives in clinical and translational research and provide needed resources and flexibility to cancer centers. Building the infrastructure and approaches to implement translational and clinical research and cancer control will require new models such as employed by NASA and other agencies to accomplish specific national goals.

Finally, spearheading the efforts required for an urgent national effort to accelerate progress toward our national goal to conquer cancer requires that the NCI must be in a position to attract and keep top management and scientific talent. This means that the NCI must be able to be competitive for personnel in all respects with the academic, and, in selective areas, with the private sector for personnel.

Empowering the NCI to move rapidly and efficiently, without a number of the constraints that currently limit its ability to act, is critical to winning a national “war” to conquer cancer. There are other federal models that could serve as guideposts for these changes. In fact, it would be prudent to utilize the NCI as a “reinvention laboratory,” as has been done with other government agencies.

Recommendations

- ❖ **Remove burdensome policy constraints that represent significant barriers** to achieving the authorities, flexibility, efficiency and effectiveness required to optimize the efforts of all sectors and accelerate progress toward our national goal of curing and preventing cancer.
- ❖ **Empower the NCI and provide additional resources to facilitate the development of and participation in the novel system partnerships required to optimize and leverage discoveries** into new cancer detection treatment and preventive strategies and products and provide flexibility and needed resources to cancer centers.
- ❖ **Use the NCI as a “reinvention laboratory”** as one approach to relieve bureaucracy and achieve these aggressive goals for the Nation.

Estimated Resources Required – To Be Determined.

EXPECTED RETURN FROM OUR INCREASED INVESTMENT

It is critical that we address the increasing burden of cancer that will certainly become an unprecedented health care crisis in the next 10-20 years, unless we take steps to change it now. We have shown that cancer incidence and mortality can be reduced through basic, clinical and population-based behavioral research. We have cured some cancers, but much of the job remains in front of us.

The March Research Task Force recommends that we initiate a **National strategy - to significantly increase our federal investment in cancer research**. Our goal is to achieve a federal funding level of \$10 billion per year in five years to support the basic and clinical research required accelerating progress in a National campaign to cure and prevent cancer. It is recommended that we launch this strategy in 1999 by doubling the current budget (\$2.5 billion in 1998) for cancer research to a level of \$5.0 billion and increase the budget by approximately 20% per year for the ensuing four years until we reach the \$10 billion goal. This would mean an increase from the current 1-cent for every \$10.00 paid in taxes that are dedicated to cancer research to approximately 4 cents in the next 5 years. A thorough analysis should be undertaken annually and in five years to assess progress and determine our goals for the subsequent five-year periods and the required investment. Reassessment of our strategy, investment levels and priorities should be undertaken at regular intervals to insure the success of our unified national strategy to address this cancer health care “iceberg” that is expected to hit America the hardest in the next 10-25 years.

If the plan of The March Research Task Force is implemented and the budget is increased as recommended, we believe that the annual incidence of cancer can be reduced 20% in 10 years and as much as 30% in 20 years. Using today’s incidence levels as a baseline, we would **expect 246,000 fewer cases in 10 years and 369,000 fewer cases annually in 20 years**. We also believe that death from cancer can be reduced from 25-40% over this same time period. At current mortality rates, **we could save 150,000 -225,000 lives each year in the United States and countless lives around the world from the application of research discoveries**. The impact of these reductions in cancer incidence and mortality will be staggering in lives saved and pain averted, not to mention the gains in productivity and long-term reductions in healthcare costs.

Not only will lives be saved, medical costs avoided and productivity maintained, but a significant reduction in fear of the disease can be accomplished and the lives of those who do get the disease will be of much higher quality. While it is not possible to predict how long it will take to cure and prevent all cancer, we surely will significantly improve the quality of life of cancer patients so that it is regarded as a chronic and manageable condition - not a death sentence.

Imagine the change in outlook for every American when physicians can say, “Yes, you have cancer, but after a few weeks of therapy and some periodic maintenance you should live a pain-free, productive and normal life.” And because the root causes of cancer will be better defined and prevention begun early in life, these prevention strategies will have positive effects beyond cancer – leading to healthier and longer lives for all Americans.

Cancer is perhaps the most difficult problem that we have tried to solve to improve the health of our Nation. Although cancer remains a fearsome enemy, there is optimism in all areas of cancer research that we can turn the tide against cancer. The message from cancer survivors is **no more** – “no more” cancer and **no more waiting**. We have cured several other cancers, and we are confident that this dream can be achieved, but only if we redeclare a “War” to conquer cancer and we stand together as a Nation to do it **NOW**.

THE MARCH – RESEARCH TASK FORCE*

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* Complete Task Force Membership Listing in Final Report

INTERIM REPORT*

Recommendations of

THE MARCH – Research Task Force

Commissioned by

THE MARCH – Coming Together to Conquer Cancer

September 25-26, 1998

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NOT FOR RELEASE OR DISTRIBUTION

* Final Report Pending

EXECUTIVE SUMMARY

Cancer has reached epidemic proportions in the United States, with an estimated 1,228,600 new cases and over 560,000 Americans lost in 1997 at an annual economic cost of over \$104 billion. If these rates continue, one quarter of our population will die from the disease. The effect of the changing demographics in America and our aging population will cause cancer rates to reach staggering proportions as early as 2010 with the incidence of cancer conservatively estimated to increase by 29% and deaths by 25% at an annual cost of over \$200 billion. **Although defeating cancer remains in every sense a daunting task, we can change the future. We now have unprecedented opportunities to achieve essential progress against cancer, but only if we move with real urgency to provide the necessary resources**

President Richard M. Nixon signed into law the National Cancer Act in 1971 and declared a “war” – to eradicate cancer. This was a bold first step, unfortunately a “war” was never fully launched or funded in relation to the complexity, size and cost of the problem. We currently invest approximately \$2.5 billion per year in cancer research through the National Cancer Institute (NCI), which represents only 2% of the economic burden of the disease and translates to about 1 cent invested in research for each \$10.00 paid in taxes.

We could not have predicted in 1971 that solving the mystery of cancer would require that we literally “unravel” the basic secrets of normal life processes. Despite chronic underfunding, in the ensuing years our ever-increasing understanding of the fundamental differences between normal and cancer cells has finally given us the weapons we need to conquer cancer and many other diseases. It is an optimistic and hopeful time in cancer research.

This hope provided the energy for individuals from all walks of life to unite in a movement called “The March” – Coming Together to Conquer Cancer (hereafter The March). As part of The March, a group of experts that included basic and clinical scientists, behavioral and psychosocial researchers, cancer survivors and executives from academia, government, industry cancer research organizations and professional societies came together as “The March” Research Task Force to define what is essential and possible in all areas of cancer research.

RECOMMENDATIONS

The Research Task Force Report includes 40 specific recommendations aimed at expediting cancer prevention and treatment research and advancing the prospect for conquering cancer. These recommendations address issues ranging from funding to information sharing and streamlining, from the creation of private-public partnerships to quality of life improvements. They appear under the following headings in the Report:

- Status of Cancer Research: Unprecedented Opportunities for Progress
- Necessary Actions to Realize Essential Progress

- Expected Return from Our Increased Investments

The following recommendations are fully supportive of the National Cancer Institute's (NCI) Bypass Budget that delineates the needs and opportunities of the Nation's National Cancer Program. The Research Task Force recommendations represent broad research initiatives and actions needed to fully support an accelerated "war" to address the looming cancer crisis and ultimately to cure and prevent cancer for all Americans. The projected costs of these initiatives are estimates based on the status of current areas of cancer research and recommended levels of effort required.

Opportunities for Essential Progress

Basic Research. Unfortunately only 25% * of approved grants are currently funded and many excellent ideas and investigators with great potential are lost. **We must increase this level to a minimum of 45%** and fund more investigators and all areas of cancer research, especially in historically underfunded areas such as cancer prevention, behavior and psychosocial research. It is also critical that we attract young and minority investigators to cancer research and fund the most innovative ideas. The complexity of cancer and convergence of disciplines mean that the future belongs to teams of scientists working together to make discoveries and translate them into clinical applications. Therefore, current mechanisms to fund **multidisciplinary research teams and "centers of excellence"** (focused around the strengths of the Nation's cancer centers) to **accelerate translational/clinical research must be expanded and new mechanisms developed as appropriate.**

Cancer Therapeutics. **There is currently an unprecedented necessity and real opportunity to link discovery to commercialization of new cancer therapeutics by forming a public-private consortium that can validate cancer targets and accelerate new cancer drugs through preclinical and clinical development. ** We must provide incentives, such as periods of exclusivity and tax credits, to fully leverage the strengths of the private sector, especially in the development of new cancer therapeutics. To fully implement this concept we must also empower and fund the NCI and other federal agencies and academic sectors to participate fully in this partnership.**

* Most of our past investments in cancer research were utilized to build an incredibly powerful discovery resource, and the experts agree that we must accelerate our efforts to achieve the additional necessary breakthroughs required in basic research. For example, genetic changes in cancer, mechanisms by which cancer cells become immortal, pathways by which they signal and communicate and the process by which tumor cells spread all represent high potential pay-off areas that require increased support. The foundation of our unparalleled capability in basic biomedical and behavioral cancer research is the ideas that come from individual scientists.

** Basic research has provided us with a wealth of exceptional opportunities to develop new and better drugs to treat cancer successfully. . Drugs can now be more rationally designed and the process accelerated through the use of new technologies such as "combinatorial chemistry", computer modeling and "high-throughput screening". A new concept of chemical-cellular biology holds the promise of allowing us to convert our knowledge of biological molecules into cancer drugs that will be more effective in humans. There are hundreds of new compounds being studied in academic and private laboratories for application to the treatment of cancer, but new resources must be provided to realize these benefits for cancer patients.

Early Detection of Cancer. Our increased understanding of the genetic and other changes that occur in cancer cells has provided “signposts” or markers that will facilitate the development of risk profiles and screening tests to determine cancer risk. Once risk is determined, intervention strategies can rationally be used to prevent cancer. **Funding a national initiative to accelerate the development of these early detection technologies and developing public-private partnerships to make these tests widely available will save hundreds of thousands of lives each year.**

Cancer Prevention. Cancer is a preventable disease. Cancer prevention is multifaceted, ranging from research on behavior modification and diet control to chemoprevention and environmental exposures. For example, the potential causative role of the environment in many forms of cancer must be thoroughly studied. **Overall funding for cancer prevention research should be doubled and “centers of excellence” established to accelerate a proactive approach.** Chemoprevention research can be performed using the same public-private model that we will employ for developing cancer therapeutics, but we must be prepared to **pay for the large, expensive clinical trials required to engage the private sector** in developing chemopreventive agents for cancer.

Success in cancer prevention depends in large measure on the extent to which research can help people change destructive behaviors such as smoking and poor diets. To reduce cancer incidence and mortality from all tobacco related cancers, **we must develop and implement a major new nationwide tobacco research and control initiative.**

Improved Quality of Life. **With the necessary additional resources, we can understand and control the physical symptoms of cancer and the side effects of cancer therapies.** Psychosocial and behavior research related to cancer has not received adequate research attention in the past, but we have the opportunity to change this picture by **supporting important grants in these areas, training more scientists and addressing critical research issues such as controlling symptoms at the end of life.**

Minority and Medically Underserved Populations. **We must support the research required to understand why cancer occurs in disproportionate rates in certain minority and medically underserved populations such as the poor and the elderly.** We must apply what we already know from previous research, such as breast, cervical and colorectal cancer screening technologies, to detect and treat cancer earlier in these populations. In addition, we must ensure that the technologies and new medicines that derive from the discoveries and advances in clinical research detailed in these opportunities for progress are applied to all populations, so that rates of cancer incidence and mortality cannot only be reduced, but also equalized across all populations. Finally, we must support high quality registries to provide a basis for cancer control and assessment of our progress.

Necessary Actions

We must take immediate actions to remove a few key barriers. In short, we must develop novel public-private partnerships, increase the participation of cancer patients in clinical

trials, train the required cadre of clinical investigators and empower the NCI to spearhead a full national effort to accelerate progress to cure and prevent cancer.

A New Culture and a New "System". We need to establish a new culture where "translational" research can flourish – centers of excellence that leverage the basic and clinical research strengths of our National cancer centers. We must also urgently develop a new system to translate laboratory discoveries into new products and technologies to cure and prevent cancer. This will require new models that optimize and speed this process. The current system is too slow and significantly underfunded to expedite laboratory discoveries into new drugs and technologies that will reduce the incidence and mortality of cancer. There is a real and immediate need to establish highly effective relationships and partnerships among the three sectors involved (government, academia and the private) with a special focus on leveraging the strengths of the private sector in our national effort to conquer cancer. To do this we need to **offer incentives such as increased periods of product exclusivity and federal tax credits, and take specific actions such as support for large, expensive prevention clinical trials.**

Reform and Expand Cancer Clinical Trials. **An unacceptably low 2% of cancer patients are enrolled in clinical trials to test new agents. This number needs to be increased to 10% through better public education, a simplified enrollment process and incentives for clinical cancer researchers to enroll cancer patients in trials. A renewed national effort at an unprecedented scale must be made to attract and train these new clinician researchers and provide them the necessary resources to do their work.**

Empower the NCI. Finally, the implementation of the recommendations of the Research Task Force requires that the National Cancer Institute will have the increased resources, flexibility and authority required to plan, coordinate and implement the unified national initiative to cure and prevent cancer envisioned by the National Cancer Act. The NCI must be able to make rapid decisions, provide expeditious support for critical research and our Nation's cancer centers and build the partnerships required to leverage discoveries into the clinic and, subsequently, into new products to cure and prevent cancer. **This required level of "readiness" means that the NCI must be freed of burdensome policy constraints and empowered in all respects. In fact, it should be considered as a potential national "reinvention laboratory" and/or empowered through the use of other models employed to meet similar goals.**

Return on Investment

The Research Task Force recommends that we initiate a National strategy – Cancer Reduction 2010-2025 – and incrementally increase our investment in all areas of cancer research. It is specifically recommended that we **increase our annual investment in cancer research to \$10 billion over the next 5 years. Implementation would begin in 1999 by doubling the current NCI budget to \$5.0 billion and increasing the budget by approximately 20% per year for the ensuing five years.**

The Research Task Force believes that if its recommendations (and those detailed in the Bypass Budget of the NCI) are implemented and the required resources are dedicated now, that required reductions in cancer incidence and mortality can be achieved. At current levels, it is anticipated that **cancer incidence could be reduced 20% in 10 years and as much as 30% annually in 20 years.** This translates into **246,000 and 369,000 fewer cases of cancer annually in 10 years and in 20 years respectively.** The Research Task Force also projects that **deaths from cancer could be reduced from 25-40% over this same 20 year period, a savings of 150,000–225,000 lives each year** in the United States and countless lives around the world from the recommended application of research discoveries and research-based initiatives such as tobacco control.

Through research we have cured several cancers such as testicular cancer, Hodgkin's disease, and certain types of leukemias, and we are hopeful that many more cancers can be cured in the next few years. The clear message from the members of the Research Task Force is - **don't let this moment pass; seize this opportunity to launch an inclusive, national, full-scale "war" to eradicate cancer for all Americans NOW.**

As a Nation, we know what this challenge means and how to meet it. We have done it before and we can do it again - to defeat cancer. We have supported the level of commitment it took to win World War II, put a man on the moon and triumph in the Gulf War. These campaigns required decisive commitment by our government and the American public, full engagement of our best research minds in the academic, government and private sectors, freedom to act by the federal sector, full participation and support from the private sector and dedication of the required resources. A full-scale, coordinated national effort to cure and prevent cancer will require no less.