

Discovering More Innovative and Effective Treatments to Make Cancer a More Treatable Disease

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Good morning. I am Dr. Michaele Chamblee Christian, Associate Director of the Division of Cancer Treatment and Diagnosis for the Cancer Therapy Evaluation Program, in the National Cancer Institute (NCI), within the National Institutes of Health (NIH) and the Department of Health and Human Services. I am a medical oncologist.

Thank you, Mr. Chairman, Representative Waxman, and distinguished Members of the Committee, for the opportunity to discuss NCI's efforts to deliver innovative and effective cancer treatments to the public and the steps being taken to turn cancer into a more treatable disease.

Recent advances across the biomedical research enterprise have set the stage for unparalleled progress in biomedicine early in the 21st century. Basic research has given us an understanding that cancer is a disease process where normal cells are transformed into cancer cells through a series of defined steps that begin with small changes in cellular DNA. If left unchecked, these transformed cells can progress and spread to cause the suffering and death that we recognize as the horrible burden of cancer. Fortunately, our growing understanding of this disease process has revealed multiple opportunities to intervene.

New intervention strategies include preventing initiation of the disease process; early detection, when the disease is most amenable to elimination; and arresting the process to stop the spread (metastasis) of the disease, which is the primary reason that patients suffer unduly and die. In short, we are rapidly learning how to modulate the cancer disease process. This ability to intervene will ultimately eliminate some cancers and transform others into chronic, manageable diseases that patients do live with and not die from.

Scientific advances in genomics, nanotechnology, proteomics, immunology and bioinformatics may soon allow us to profile a patient's genetic, lifestyle, and environmental risk for cancer and to be able to combine effective prevention and early

intervention strategies for those at high risk. For example, genomic analysis of a patient's tumor and proteomic patterns obtained from a patient's serum, as well as sophisticated imaging technologies designed for molecular detection, will be used to identify cancers at the earliest stages. Precise molecular diagnosis and patient-specific profiling will allow physicians to predict responses to specific interventions and provide a rational basis for tailoring treatments. The result will be more effective and less toxic, targeted agents delivered to patients, which will greatly change the outcome of many cancers and which is attainable in the foreseeable future.

Given these extraordinary opportunities, the NCI is focused on accelerating the pace of therapeutics development through better integration of its translational research and clinical trials components and better collaboration with our partners in academia, the community, the pharmaceutical industry, and other federal agencies to ensure that we are optimally positioned to address the most compelling scientific and medical challenges facing patients with cancer.

Bringing Innovative Treatments to the Public

The National Cancer Institute (NCI) has an extensive clinical trials program that is dedicated to developing more effective treatments for cancer patients using novel investigational (experimental) agents and new applications of commercially available drugs. In fact, the NCI is the largest sponsor of cancer clinical trials in the world and works extensively with the biotechnology and pharmaceutical industries, that are the source of many of these new agents, to accelerate the pace and scope of development. At any given time, the NCI has over 500 clinical trials actively enrolling patients and several hundred more still in analysis. Over 31,000 patients are enrolled on NCI-sponsored treatment trials each year, and many additional patients participate in clinical trials at NCI funded cancer centers across the country and in clinical trials sponsored by biopharmaceutical companies. Nearly 18,000 patients participate in NCI-sponsored cancer prevention and control studies. NCI treatment trials alone involve 3,300 clinical sites and approximately 11,000 investigators.

NCI has many initiatives underway to involve local healthcare providers, both at academic centers and in community practice settings, in clinical trials to allow patients everywhere to participate in the development of innovative treatments. Beginning in 1999, the NCI undertook two important pilot projects designed to increase both the speed of accrual and overall access to its large, phase 3 treatment trials. Phase 3 trials are, in large part, performed by the NCI's Clinical Cooperative Groups. Before 1999, the Groups had traditionally limited participation in their trials to their own membership. In a pilot project, the Cancer Trials Support Unit (CTSU) was created to open the trials of the 8 Adult Cooperative Groups to participation by any NCI-registered physician, whether or not they were members of the Cooperative Group leading the trial. In order to make this a practical reality, and not overburden investigators with regulatory and audit requirements related to participation in trials led by different organizations, the CTSU consolidated the regulatory and data management activities for all the Cooperative Groups. This allowed the CTSU to provide access to the majority of the Group's Phase 3 trials in a consistent

and uniform format. The CTSU now provides all Group members access to any of the Group's trials, thereby adding flexibility and access to the NCI system that did not formerly exist. To spur even greater participation in NCI-sponsored trials, since 2002 the CTSU has permitted physicians not affiliated with any Group to join and provide access to all trials on the CTSU menu to their patients.

This new approach to participation in trials via the CTSU has required substantial changes on the part of investigators and their staffs, reflected in the use of new informatics systems and in new management processes. There is growing evidence that this new approach is achieving its goals. Enrollment via this mechanism has steadily increased over the past 2 years and approximately 350 patients are currently being entered each month by this CTSU mechanism. In addition, the potential now exists for regulatory and many administrative documents for all Group trials to be handled exclusively by the CTSU. NCI would like to expand this effort by adding more trials to the CTSU menu and providing more efficient, automated systems (online registration and data management) to facilitate enrollments. This approach allows NCI to make its most important treatment trials widely available to patients across the country treated by experienced physicians in any setting, whether academic-centered or community-based, and regardless of their oncologist's affiliations.

A second pilot project, termed the Central Institutional Review Board (CIRB), was developed by NCI in direct response to repeated requests from the investigator community. Cumbersome and time consuming paperwork and IRB review process for clinical trials had to be completed separately at each of many hundreds of sites, even though many smaller sites might enroll only 1-2 patients on a trial, particularly for less common cancers (like Gastrointestinal Stromal Tumor [GIST]). The burden posed by local IRB review was frequently cited by investigators as a major reason for limited participation in clinical trials. While there can be no substitute for local IRB review for research being performed at a single institution, the CIRB primarily reviews large, Phase 3 studies performed at hundreds of sites across the country. By assuming the primary responsibility for review, adverse event monitoring, and follow-up paperwork for these national protocols, the investigators and local IRBs are spared duplicative application and review work and the process of gaining approval to enroll the first patient on a trial can be reduced from many weeks to as little as one to several days. This initiative has made important strides since its inception in 2000 and now consists of over 165 participating IRBs. The NCI has developed this project in close consultation with the HHS Office for Human Research Protections (OHRP). The CIRB members who perform the reviews are highly qualified oncologists, statisticians, patient/consumer advocates, pharmacists and nurses from across the United States who have volunteered to assist NCI by performing this task. While a formal evaluation of progress to date is currently underway, NCI hopes to expand the initiative this year to include 500 sites and, at the request of the Children's Oncology Group, has initiated the formation of a second Board that will focus on reviewing pediatric multi-center trials.

In addition, NCI has major initiatives to disseminate information about state of the art treatments into the community. For example, since 1999 NCI has supported the HMO

Cancer Research Network (CRN), a consortium of eleven research organizations affiliated with integrated healthcare delivery systems located across the U.S. that provide healthcare to over 10 million members. The CRN is engaged in a wide variety of population-based cancer control research ranging from exploring factors related to cancer occurrence and prognosis to health system design issues related to optimizing the performance of cancer prevention and screening services, to assessing the impact of cancer treatment on the quality of life of cancer patients. During its first funding cycle (1999-2002), with targeted support from NCI, CRN investigated barriers and facilitating factors related to participation of CRN physicians and members in cancer clinical trials. The results of this study have been submitted for publication, and based on these results CRN is currently designing an intervention trial to test organizational methods to enhance participation in clinical trials at CRN institutions. At the urging of NCI, in its renewal application (2003-2006) CRN will initiate a series of "cancer diffusion studies" that will document the rate and determinants of the dissemination of evidence-based cancer treatments in the community care settings of the CRN healthcare delivery organizations.

Public/Private Partnerships to Enhance Clinical Trials

NCI is continually working to expand its role in public-private partnerships as more private-sector companies begin to develop anti-cancer drugs. Many of the most promising new agents to treat cancer now come from the research and development efforts of the biotechnology/pharmaceutical industry. Over the past 10 years, the number of new agents being developed by industry has grown over threefold, from 124 to 395. The current status of working relationships between NCI and private industry is excellent. These collaborative relationships have resulted in many pharmaceutical agents that are highly effective in the treatment of cancers and precancers. The Cancer Therapy Evaluation Program of the NCI, which coordinates NCI's clinical treatment trials, has formal relationships with more than 60 biotechnology and pharmaceutical companies, including 34 Cooperative Research and Development Agreements (CRADAs), 54 Clinical Trials Agreements (CTAs), and 9 Clinical Supply Agreements (CSAs). Similar arrangements exist within the Division of Cancer Prevention, which has 26 CTAs and 37 Investigational New Drug Applications (INDs), and NCI's intramural research program, which also supports or conducts clinical trials. NCI staff work closely with these corporate collaborators to ensure that the most important medical and scientific questions are addressed in the collaborative development of these agents and that duplication is avoided. Companies are often narrowly focused on the development path most likely to result in FDA approval, which may involve a single cancer type. NCI can accelerate the pace of broader development substantially to explore the many other cancer settings where an agent may have potentially important uses. Examples include the collaboration between Novartis and NCI-supported researchers that led to the development of **Gleevec** as a remarkably effective treatment for chronic myelogenous leukemia and now also for gastrointestinal stromal tumors. NCI is sponsoring clinical trials with Gleevec in many other tumor types that express the relevant targets. Likewise, in an ongoing partnership with Genentech, NCI-supported clinical investigators are testing a promising molecularly targeted drug, **Avastin**, in patients with a variety of different cancer types, including those with advanced colorectal cancer who were previously treated with chemotherapy

alone. Through a collaborative relationship with Searle and Pfizer, Inc., researchers found that the arthritis drug **Celebrex** can reduce the number of pre-cancerous colon polyps in patients with familial adenomatous polyposis, an inherited syndrome that predisposes them to colon cancer. NCI is exploring this important lead in a number of clinical trials. These specific examples represent only a small fraction of the clinical trials that NCI is supporting this year and the many industry partnerships that are predominantly for non-marketed investigational agents.

Because of its extensive relationships with bio-pharmaceutical companies, NCI is in the unique position of being able to broker and sponsor studies of combinations of investigational agents owned by different companies. It is widely believed that many of the promising new molecularly targeted agents will demonstrate their optimal utility in combinations that inhibit or modulate multiple targets in critical cancer cell pathways. NCI has worked with over a dozen industry collaborators to arrange 22 trials of novel investigational combinations to date and has commitments for additional high-priority trials, some containing 3 or 4 novel agents. Without these collaborations, many of these regimens would not have been evaluated until one or more of the agents had received FDA marketing approval, potentially resulting in years of delay. NCI continues to seek opportunities to provide additional incentives for bio-pharmaceutical companies to collaborate in the development of promising new agents and to further accelerate therapeutics development in the public interest. NCI is carefully following the impact of incentives such as the extension of exclusivity provided in the Best Pharmaceuticals For Children Act of 2002, as one example.

NCI/FDA Collaboration

For the past year, NCI has also been working aggressively with the Food and Drug Administration via the NCI/FDA Interagency Oncology Task Force (IOTF) to increase collaboration and eliminate impediments to accelerated therapeutics development. The formation of the IOTF was an important strategic step toward achieving NCI's challenge goal of eliminating suffering and death due to cancer by 2015; and the FDA's goals of increasing the availability and use of safe and effective treatments for cancer. The goal of the IOTF is to leverage the expertise and capabilities of both agencies in order to streamline and accelerate the overall development of diagnostic, preventive, and therapeutic interventions for cancer.

Since its formation, the members of IOTF have identified several specific initiatives that are directed toward optimizing drug and device development. The NCI is working to specifically gather and synthesize the scientific support needed by the FDA to address specific regulatory issues. The IOTF is working through a series of specific subcommittees that are actively engaged in the following areas:

- **Joint Training and Fellowships:** The IOTF is focused on significantly increasing the number and quality of training of physicians and scientists that are expert in clinical research, the clinical approval process, and the translation of laboratory science into new products for cancer. To that end, the IOTF Training Subgroup

- has developed a series of fellowship programs that will allow NCI fellows to train at the FDA and has established fellowships for personnel from both agencies to train in areas such as oncology product research for cancer detection, treatment, and prevention. These programs will be initiated in 2004.
- **Developing Markers of Clinical Benefit:** Work in this critical area includes the use of imaging in oncology drug development, collaborative development of the scientific data needed to establish surrogate endpoints for cancer clinical trials, and the potential utilization of advanced technologies such as genomics, proteomics, nanotechnology and immune monitoring to speed drug discovery and development, especially the regulatory phases. The subcommittee is organizing background materials to capture the state-of-the-science in specific types of cancer and technologies. These projects are all underway and will engage scientific input through publications, meetings, and workshops.
 - **Common Bioinformatics Platforms:** NCI has recently launched a pilot program to connect the cancer research community through a new bioinformatics platform known as the Cancer Bio-informatics Grid (caBIG). One of the primary goals of this unprecedented effort is to improve the organization and reporting of data derived from oncology clinical trials. Among other projects, the NCI and the FDA are collaborating through the IOTF to utilize this common infrastructure to implement electronic INDs. As part of their participation in caBIG and the IOTF, the two agencies will pursue the development of standards to support the submission of clinical data and other electronic filings to shorten the time frame for processing and alleviate investigator workloads.
 - **Process Improvement:** The IOTF has undertaken a series of projects to address specific issues or barriers that arise in the regulatory processes of oncology drug development. These projects range from preclinical development through the range of clinical trials required for drug approval. Among the notable accomplishments are: the development of an NCI-FDA leadership group that can act to address questions from NCI-supported investigators during any phase of the regulatory review process; scientifically driven review of the preclinical requirements for IND filings; and the development of a more consistent process for the review of cancer prevention agents.

The IOTF meets regularly and actively addresses issues that can ultimately speed the development of new interventions for cancer. The IOTF subcommittees are currently framing new issues and developing resource materials that will facilitate investigators in preparing the data needed for the regulatory processes. In some cases, the FDA has already responded with guidance documents (such as a recent guidance on pharmacogenomics) and process changes, and the NCI is actively working to develop and synthesize the science needed to make regulatory decisions.

NCI Partnerships with Academic Health Centers and Cancer Centers

Because funding and sponsoring cancer research is fundamental to NCI's mission, there are extensive collaborations with cancer centers and academic health centers, both in drug discovery and development. NCI's Rapid Access to Intervention Development

(RAID) Program is an example of a partnership with academia to accelerate the development of the most promising new agents from academic laboratories by providing the pre-clinical resources, such as drug formulation and toxicology studies, that often present significant obstacles to university laboratories that do not have the resources typically present in pharmaceutical companies. To date, **91** new agents have received pre-clinical support through this program and many have entered clinical trials. The Division of Cancer Prevention has a similar program called RAPID (Rapid Access to Prevention Intervention Development) that has an additional 26 projects.

NCI has expanded its established working relationships with academic health centers and cancer centers to accommodate the increasing need for collaboration with laboratory scientists in conducting clinical trials for molecularly targeted agents. The cellular pathways and interactions involved in these molecular targets are extraordinarily complex and interrelated. These complexities require scientists to develop new techniques and tests to identify patients whose tumors contain the relevant targets and to monitor drug effects during treatment. More than half of NCI-sponsored cancer treatment trials initiated over the last 2 years have included correlative studies with laboratory scientists, and this trend is being seen increasingly in cancer prevention trials.

Clinical trials and much of the translational research that accompanies them are carried out in a variety of specialized mechanisms including: 1) **25** early therapeutics development contracts and cooperative agreements for Phase 1 and 2 trials, which are overwhelmingly based in cancer centers; 2) **56** Specialized Programs of Research Excellence (SPOREs), of which all but 3 are in cancer centers; 3) highly specialized disease specific consortia such as the AIDS Malignancy Consortium, and brain tumor consortia are located in cancer centers and academic health centers; 4) the 9 Cancer Cooperative Groups that conduct almost all Phase 3 trials and the pilot trials leading to them. The Groups are extensive national networks that include cancer centers and community sites. There are 9 adult national cooperative groups including 4 multi-specialty/multi-modality groups, 2 surgical groups, 1 each in gynecologic oncology, radiation oncology and a diagnostic imaging group, as well as the Children's Oncology Group. Most cancer centers belong to several or many cooperative groups; 5) and the Community Clinical Oncology Program (CCOP), a large network of community oncology practices that conducts cancer treatment, prevention and control research and is not based primarily in academic centers, though the coordinating research bases are cancer centers. The CCOP program has grown rapidly over the past 10-15 years and now includes 61 individual grants to community based clinical trials research organizations in 39 states, Washington, D.C., and Puerto Rico. CCOP accrual has risen steadily over the past 10 years as a percentage of all Cooperative Group accrual and accounts for about 30% of accrual to treatment trials.

There is extensive involvement of cancer centers and academic health centers in most clinical trials mechanisms and in other activities supporting translational research, as described above. In an effort to accelerate clinical development and enhance collaboration and resource sharing, NCI is currently examining new approaches to integrating the clinical research that is conducted across these mechanisms to help ensure

rapid and seamless progression of new agents and regimens through this process. A broadly representative Clinical Trials Working Group has been formed and includes senior NCI staff and external experts from across the clinical research spectrum, including academia, biopharmaceutical industry, and other federal agencies (FDA and the Center for Medicare and Medicaid Services) who will have an ongoing role in working together to improve the clinical trials process. The goal is to better integrate information, resources, and infrastructures so that the information gained in one venue is exploited most appropriately in the others. For example, when the basic research ongoing in an NCI-designated cancer center or SPORE identifies a new molecular target in a specific disease, work can begin immediately on: identifying an assay to detect the target in tumor specimens from cancer patients; beginning clinical trials with agents that inhibit or modulate the target; and, on collecting tumor specimens from the patients on those or other clinical trials to further examine the impact of the target and its inhibition on the patient's tumor. Studies can also be initiated to examine the potential of new imaging techniques to identify these target effects non-invasively and to begin new pre-clinical studies of the targeted agents with other treatment approaches. One major aim of the NCI's current efforts to enhance cancer clinical research is to make many of these research processes, which have been sequential in the past, and proceed concurrently, thus enhancing the timeliness of the translation of new laboratory findings into clinical trials.

Rates of Participation in Clinical Trials

NCI was asked to comment about the differences in adult (about 3% of newly diagnosed cancer patients) and pediatric (about 60%) participation rates in cancer clinical trials. The rate of enrollment of children with cancer into clinical trials obviously far exceeds that for adults with cancer, although the absolute numbers of adults participating in trials is far higher. Most children with cancer are treated in tertiary care centers, the majority of which are associated with medical schools, whereas the vast majority of adult cancer patients are treated in community practice settings. The higher priority that academia places on research compared to the community setting facilitates the enrollment of children with cancer into clinical trials. Another important factor is the culture of the pediatric oncology discipline. This culture is driven by a history of progressive improvements in childhood cancer outcomes that has reinforced in these specialists the belief that the best way to identify more effective treatments is through well-designed clinical trials. A key characteristic of the pediatric oncology culture is the willingness of researchers to collaborate in conducting multi-institutional clinical trials, which are essential since few single institutions see sufficient children with cancer to conduct the clinical trials that are needed to reliably identify more effective therapies. The remarkable efficacy of many pediatric cancer treatments and the dramatic progress that has been achieved by application of the pediatric oncology paradigm has created incentives for childhood cancer researchers to maintain their high rates of participation in clinical trials in the hope of continuing progress into the future. Because adult patients are predominantly treated in the highly competitive community setting, NCI has focused its attention and resources on building a far-reaching clinical trials infrastructure that is user-friendly for community physicians.

Educating the Oncology Community and Patients about Clinical Trials

Since the NCI introduced its Clinical Trials Education Series (CTES) in 2002, the NCI's Cancer Information Service (CIS) staff has been training health professionals and community organizations in how to use this excellent resource to educate patients and community groups about clinical trials. To increase awareness and education about clinical trials to the public and special populations, the CIS works in partnership with local, state, and federal agencies to expand the reach of NCI programs and services. The CIS Partnership Program strives to increase partners' awareness that cancer is a major public health problem and that the burden of cancer falls disproportionately on certain racial, ethnic, and socioeconomic groups. The CIS forms partnerships with organizations to deliver information that motivates people to improve their health and connects partner organizations working in clinical trials education and outreach to build the capacity of those organizations in order to further the reach of their programs and services.

Leukemia and Lymphoma Society chapters across the U.S. and NCI grantees known as the Special Populations Networks (SPNs) have been active participants in clinical trials education by involvement in train-the-trainer sessions offered by the CIS to become familiar with the CTES materials so that they can use the materials to inform their communities. The purpose of the SPNs is to build relationships between large research institutions and community-based programs and find ways of addressing important questions about the burden of cancer in minority communities. In particular, the SPNs and the CIS collaborate to increase awareness of and accrual to clinical trials.

The NCI's Cancer Information Service interacts directly with cancer patients and their families through its toll free number (1-800-4-CANCER), through the Internet using real-time instant messaging technology (*LiveHelp* in NCI's web site [cancer.gov](http://www.cancer.gov)), and by e-mail (through NCI's Web site, <http://www.cancer.gov>). One of the most common reasons that patients, their families, and health professionals contact the CIS is for information about clinical trials. When appropriate, CIS proactively offers information on clinical trials to individuals seeking information on treatment options and conducts a customized search of NCI's database of clinical trials. The clinical trials search is provided directly to the patient so that they can discuss the trials with their physician. Accompanying clinical trials patient education booklets and materials are also offered to the individual.

The NCI also provides extensive internet access to information. The NCI's Web site (<http://www.cancer.gov>) provides the public with access to the PDQ database, consisting of cancer treatment summaries and cancer clinical trials, including approximately 2,000 cancer clinical trials open to patient accrual. These include trials sponsored by NCI, as well as those submitted by the pharmaceutical industry. The information summaries are developed through peer review and application of levels of evidence. A parallel summary is written for the lay public; both the health professional and patient versions are also available in Spanish. This registry is easily accessed through NCI's Web site, where users are able to narrow their search based on multiple parameters, including disease characteristics and geographic location. The Web site provides contextual material about clinical trial participation, to help users easily find information to help them make

informed decisions regarding cancer treatment. The Web site is currently being redesigned to make it even easier for the public to find the information they need, including easier access to information regarding cancer treatment and clinical trials.

Improving the Clinical Trial Process

The Clinical Trials Working Group (CTWG) will attempt to better integrate the many diverse components of NCI's vast clinical trials program to ensure that the most important scientific questions are being addressed expeditiously, that duplication is avoided, resources are optimally distributed, and the structures in place are appropriate for 21st century science and technology.

Regarding increasing funding for the clinical trial cooperative groups to levels approved by peer review, it is important to note that the total funding for the cooperative groups rose by over 60% during the period FY98-03 to peer-review-recommended full funding at that time, and the amount of funding to cover the costs associated with enrolling a patient in a trial more than doubled from less than \$1000 at most sites to \$2000 at all sites currently. The cooperative groups, albeit extremely important, are only one component of the complex clinical trials system described above. While they are responsible for accrual to crucial definitive Phase 3 studies which enroll the largest number of patients overall, they are also the largest individual grants in NCI's portfolio. The Clinical Trials Groups undergo peer review once every 6 years. At this review, both major accomplishments of the past 6 years and general scientific plans for the next 6 years are presented along with a budget to support these planned efforts. However, the specific number of clinical trials that will actually be conducted is not predictable, nor is the size of each trial or its accrual rate known at the time of peer review. Since these two factors are critical determinants of the funding, administrative support, and resources required to complete the research agenda, the annual budget of each Group fluctuates. Each Phase 3 trial costs anywhere from \$2 million to \$10 million, depending on its size. Therefore, the budget approved at the time of peer review is seen as a future projection based on an optimal set of provisional plans. Not all these plans will come to fruition for multiple reasons - some are duplicative of other efforts not known to peer reviewers at the time of review, and, not infrequently, unanticipated scientific developments and opportunities occur. Therefore, on an annual basis, NCI staff assesses the actual needs of each Group, prioritizes studies among the various Cooperative Groups, and allocates funds to each Group based on the total pool of available resources. While peer review does a good job of assessing the infrastructure and track record for these large cooperative groups, it is not able to assess the relative merits and prioritization of all of a group's proposed research projects against the available NCI resources. NCI staff attempt to look across all the existing projects, research priorities, and proposed projects to make that assessment. The CTWG will enhance that process by suggesting areas where resources can be conserved and re-aligned to get the highest priority research done most efficiently, thereby accelerating the delivery of promising new treatments to patients.

The Role of www.clinicaltrials.gov

In 2000, the National Library of Medicine (NLM) launched a new Web site, www.clinicaltrials.gov, which aims to be a complete listing of all U.S. Government- and industry-sponsored clinical trials, including cancer trials. The NIH, through the NLM, has developed this site in collaboration with the Food and Drug Administration (FDA) as a result of the FDA Modernization Act, which was passed into law in November 1997. Although no single resource lists every cancer clinical trial being conducted in the United States and abroad, ClinicalTrials.gov currently contains approximately 10,200 clinical studies sponsored by the NIH, other federal agencies, and private industry.

Studies listed in the database are conducted in all 50 States and in over 90 countries. For each trial, the website presents a description of the purpose of the experimental trial, eligibility criteria for participation in the trial, location of the trial, and a point of contact for those who would like to enroll. ClinicalTrials.gov receives over 2.5 million page views per month and hosts approximately 16,000 visitors daily. In addition to helping patients find clinical trials in which they might participate, this website also educates users about clinical trials research, regulatory issues, and the meaning of informed consent. It provides links to background and related research and allows mining of statistics related to clinical studies.

NCI's cancer.gov website is a disease specific portal that includes extensive additional information about cancer, its prevention and treatment, and other material of interest to cancer patients and professionals, as described above. All clinical trials information in cancer.gov is downloaded to and available through www.clinicaltrials.gov as well.

NCI's Commitment to the 2015 'Challenge Goal'

The NCI is taking steps to achieve the 2015 challenge by accelerating the pace of progress across the entire cancer research continuum. Basic research, which is aimed at *discovering* the pathways that lead to cancer, represents the beginning of the continuum that proceeds through *development* of new agents and technologies and ultimately to the *delivery* of these new interventions to patients. Increasing our knowledge of the molecular defects in cancer cells and their microenvironment and identifying the biomarkers that characterize the cancer process will enable the development of new targeted interventions for preventing, detecting and treating cancer.

The NCI has identified six "mission-critical" research areas that offer significant potential for accelerating progress across the cancer continuum and for realizing our 2015 goal. These include: harnessing the power of the newly emerging science of molecular epidemiology to better identify risk populations; developing an integrative understanding of cancer (systems) biology to discover key biomarkers and targets; facilitating the development of strategic cancer interventions for targeted prevention, early detection, and treatment; creating a national integrated clinical trials system to more effectively test these interventions; overcoming health disparities to deliver these advances to those in greatest need; and developing a bioinformatics network to connect the cancer research community and optimize the collection, analysis, and use of the enormous amount of data that must be managed and shared.

A key example of progress in a mission-critical area is NCI's launching of the Cancer Biomedical Informatics Grid (caBIG). This pilot initiative has the potential to transform the pace of cancer research by providing the tools needed to share information and data, by initially connecting 50 of our NCI-designated cancer centers through an NCI-developed open source system to become, in effect, the "World Wide Web" of cancer research. This platform eventually will link individual cancer researchers and research institutions across the nation, and around the world, in an open source, federated network that will enable researchers to share tools, standards, data, computing applications, and technologies. This bioinformatics initiative will allow researchers to answer research questions more rapidly and efficiently and will accelerate progress in all aspects of cancer research.

Conclusion

NCI-supported clinical trials provide a crucial infrastructure for moving new cancer interventions from the laboratory to studies in people with, or at risk for, cancer and then to the health care setting. These clinical trials have always included investigations of a broad set of interventions - chemoprevention, chemotherapy, radiation, and surgery - sometimes used alone and sometimes in combination. With recent advances in deciphering the molecular changes that cause cancer, a new paradigm of cancer treatment and prevention research is emerging and bringing with it the promise of an exponential growth in effective cancer interventions.