THE CANCER LETTER

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NCI Outlines Need For $3.873 Billion To Seize Cancer Research Opportunities

The National Cancer Institute says it needs a budget of $3.873 billion for fiscal year 2000 to sustain its research programs, seize extraordinary *opportunities* in cancer research, and translate those findings into practical applications.

The funding request is $946 million above the $2.927 billion FY1999 appropriation approved by Congress and signed into law last week.

NCI submitted the budget request to the White House on Oct. 23, just two days after President Clinton signed a spending bill that gave NCI the largest increase in its history.

"Our ability to act on the new initiatives that we have spent the last

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In Brief:

WHO Begins Project To Urge Governments To Establish "National Cancer Programs"

WORLD HEALTH ORGANIZATION has begun a Program of Cancer Control to reduce the global incidence, morbidity, and mortality from cancer through the development of National Cancer Programs in each of the 191 member states of the United Nations. Each National Cancer Program would establish cancer control priorities, taking into account the prevalence of certain types of cancer and the country's economy. To help national health departments set priorities, WHO has established a cancer control "priority ladder," starting with tobacco control. "Action is needed now from health ministries across the world to collaborate with the private sector in order to make a difference through focused National Cancer Programs," said **Karol Sikora**, WHO cancer program chief, announcing the new program at conference at the Royal College of Physicians, London, on Oct. 19. The WHO director-general and former prime minister of Norway, **Gro Harlem Brundtland**, was scheduled to discuss the cancer program and other WHO initiatives at NIH in Bethesda, MD, on Oct. 29. . . . **HAROLD MAURER**, the immediate past chairman of the Intergroup Rhabdomyoscarcoma Study Group and dean of the College of Medicine of the University of Nebraska Medical Center, was appointed chancellor of the University of Nebraska Medical Center effective Dec. 1. . . . **SPACE SHUTTLE** Discovery, launched Oct. 29, carries pharmaceutical production experiments designed by Bristol-Myers Squibb Co. to test rates of fermentation in weightlessness. "In a zero-G environment, we want to determine if it's

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NCI Bypass Budgets Guide Institute's Funding Initiatives

(Continued from page 1)

few years articulating, through an enormous amount of effort by hundreds of advisors, is certainly made much more possible by the fact that the NCI received the largest increase that we've ever received, a 15.1 percent increase," NCI Director Richard Klausner said to the NCI Director's Consumer Liaison Group earlier this week.

"It's an enormous measure of expectation, and a vote of confidence, that we actually have a program that we can articulate and defend," Klausner said at the Oct. 26 meeting. "It's important that we come back next year to Congress and be very clear about what we've done."

The $385 million increase amounted to about half of the increase the Institute requested in last year's Bypass Budget, Klausner said.

The new Bypass document requests $2.99 billion as a "core" amount to sustain the Institute's research programs, plus $189.5 million to "seize extraordinary opportunities to further progress," and $693.5 million to "create and sustain mechanisms that will enable us to meet the challenge of rapidly translating our findings from the laboratory into practical applications."

The National Cancer Act of 1971 requires the NCI director to send a document each fall directly to the President outlining the Institute's professional judgment of the funding needs in cancer research. Because the document skips over the usual review levels at NIH and the Department of Health and Human Services, it is referred to as the "Bypass Budget."

Klausner's Third Bypass Budget

The FY2000 Bypass Budget, Klausner's third since being appointed NCI director in 1995, represents the third volume of what Klausner has said he envisions as a Bypass trilogy.

Once identified, the four or five major areas of scientific opportunity outlined in the Bypass Budget should not change much from year to year, but should be reconsidered about every three years, he said.

Over the next year, NCI and its external advisors will write "the first of the second cycle of the three-year cycle of the Bypass," Klausner said to the DCLG.

Cancer research advocates have praised Klausner for completely revamping the Bypass Budget, which had grown over the years to a 600-page reference work that painstakingly described hundreds of research programs and proposals, but failed to communicate a coherent vision of the Institute's priorities.

Klausner's first Bypass Budget, for FY97/98, requested $2.7 billion, and outlined five areas of "Extraordinary Opportunity" for cancer research, in only 80 pages (**The Cancer Letter**, March 29, 1996).

The document and its successor, the FY99 Bypass, have guided the Institute's new research initiatives, Klausner said. The results are evident in the third volume of the trilogy, the FY2000 Bypass, which lists the projects that have gotten underway in the past three years.

"Over the last few years we have put in place an entirely new National Cancer Program, in terms of new structures and new initiatives," Klausner said to the DCLG. "Through these 'Extraordinary Opportunities,' NCI has become a very proactive scientific institution, creating new types of resources, reagents, intellectual information, that we think are going to dramatically speed the discovery process."

Perhaps that explains why the new Bypass document is 90 pages long, 10 pages more than the FY99 and FY97/98 documents. Also, the margins, the typeface, and the leading, or space between the lines of copy, are noticeably smaller than the initial Klausner-era document.

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"It's longer," Klausner said to the National Cancer Advisory Board last month. "We will work to get it back down next year."

Extraordinary Opportunities

The FY2000 Bypass request for the Extraordinary Opportunities includes:

Cancer Genetics: $67 million. Objectives are to expand research and training in cancer genetics, develop informatics to collect data, develop diagnostic tests for gene alterations, provide the infrastructure to establish interventions, establish approaches to study the interaction between genes and individual genetic variations and the environment, and provide training in genetic counseling for health professionals.

The funding would support six areas of investment, including:

—$8 million for the Cancer Genetics Network, for which NCI recently announced awards (**The Cancer Letter**, Oct. 23 and July 31), to conduct studies on the genetic basis for cancer susceptibility, develop cancer genetics educational programs, and develop informatics.

—$12 million to expand existing population and family-based registries, increase access to these registries, and use the registries for gene discovery.

—$5 million for the Genetic Annotation Initiative, established as part of the Cancer Genome Anatomy Project, to identify genetic variations in cancer-related genes and adapt technologies for clinical detection and measurement of genetic variation.

—$11 million for comprehensive molecular analysis, to integrate cytogenetic and physical maps of the human genome, develop technologies for analysis of chromosomal aberrations, translate technologies for use in clinical and population studies, conduct pilot studies linking molecular analysis of tumors to population-based studies and clinical data, develop informatics and make available a database of cancer chromosomal aberrations.

—$19.5 million for gene-environment interactions, to collect and maintain a population-based repository of biological specimens, develop and implement a questionnaire for environmental risks, measure exposure to environmental risk factors, develop tools for molecular analysis of environmentally induced alterations of genes, assess impact of complex interactions between genes, environment, and lifestyle on cancer risk, and develop informatics.

—$7.5 million for training and education programs and $4 million for management and support.

Preclinical Models of Cancer: $41.3 million total. Objectives are to develop new preclinical models of cancer to study gene mutations and provide a natural setting for studying all stages of tumor development, and facilitate more rapid testing of cancer prevention and detection strategies and new treatment regimens.

The funding would support the following:

—$4.3 million for the Mouse Cancer Genome Anatomy Project to produce 50 cDNA libraries from mouse cancer models, 100 cDNA libraries from different stages of mouse development and anatomical sites, and sequence tag 400,000 mouse gene transcripts.

—$21 million for mouse models to study the biology and treatment of human cancers, to improve technology for development and validation of mouse models, establish a database, use mouse models for identification and evaluation of detection, treatment, and intervention strategies, improve access to validated mouse models, and training in genetic manipulation of mice.

—$6 million to develop a new initiative to identify genes that modify cancer phenotypes in mice.

—$9 million for non-mammalian organism models to find oncogenes, cancer pathways, and screens for anticancer drugs.

—$1 million for management and support.

Imaging Technologies: $43.5 million total. Objectives are to improve diagnostic imaging technology so that it is both sensitive and specific enough to detect very small numbers of tumor cells, develop functional imaging to observe the characteristics of tumors and the effects of therapy, and create an infrastructure to rapidly assess new imaging technologies.

The funding would support the following:

—$14.5 million to develop multidisciplinary centers for molecular and functional imaging that would develop technologies and reagents, and establish conferences on in vivo molecular imaging.

—$7 million to develop and refine image-guided therapy for various cancer sites, and develop and apply imaging agents and technologies for the assessment of cancer drugs.

—$5 million for a Diagnostic Imaging Network

for the comprehensive clinical evaluation of new and refined imaging technologies.

—$11 million for small animal imaging facilities.

—$4 million for training.

—$1 million to establish a national forum for information exchange on imaging technologies.

—$1 million for management and support.

Defining the signatures of cancer cells—Detection and diagnosis: $75 million. Objectives are to improve early detection of cancer by identifying in body fluids tumor-specific secreted proteins and mutant genes that may signal the presence of small numbers of premalignant cells, and to use new knowledge of the molecular traits of tumor cells to improve the ability to diagnose and treat cancer.

The funding would support the following:

—$21.5 million for the Tumor Gene Index, planned as a complete index of all expressed genes in cancer cells.

—$8 million for molecular discovery, to develop methods to identify gene mutations, changes in gene expression, and to identify signaling and regulatory pathways, and to develop tools to interpret information from molecular analysis.

—$7 million for tissue repositories and secure informatics systems.

—$10 million for diagnostic assays and the development of new molecular classification schemes for all cancers.

—$20.5 million in detection, to determine secreted proteins that correlate with the presence of cancerous lesions, develop assays, and develop a detection research network.

—$6 million to fund long-range, high-risk projects for the development of remote detection technologies.

—$2 million for management and support.

Support For Research, Centers, Trials

The Bypass Budget document proposes spending $693.5 million over the funding request for core programs and extraordinary opportunities to provide additional support for investigator-initiated research, cancer centers, clinical trials, informatics, and training.

The additional funding would provide:

—$138.9 million enabling NCI to fund 1,800 new and competing renewal research project grants at peer-reviewed recommended levels, at an average cost of $355,000; funding the top 45 percent of single investigator grants; increase the average cost of a grant by 10 percent; double the number of program project grants and collaborative agreements; and fund more translational research projects.

—$79.5 million to expand existing NCI-sponsored cancer centers; fund six new cancer centers; help five more cancer center planning grants; expand the Specialized Programs of Research Excellence; and plan new types of centers linking academic institutions with community hospitals.

—$316.5 million to support investigator-initiated cooperative clinical trials; cover research costs to accrue an additional 20,000 patients in clinical trials conducted by the cooperative groups; bring current cooperative groups to full funding levels; support cancer prevention trials; fully fund participants in the Community Clinical Oncology Program; fund clinical trials conducted by the NCI Intramural Research Program; and enhance the national capacity to translate discoveries into new drugs.

—$35 million for informatics and information flow, to support multicenter clinical trials and the widespread availability of cancer information for patients.

—$28.5 million to study emerging trends in cancer, including data collection for the Breast Cancer Surveillance Consortium, surveillance research, and expansion of Surveillance, Epidemiology and End Results special studies.

—$95.1 million to facilitate training, education, and career development, including activities devoted to trainees from underserved populations.

Copies of the FY2000 Bypass Budget, "The Nation's Investment in Cancer Research," may be ordered by fax at 301-330-7968, by e-mail at cisocc@nih.gov, or by phone at 800-4-CANCER. The document and previous Bypass Budgets may be viewed online at http://www.nci.nih.gov by clicking on "What's New."

Congress Tells NCI: Fund More Prostate Cancer Research

The appropriations bill signed by President Clinton last week gives NCI the highest increase in its history—15.1 percent percent over last year—as well as a strongly worded mandate to spend more on prostate cancer research.

The Institute received $2.927 billion, the

appropriation proposed in the Senate bill. The NIH appropriation was $15.582 billion, a $1.96 billion increase from last year.

The legislation urges NIH to make prostate cancer a "a top priority in allocating funding increases." However—unlike the Senate bill—the measure does not include any earmark.

A provision inserted into the Senate bill by appropriations committee chairman Ted Stevens (R-AK) directed NIH to spend $175 million on prostate cancer research. Altogether, NIH spent about $114 million on prostate research last year.

The language of the NCI section of the appropriations bill follows:

"The conference agreement includes $2,927,187,000 for NCI, as proposed by the Senate instead of $2,787,830,000 as proposed by the House.

"The conference agreement deletes without prejudice the Senate bill language specifying $175 million for prostate cancer research at the NIH. The House bill contained no similar provision.

"It is agreed that spending for prostate cancer research over the years has not kept sufficient pace with the scientific opportunities and the proportion of the male population who are afflicted with this disease.

"This has resulted in significant gaps in scientific and clinical knowledge that contribute to the ongoing morbidity and mortality directly attributable to prostate cancer. To address this shortcoming, NIH is strongly urged to make prostate cancer a top priority in allocating funding increases.

"The agency is expected to accelerate spending on prostate cancer, taking into account the recommendation contained in the Senate report and bill. It is further expected that NIH will consult closely with the research community, clinicians, patient advocacy groups, and the Congress to identify promising new avenues of basic and clinical research.

"The agency is directed to develop a report to be presented to the House and Senate Committees on Appropriations within six months outlining the professional judgment for prostate cancer research for the next five years. The Secretary and the Director should also be prepared to discuss actions taken in planning, funding, and implementing the agency's prostate cancer research portfolio for fiscal years 1999 and 2000.

"Despite impressive NIH progress in the area of brain cancer research and development, there are still concerns with the growth rate of such tumors and NCI should continue to place a high priority on brain tumor research.

"The conference agreement supports the approach of using centers of excellence to conduct basic, translational, and clinical research to determine the cause, mechanisms of development, and better methods of treatment and prevention of primary and secondary brain tumors.

"The conference agreement concurs with Senate report language regarding the need for a comprehensive initiative designed to assist in minority cancer control, prevention, and treatment and notes that the Early Detection Breast Cancer Program consortium in south Florida is currently addressing the needs of the minority population with a concentrated and coordinated research and treatment effort.

"NCI is encouraged to provide increased funding for a breast cancer research initiative designed to assist in minority cancer control, prevention, and treatment.

"The Institute is urged to work with NIOSH to enhance extramural research in relevant NORA priority areas such as cancer research methods, special populations at risk, mixed exposures, risk assessment methods, and exposure assessment methods."

In other highlights of the appropriations legislation:

—The appropriations measure designated $50 million for the newly established NIH Center for Complementary and Alternative Medicine. At least $20 million of these funds would be expected to support "peer reviewed complementary and alternative medicine research grants and contracts that respond to program announcements and requests for proposals issued by the center."

—The NIH appropriation includes $237.5 million for buildings and facilities. This includes $90 million for the Clinical Research Center in fiscal 1999 and $40 million in fiscal year 2000, as proposed by the Senate. The House bill provided funds for 1999 only.

—The measure "encourages" the NIH director "to establish partnerships between new and existing centers to expand the scientific base in the field of mind/body medicine and teach and train health care professionals in these approaches."

—The NIH director is "urged to provide funding to the Office of Research on Minority Health for the purpose of increasing the number of African

American principal investigators to conduct HIV behavioral and clinical research targeting the links between substance abuse, sexual behaviors and the extraordinary HIV infection rates in African Americans." The document said emphasis should be placed on research into ways of breaking this linkage."

—The document instructs NIH "to cooperate in completing the Institute of Medicine study on cancer among minorities and the medically undeserved, and to provide timely access to requested data to enable the IOM to complete the study in an expeditious fashion." The director would be expected to report on the study's progress during the hearings on next year's budget request.

—The NIH Building 50, Consolidated Laboratory Building, was named the Louis Stokes Laboratories.

—The Centers for Disease Control and Prevention will receive $25 million for CDC to carry out the American Stop Smoking Intervention Study (ASSIST). These funds will not be transferred from NCI, the document states. The Senate report said the funds would be transferred from the Institute to CDC. The document provides $145 million for the CDC breast and cervical cancer screening program, but does not provide funds for women who were diagnosed through the program, but who lack funds to obtain treatment.

—The Health Care Financing Administration is urged to "act as soon as possible" to increase the Medicare payment for the screening Pap smear. "The agency is further urged to provide for a commensurate increase in the payment rate for new cervical cancer screening technologies," the document states. "It is recognized that access to the best cervical cancer screening techniques is particularly important to low-income, minority, and elderly women covered by Medicare who in too many cases do not receive regular preventive screenings."

—HHS is urged "to consult with the National Academy of Sciences to assess the current scientific knowledge on the potential environmental causes of breast cancer, and to identify research needs, establish research priorities, and make recommendations about the implementation of the research plan identified." The legislation said the consultation should include scientists, outside agencies, and community advocates.

—The HHS Office on Women's Health, the intelligence community and the National Information Display Laboratory are instructed to continue their technology transfer program aimed at developing computer-aided diagnoses of mammography. "OWH is strongly urged to continue the technology transfer effort with the NIDL to improve breast cancer detection, conduct clinical evaluations of promising technologies, conduct medical research on topics that show promise for future benefit in breast cancer detection and expand the technology transfer to other priority medical problems," the document states.

—HHS is told to cooperate with the Department of Energy and Nuclear Regulatory Commission to conduct "an independent scientific and management review and audit of the thyroid and leukemia studies being conducted by the US and the governments of Belarus and Ukraine."

—Last month, the Department of Defense appropriations bill committed $135 million to peer reviewed research in breast cancer and $50 million to prostate cancer.

The appropriations for all NIH institutes and centers follow:

National Heart, Lung and Blood Institute: $1,793,697,000

National Institute of Dental and Craniofacial Research: $234,338,000

National Institute of Diabetes and Digestive and Kidney Diseases: $994,218,000

National Institute of Neurological Disorders and Stroke: $903,278,000

National Institute of Allergy and Infectious Diseases: $1,570,102,000

National Institute of General Medical Sciences: $1,197,825,000

National Institute of Child Health and Human Development: $750,982,000

National Eye Institute: $395,857,000

National Institute of Environmental Health Sciences: $375,743,000

National Institute on Aging: $596,521,000

National Institute of Arthritis and Musculoskeletal and Skin Diseases: $308,164,000

National Institute on Deafness and Other Communication Disorders: $229,887,000

National Institute of Nursing Research: $69,834,000

National Institute of Alcohol Abuse and Alcoholism: $259,747,000

National Institute on Drug Abuse: $603,274,000

National Institute of Mental Health: $861,208,000

National Human Genome Research Institute: $264,892,000

National Center for Research Resources: $554,819,000

John E. Fogarty International Center: $35,426,000

National Library of Medicine: $181,309,000

Office of the NIH Director: $306,559,000

Letters to the Editor:

Burzynski Says Reviewers Sought To "Discredit" Therapy

To the Editor:

In an unprecedented move last April, FDA acting commissioner Michael Friedman violated the confidentiality of the agency's communications with regulated companies by releasing parts of Burzynski Research Institute's annual report during a hearing conducted by Rep. Dan Burton (R-IN).

Friedman's report was so inaccurate that it prompted a response from us (**The Cancer Letter**, May 22). Subsequently, **The Cancer Letter** requested copies of the annual report to have its own review of the data, and submitted the report to three oncologists (**The Cancer Letter**, Sept. 25). Surprisingly, to quote **The Cancer Letter**, "the reviewers did not audit the data in the annual report."

"The reviewers first assessed protocol design and the quality of data," the story states. "After enumerating fundamental errors in protocol design and data collection, the reviewers concluded that the studies were so flawed that auditing them was meaningless."

It appears that the efforts of the reviewers were concentrated on discrediting the protocols and assuming that since, according to them, the protocol design was wrong, the data are not good and it is impossible to say that treatment with antineoplastons is effective.

Most of the article deals with the supposed errors in the protocols. It may come as a surprise to the reviewers that the protocols they are criticizing were designed by doctors from Memorial Sloan-Kettering Cancer Center, and used in phase II studies of antineoplastons sponsored by NCI.

The reviewers did not even care enough to review the data in the annual report, yet they expressed negative opinions. Since they did not review the data on the treatment with antineoplastons, their review is scientifically invalid.

Two experts mentioned in the article, Drs. Mark Malkin, of MSKCC, and Jan Buckner, of the Mayo Clinic, were institutional principal investigators who used the protocol. Additional patients were treated according to the same protocol by Dr. Eddie Reed at NCI. Additional co-investigators listed in NCI study included well-known experts such as Drs. Jerome Posner, Frank Lieberman, Charles Young and William Tong from MSKCC, Joel Reid and Randal Millikan from the Mayo Clinic and William Figg from NCI.

The protocol has been approved by the institutional review board at MSKCC, NCI and by the FDA. The identical protocol has been used as a prototype for protocols in clinical studies sponsored by BRI. Thus, if our protocols are flawed, then so were those by the NCI and its chosen investigators. We have always attempted to live by the standards set by the NCI.

Initially, protocols used by Dr. Stanislaw Burzynski were identical to NCI protocols. Subsequent changes have been made based on FDA request. The protocols were accepted by NCI and two leading cancer treatment centers, MSKCC and Mayo Clinic. In this respect, we have the opinion of 11 experts from NCI, MSKCC, and Mayo Clinic listed as the investigators on NCI protocol versus three experts selected by **The Cancer Letter**. Certainly, the opinions of 11 experts is that this was the right protocol, since they approved it and used it in clinical studies of antineoplastons. It is clear then that most of the negative opinions expressed in **The Cancer Letter** can be dismissed, since the protocols were designed by some of the best experts in the U.S.

The article creates a dilemma: should we follow the designs of NCI, FDA, MSKCC and Mayo Clinic or should we obey the teachings of Drs. Friedman, Ozer and Eisenberg? I believe the readers will agree that we should use design of the first group.

The next largest issue is the criticism of the annual report. Despite the fact that the oncologists selected by **The Cancer Letter** decided not to review the annual report, they expressed negative opinions about it. Their approach suggests they may never have seen or prepared an annual report to the FDA. This should be no surprise, because the annual report is prepared by the sponsor of a clinical trial, which is usually a pharmaceutical company.

Our report was prepared exactly according to instructions from the FDA. The FDA did not have even a single objection regarding the annual report

and requested that future annual reports be prepared the same way. Basically, the report lists data on the treatment with antineoplastons after approximately one-year existence of clinical trials. Every patient treated is listed. Many of these patients are not yet evaluable because the time was too short for evaluation. Nevertheless, even the patients who took the treatment for only a day must be listed. Therefore, the criticism of the annual report can be dismissed based on the fact that the report was prepared as the FDA wanted and they were satisfied with it.

The third major issue of criticism is hypernatremia occurring in patients taking antineoplastons. Our answer to this issue is that serious hypernatremia occurred in fewer than 1% of the patients. In the other patients, hypernatremia was only a laboratory result without any clinical change in the patient's condition, and was reversed by simple measures such as hydration. To fulfill FDA request, the slightest increase of sodium concentration in the serum which constitutes hypernatremia was reported by us to the FDA. The standard practice is that such small change which occurs in clinical trials using chemotherapy is usually not reported because it is of no clinical significance.

Pharmacokinetic studies with antineoplastons reveal that the entire sodium load, due to antineoplastons, is rapidly eliminated from the body through the kidneys. There were no cases of hypernatremia in patients in pharmacokinetic studies of antineoplastons, even after administration of high dosages of antineoplastons. Only in 0.1% of all patients (2 patients) hypernatremia was not reversed. One of these patients died as the result of a stroke before hypernatremia could be treated and another patient refused any treatment. Ozer, one of the experts selected by **The Cancer Letter**, admits that he has never seen severe hypernatremia in his practice, yet he is expressing an opinion in this area.

The fourth issue repeatedly discussed in **The Cancer Letter** article is "stable disease." In the treatment of astrocytoma, which is the most common in our clinical trials, we do not need to include stable disease as an objective response. We believe we have a sufficient number of complete and partial responses to prove that antineoplastons have anti-tumor activity.

It should be noted, however, that it is customary to include stable disease as objective response in peer reviewed articles describing clinical trials in brain tumors.

Following is a point-by-point refutation of the criticism expressed in **The Cancer Letter.**

—*"Working outside peer review Burzynski is conducting 71 concurrent, preliminary phase II trials."* Dr. Burzynski is not working outside peer review. Clinical trials are supervised by the FDA and the Institutional Review Board. Cancer diagnosis is confirmed by outside pathologists, and the results are reviewed by outside radiologists.

—*"[Burzynski] is under a court order to administer antineoplastons exclusively through clinical trials or through 'special exceptions' from FDA."* This is completely untrue. The case of FDA vs. Burzynski ended in not guilty verdict for Dr. Burzynski. There is no court order in force now to order administration of antineoplastons in clinical trials or through special exceptions.

—*"[C]o-investigators who follow his patients ... have no knowledge of Burzynski's protocols."* All co-investigators are given copies of the protocols.

—*"CAN-1 is so distinctly unconventional that frustrated prosecutors promptly began to refer to it as 'the garbage can.'"* This charge is no more valid as the other charges [former prosecutor Michael] Clark made, which were rejected by the jurors. The accusation is that CAN-1 contains too many varieties of cancer to be treated. In fact many cancer treatment protocols treat a number of different types of cancer. The protocol for phenylacetate, sponsored by NCI, includes many different types of cancer.

—*Dr. Norman Wolmark states: "To justify this kind of an effort, the investigator has to have 71 legitimate research questions."* We certainly have 71 legitimate research questions; one key question for each of the 71 protocols. The main question in each case is whether antineoplastons A10 and AS2-1 are safe and effective in the treatment for the type of cancer for which the protocol has been designed.

—*Dr. Robert Young states: "The problem with 71 pilot trials is that it is so diffuse that it becomes no trial at all."* It is not unusual for a medical institution to run more than 71 clinical trials. If the trials are conducted according to the protocol then the results can be scientifically evaluated. How many trials are conducted at Fox Chase Cancer Center? [The Burzynski Research Institute] employs between 110 and 130 employees with the number varying from time to time.

—*"In a statement, FDA officials indicated that the trials being conducted by Burzynski could not support a New Drug Application."* We believe this

statement concerns only one protocol, which is not even included in the 71 protocols mentioned in **The Cancer Letter**. In fact there are 71 prospective protocols and 1 retrospective protocol.

—The story quotes an FDA's statement: "[Burzynski]...has administered antineoplastons to several thousand patients without, for the most part, gathering enough information to determine whether the product is safe and actually works." All information gathered in the treatment of all patients is compiled to be submitted to the FDA in support of safety and efficacy of antineoplastons. Because the FDA delayed, for years, giving us an Investigational New Drug exemption, we have only recently been able to gather the sort of detailed information, the agency says it wants.

—Dr. David Parkinson states: "The reviews suggest that, at best, this extraordinarily large experience of treated patients ... is a collection of anecdotes." It is difficult to find logic in Parkinson's statement, since his former agency approved an identical protocol for antineoplaston studies sponsored by the NCI, at the time he worked there. Did the NCI purposely approve the protocol to deliver a collection of anecdotes?

—Dr. Janice Dutcher states: "From the comments, it seems that it's all commerce: Whoever wants it gets it. It's impossible to tell from anecdotal data, without controls, what is happening." As stated in all protocols approved by the FDA, the main objective is "to study the safety and possible effectiveness of antineoplastons in patients with cancer "and "to describe the patient's response, tolerance, and the side effects of this regimen." The patients are admitted according to strict entrance criteria approved by the FDA, which were designed primarily by the NCI.

—Dr. Barrie Cassileth states: "The reviews carefully delineate deficiencies in Dr. Burzynski's protocols. The reviews are sufficiently detailed and instructive to enable collaborative development of properly designed protocols." I did not submit any protocols for the review to Drs. Ozer, Friedman, and Eisenberg. Our annual report to the FDA compiled after one year of duration of 71 clinical trials. It is obvious that the annual report could not include complete information on the results of clinical trials, because these clinical trials had barely begun.

—"As a clinical investigator, Burzynski enjoys considerable leeway. FDA does not verify whether patients who are enrolled on protocol actually fit the entry criteria." The FDA requires more information on patient enrollment from us than from any other investigator. They are requesting not only an annual report, but also weekly and monthly reports, and we provide these.

— "The metabolic consequences of this therapy could be disastrous, said Bruce Chabner." As proven by the treatment of thousands of patients for many years the metabolic consequences of the therapy are certainly not disastrous. Most of the patients do not experience any toxicity.

—On the issue of "Accidental Co-Investigators," raised in ***The Cancer Letter:*** We can easily prove that doctors listed as co-investigators signed FDA Form 1572 to confirm that they were co-investigators.

—Ellen Stovall states: "I would like to see Dr. Burzyski's Congressional patrons apologize to the American people. Now that the truth is out, nothing less than an apology will suffice." This statement is based on the fact that the so called "patients groups" have never saw or analyzed any of our information on their own, but are blindly accepting the flawed analyses of the physicians consulted by **The Cancer Letter**. Apparently so-called "patient groups" quoted in **The Cancer Letter** have no idea that the protocol for studying antineoplastons was designed by MSKCC, and approved by the NCI and the FDA. They have never asked us for any protocol or any research data.

The Ozer Review

—"Dr. Burzynski is studying a heterogeneous, ill-defined patient population. He treats patients who come through the door and only patients who come through the door.... He organizes data by disease site, whatever the patient's stage, and whatever treatment they received prior to walking through the door of his clinic." The reviewer ignores the fact that a protocol is designed for the treatment of a specific type of cancer, i.e. separate protocol for treatment of pancreatic cancer, separate protocol for treatment of esophageal cancer, etc. The protocols define exactly what stage of the disease is accepted for the treatment and define what previous treatment patients are allowed to have received. Only some patients who come through the door are accepted into clinical trials. In fact most are not accepted. We can prove this.

—"The protocols are evaluating a single statistical endpoint: response. He doesn't evaluate disease-free survival, time to progression, quality of

life, or overall survival." The reviewer is wrong. We evaluate all these additional parameters. For instance, the survival analysis for one of the protocols was submitted to **The Cancer Letter**, but Dr. Ozer earlier stated he didn't bother to read this.

—*"Dr. Burzynski presents no baseline data. He presents no control data. He presents no description of methodology employed to measure active agents in the blood. How are these values affected by other variables, such as how recently these patients have been on other chemotherapy?"* All of these data are either included in the annual report or are now in preparation to be reported to the FDA. Dr. Ozer apparently did not read them, either.

—*"[T]he investigator would have to show stable disease not for a month or three months."* The reviewer might not be aware that three months (12 weeks) is the standard time necessary to claim stable disease, as accepted by NCI. The additional question is the duration of stable disease, which could be 3 months or 3 years etc.

—*"In the annual report to the FDA, I see problems of adherence to protocols. While protocols call for evaluation of response every 90 days, in some instances I see Dr. Burzynski making these evaluations monthly."* Most of our protocols call for clinical evaluation monthly, but some only every 90 days.

—*"I do see patients with responses who subsequently withdraw from the study. That means to me that the patient's perception of their benefit is less than what Dr. Burzynski is interpreting."* Some of the patients felt so well that they decided to discontinue the treatment sooner than advised. Their tumors disappeared and they did not feel it was necessary for them to continue the maintenance treatment.

—*"In the data presented to the FDA, I see a 4% death rate that may be attributable to the therapy. That's a very significant grade 5 toxicity rate."* During the entire 22-year clinical experience with antineoplastons, no grade 5 toxicity was ever identified. There was never a case of death which can be proved attributable to antineoplastons.

—*"By that token, 180 mEq/L [hypernatremia] is truly remarkable. I have never seen it."* By his own statement, the reviewer does not have any experience in the treatment of hypernatremia. Hypernatremia of this magnitude occasionally occurs in advanced brain tumors and liver cancer.

—*"The pharmacokinetic data are reported, but are impossible to interpret."* We can help the reviewer to interpret this data if he so desires. The pharmacokinetic data clearly indicate that hypernatremia does not occur even during administration of large dosages of antineoplastons.

—*"About 80% of Dr. Burzynski's patient population is too early to evaluate, and yet he evaluates them, and he does include the data from that evaluation."* The reviewer appears to be completely confused. We are required to report in the annual report all cases of patients, even those who are too-early-to-evaluate. The fact that 80% of patients are too early to evaluate, clearly indicates that clinical studies just began. They were far from being finished and the FDA should have never made an evaluation of the treatment based on such preliminary results, nor should it have counted these too early to evaluate cases as failures. Currently, almost a year after the date of the annual report, a number of clinical trials have reached an endpoint.

—*"Compassionate use should be preserved for cases when you know that a treatment is likely to benefit the patient, but the patient doesn't meet the protocol criteria."* Compassionate exception is applied for patients when the patient is likely to benefit from the treatment, but does not meet the protocol criteria.

—*"I would not allow Dr. Burzynski to continue enrollment of new patients in his study."* This clearly shows the discriminatory attitude of the reviewer. Despite the fact that a few clinical trials have reached an endpoint, most of the studies are not yet completed. There is no reason to discontinue the trials before accrual of the proper number of patients listed in the protocols.

The Friedman Review

Friedman makes numerous references to hypernatremia, as if it was major problem. Despite the reviewer's comments, hypernatremia was reversed without any complications in 99.9% of patients.

—*"Dr. Burzynski is collecting data in anecdotal fashion."* The data are collected exactly the way that NCI and the FDA requested.

—*"I see no data that would support the activity of this agent in brain tumors in any way, shape or form."* Since by their own admission the reviewers did not even see the data, certainly they were not able to see responses. Therefore, any statements of the reviewers about supposed lack of anti-tumor activity are completely invalid.

The Eisenberg Review

—Dr. Eisenberg made several criticisms of acceptance criteria of our clinical trials.

The patients admitted to our clinical trials meet all criteria recommended by the reviewer.

—*"The results of his studies should be presented in a peer-reviewed, published paper..."* The results of the studies have already been submitted to peer review journals and some of them are in press.

—*"Dr. Burzynski has studied hundreds of patients without publishing his results...."* Burzynski has published 104 papers, many of them describing results of treatment with antineoplastons in cancer patients.

—*"The results in the annual report are presented in the form of raw data: many, many pages of charts detailing patient names, I.D. number, patient characteristics, name of disease, response to treatment and current status."* The results are presented exactly the way that the FDA has requested.

—*"I can't understand why so many of Dr. Burzynski's patients entered in the studies are classified as 'not evaluable.'"* The data are reported only after one-year duration of 71 clinical trials. For many of these patients, this was too soon for evaluation, but the FDA requires that we include them in the annual report.

—*"Oncologists use standard measurements for response."* In all treatment protocols for antineoplastons we use standard measurements for response.

—*"Dr. Burzynski's brain tumor data are impossible to interpret since all brain tumors are lumped together into a single category."* All brain tumor data are segregated by the tumor type. Apparently, this reviewer also did not read the annual report.

The Case Study of Treatment of A Medulloblastoma Patient

I can only feel sorry for the short memory of Dr. Henry Friedman, who was the first one to be excited about the response of this particular patient to treatment with antineoplastons.

Seeing the response to antineoplastons he became very interested in conducting clinical trials with antineoplastons by himself, which was witnessed by this patient's parents. This patient was admitted according to entrance criteria into an FDA approved clinical protocol.

You report that "Friedman disagrees with Burzynski's claim that the boy's tumor had shrunk."

Dr. Friedman was the first to be amazed that the tumor had shrunk; his reaction was witnessed by this patient's parents.

Stanislaw Burzynski
Houston, TX

Howard Ozer Responds: Having a single phase II trial and word-processing it into 70 different indications encompassing many stages of many diseases is the principal ingredient of scientific nonsense.

Dr. Burzynski doesn't seem to understand that cancers are different. His point-by-point "refutation" of valid scientific criticism typifies an approach that has neither clinical nor research validity: He fails to realize that protocol design requires prospective strategies and disease-and state-specific approaches.

I am struck by his unwillingness to accept even the most minor criticisms and suggestions by unbiased peer reviewers. He seems to approach his use of antineoplastons more as a business strategy—or perhaps a religion—than an effort to discover new knowledge.

Henry Friedman Responds: Dr. Burzynski's elaborate answer ignores the fundamental problem that all three reviewers are approaching in a similar fashion.

With nearly 1,000 patients treated last year alone, no one has any idea whether antineoplastons work. Since most phase II trials make their point within the accrual of 20 to 30 patients, it's absolutely unbelievable that these many patients have been exposed to the treatment, and not one of the reviewers was able to say, "Yes, Dr. Burzynski, you've made the case."

With regard to Dr. Burzynski feeling sorry for my short memory, I can say that at least I remember having done clinical trials that produce answers after completing enrollment.

Contrary to Dr. Burzynski's allegations, I was never interested in using his drug. I did call his institute once, to learn whether they were conducting rigorous trials that would produce an answer. After some discussions, it became apparent that at the end of the trial we would not know anything.

I have never made any statement of being "impressed" by what was going on with the medulloblastoma patient whose treatment was

described in the case study. Basically, the child's parents were desperate for help, and I can understand their clinging to Dr. Burzynski. To them, his treatment represented the hope of effective therapy without the side effects of standard care.

It's much less understandable how Dr. Burzynski can defend what he has done to that child. My review of the scans makes it clear that the patient had no measurable disease that would have allowed an assessment of a response to antineoplastons. I would be pleased to review the original MRIs with anyone who wants to examine this case.

In a nutshell, Dr. Burzynski used an agent of unproven activity, and no activity was seen.

Peter Eisenberg Responds: With about 1,000 patients treated last year alone, I find it unusual and distressing that Dr. Burzynski has not published his results in widely read peer-reviewed journals.

The Cancer Letter Responds: "The Antineoplaston Anomaly," in the Sept. 25 issue of **The Cancer Letter**, clearly and prominently stated that Dr. Burzynski's protocols are modeled on the NCI-sponsored phase II study of antineoplastons conducted at the Mayo Clinic, MSKCC, and the NIH Clinical Center.

Surely Dr. Burzynski realizes that there is a fundamental difference between the NCI approach, which involved conducting a single trial in a subset of astrocytoma patients, and his own efforts conducting 71 trials that span many diseases.

If Dr. Burzynski believes that he is not under a court order to administer his therapy through clinical trials and special exceptions from FDA, we suggest that he review the May 24, 1984, permanent injunction by Judge Gabrielle McDonald, of the US District Court for the Southern District of Texas. Federal courts have upheld and strengthened the McDonald injunction on two occasions:

—The 1995 ruling by the US Court of Appeals Fifth Circuit in Trustees of the Northwest Laundry & Dry Cleaners Health & Welfare Trust Fund v. Burzynski, and

—The 1996 ruling by US Judge Simeon Lake, who gave Burzynski a choice between setting up clinical trials and bond revocation in a case brought against him by the federal government. The Lake order was upheld by the Fifth Circuit.

The McDonald and Lake rulings are discussed in the story.

Dr. Burzynski is unfair to the three reviewers when he asserts that they "did not even care enough to review the data in the annual report," and instead concentrated on "discrediting" his work. The reviewers thoroughly analyzed the protocols and the data, finding fundamental design flaws that made any audit pointless. Dr. Burzynski's assertions notwithstanding, the fact that three respected experts working independently came up with *identical* conclusions is worthy of note.

Dr. Burzynski is also mistaken in stating that his protocols were "approved" by FDA. The agency does not approve protocols. It approves drugs. Generally, protocols are reviewed for safety of research subjects. *Protocol design is the* responsibility of the investigator.

We stand by the story.

To the Editor:

Dr. Burzynski's detractors are using the special issue of **The Cancer Letter** as a vehicle to orchestrate the downfall of a potential cure for cancer. They do this country no service by perpetuating the untruth that Dr. Burzynski is a charlatan.

I have three observations on what I found to be a very biased article:

1. The experts you quote have not done their homework. As a result, the article is fraught with omissions and half-truths. In some cases, the experts were untruthful. The protocols described as error-ridden were designed at NCI, Memorial Sloan-Kettering Cancer Center, and the Mayo Clinic.

2. If the data were as flawed as is described, the FDA would have forced Dr. Burzynski to close all the trials he is conducting.

3. The article fails to mention patients. It can be argued that good science is based on data, not patients. However, as defined by Webster, data are merely "measurements to be used as a basis for reasoning, discussion, or calculation." In contrast, evidence is "an outward sign that furnishes proof." Dr. Burzynski's patients are evidence, not data; they are proof that antineoplastons work. Certainly, they are not anecdotes: 1,000 patients equals evidence. Is it not illogical to ignore patients as evidence in approving drugs for untreatable cancers?

Dr. Burzynski has treated thousands of patients. Surely, if only a handful had had legitimate complaints or had died as a result of adverse events directly related to antineoplaston therapy, he would

have been stopped by the FDA long ago. If Dr. Burzynski were a charlatan, he would have fled a few miles southwest to Mexico years ago; if he were a fraud, he would have chosen to treat less rare, and thus more lucrative, cancers.

I do not hear of patients who were told to go home and die calling for more data. These are the patients Dr. Burzynski is treating.

My 49-year-old husband was diagnosed with stage IV renal cell carcinoma involving the spine and vena cava. In July, 1997, he was given 6 months to live by an oncologic surgeon who made an unsuccessful surgical attempt to remove the tumor. In August, he began treatment at the Burzynski Clinic, having had no other treatment. In November, he stopped taking morphine three times a day. He had no more pain, and he has had none since then.

Although my husband has had a heart attack, has kidney cancer, and is taking a high dosage of antineoplastons, hypernatremia never has been a problem. Recently, the remnants of his tumor were removed surgically, and he is doing fine. He is alive when he should not be, and he looks and feels healthy.

Why not ask Dr. Burzynski's patients who have had chemotherapy and radiotherapy which they prefer?

Webster defines a red herring as "something that distracts from the real issue." Hypernatremia is a red herring. In fact, most of the criticisms in **The Cancer Letter** article are distractions from the real issues; thus, they too are red herrings.

Patricia Walter
Philadelphia, PA

To the Editor:

Your article on Dr. Burzynski's clinical trials missed the real issues. The article essentially asked the question: Are Dr. Burzynski's clinical trials good?

"No, the trials aren't good," said the experts whose advice you sought. I don't want to jump into that academic spitting fight over trials design. Instead, I will stick to the important issues.

You would have made your job easier if you had stuck to the following two issues:

1. Antineoplastons will be approved based on treatment of malignant brain tumors. Approval will be based on the trials conducted on malignant brain tumors, not on any other trials. I hope you were given the results from the trial on brain stem gliomas. The current data from this trial shows that 16 patients were evaluable, two reached complete remission, three reached partial remission, and another six were classified as stable during the study period. Because antineoplastons can continue to be administered for years with the tumors continuing to shrink, the partial response and stable patients can eventually reach complete remission.

Results like these from any brain tumor treatment are unheard of. No matter how poorly designed the trial, no matter how much selection bias you apply, no matter how much tweaking of this or that, a cancer researcher would be hard-pressed to fashion a group of 16 brain stem glioma patients and document similar results over a two year period with any existing treatment. In fact, even if you started a study on, say, radiation, selecting only those patients who responded to radiation as the participants and tracked them over two years, you would probably not have any survivors.

2. Your next question should have been, "My God, is this real?" The logical approach to answering this is to pick up the phone, get the names and numbers of the 16 patients or families involved, and call each one of them. That would have been about a day's worth of work, and I'll wager to say that it would have yielded a much better article.

The article fixates on the single side effect that occasionally appears when treating people with antineoplastons: in a few cases, the sodium in blood tests is high. Had you done your homework by calling those 16 families, you would have found that increased sodium in the blood is nothing. You would have talked to parents who, prior to the Antineoplaston trial, had subjected their child to chemotherapy treatments and watched them vomit, lose their hair, suffer from bone marrow damage and decreased blood counts, nerve damage, hearing damage, liver and kidney damage—only to find that the treatment had been ineffective.

Focusing on a side effect which is seen in a few cases, is easily controlled, and has no long term effects, is irresponsible if not barbaric.

Our son has been on antineoplastons for nearly four years, and leads a relatively normal teenage life. In the realm of brain tumor treatments, I would classify the "side effects" associated with antineoplastons as "inconveniences." You want real side effects, try carboplatin.

I don't pretend to understand why you and your "experts" are so quick to abandon common sense and

work diligently to discredit this treatment. Common sense says that if even a few cases of brain stem glioma are reversed by a treatment that has no side effects, cancer researchers would jump for joy and focus all their efforts on figuring out why this treatment works. But cancer research doesn't work that way, it doesn't seem to employ common sense, which might be why it hasn't been more successful.

Next to the standard treatments for brain stem gliomas, antineoplastons offer great hope. If the FDA can approve a drug for pancreatic cancer based on a study showing it extends the life of the group by a mere two weeks, Dr. Burzynski's trials are all that are needed to justify FDA approval of antineoplastons for brain tumors.

Continuing to cloud real results with meaningless academic spitting fights about "the structure of the data" when the disease being treated is rare, incurable, and the treatments currently offered are hopeless and extremely damaging is a waste of time and a waste of children's lives.

Ted Wadman
Corvallis, OR

To the Editor:

When I retired from active cancer research in 1982, I decided to learn everything I could about the "unorthodox" alternative treatments being offered to cancer patients. I hoped I could find one that was scientifically valid, a "diamond in the rough," so I could help bring it into clinical use.

My associate in this search was attorney and medical care ombudsman Grace Ann Monaco. In 1985, we were awarded an NIH grant to produce a database containing the results of our investigations. My role was to validate the biology, biochemistry, and physiology cited as the basis for these treatments.

During the following years, we collected and studied the literature produced by about 70 "alternative treatment" practitioners. It was then that I learned about Stanislaw Burzynski and his antineoplastons. By 1990, I had read and evaluated more than 150 of Burzynski's published papers, most of his promotional brochures, and a number of his media handouts. The results of my five-year study of Burzynski's literature led me to conclude that there was no scientific basis for his claims about antineoplastons.

My conclusions and the supporting data were included in a database on alternative medicine that we sent to the NCI early in 1991. From that point on, the proponents of alternative medicine—notably Sen. Tom Harkin (D-IA)—had a complete, objective assessment of the Burzynski treatment. Nonetheless, responding to political pressure, NCI sent a team to Burzynski's clinic to assess his "best cases."

In January 1992, I published a paper about Burzynski's treatment in the Journal of the American Medical Association. The paper showed that Burzynski's explanation for how antineoplastons work had no basis in science. However, policy-makers did not regard these issues of science as significant.

Although they knew from newspaper and TV coverage that antineoplastons were being infused into patients, no one bothered to initiate an investigation into the possibility that dire clinical consequences could occur when a patient's body was flooded with these salt-laden solutions of urinary waste chemicals.

I was overjoyed when I read the four-part series on antineoplastons published in the Sept. 25 issue of **The Cancer Letter**. Readers should note that this investigation was not instigated or carried out by physicians. It took someone like Paul Goldberg, a savvy journalist and courageous editor, to confront the situation, search out the facts and make them available to the public. His series represents investigative reporting of the highest quality.

Having worked hard for 20 years to alert the public to the dangers of unsubstantiated claims, I am not so naive as to believe that one report, no matter how superbly documented, can influence the intractable mindsets of zealots and "true believers."

Goldberg's report provides compelling evidence that "special considerations" allowed off-protocol infusions of antineoplastons to be given without any of the oversight that government health care agencies are mandated to exercise over new medical treatments.

Medical consumers, health care activists, and physicians should demand that their Congressmen find out why this intolerable situation was allowed to come about.

Saul Green
New York, NY

Funding Opportunities:

Funding Offered To Groups

Title: **Request for Competing Applications From the NCI Clinical Trials Cooperative Groups To Conduct Clinical Studies on Older Cancer Patients.** The

NCI Cancer Therapy Evaluation Program and the Geriatrics Program of the National Institute on Aging are soliciting competitive cooperative agreement (U10) applications for up to five years of support from the adult NCI Clinical Trials Cooperative Groups to conduct clinical studies that promote the development of a knowledge base to produce new treatment strategies for older patients (65 years and older).

The paucity of data on age-related issues and problems at the aging/cancer interface make it difficult to provide definitive answers to many questions that arise about cancer treatment in older persons. The goal of this research initiative is to stimulate clinical trials research relevant to older persons with cancer. The risk of developing cancer increases with advancing age. Investigators are encouraged to develop information on the complexities of treating patients who are likely to have concomitant age-related conditions and other diseases and how these clinical challenges can be resolved to improve the care and treatment of older patients. The necessary resources and infrastructure consisting of access to patients and the existing tissue banks are in place within the NCI Clinical Trials Cooperative Groups such that this initiative will be able to capitalize and move research forward at a rapid pace.

NCI staff will contact the NCI Clinical Trials Cooperative Groups directly regarding application procedures and format.

Inquiries: Rosemary Yancik, Ph.D., Geriatrics Program, National Institute on Aging, 7201 Wisconsin Avenue, Suite 3E327 MSC 9205 Bethesda, MD 20892-9205; phone 301- 496-5278, fax 301-402-1784, email: ry3e@nih.gov

Richard Ungerleider, M.D., Division of Cancer Treatment and Diagnosis, National Cancer Institute, 6130 Executive Boulevard, Room 741, Bethesda, MD 20892-7436, phone 301-496-2522, fax: 301-403-0557 Email: ru4m@nih.gov

Meeting for Potential Applicants to Mouse Models of Human Cancers Consortium. RFA CA-98-013 solicits cooperative agreement and NIH intramural applications from groups of investigators who are capable of, and interested in, becoming components of the NCI Mouse Models of Human Cancers Consortium. The purpose of implementing this Consortium is to accelerate the pace at which mice with heritable malignancies that are accurate, reproducible models of human cancers are made available to the research community for further investigation or application. The full text of the RFA can be accessed at: http://www.nih.gov/grants/guide/rfa-files/RFA-CA-98-013.html

An informational session for those investigators planning to submit applications in response to the RFA will be held Nov. 19, 1998, from 1-4 p.m. in the Lister Hill Auditorium, Building 38A, at NIH. Representatives from the NCI's extramural research programs, Grants Administration Branch, and Division of Extramural Activities will be available to provide information and to answer questions relevant to applications responding to this RFA. Transcripts will be available upon request for investigators who are unable to attend.

Investigators who plan to attend should contact the NCI staff member listed below by Nov. 13 to confirm their attendance and to obtain further information regarding the site of the meeting.

Inquiries: Cheryl L. Marks, Ph.D., Division of Cancer Biology, National Cancer Institute, Executive Plaza North, Room 501 Bethesda, MD 20892-7381; phone: 301-435-5226, fax: 301-496-8656, email: cm74v@nih.gov

Program Announcement

PAR-99-006

Title: **Small Grants Program for Behavioral Research in Cancer Control**

Application Receipt Dates: Dec. 20, April 20, and Aug. 20

The NCI Division of Cancer Control and Population Sciences invites applications focused on cancer control behavioral research. The Small Grants Program is designed to aid and facilitate the growth of a nationwide cohort of scientists with a high level of research expertise in behavioral cancer control research. Small grants are short-term awards to provide support for pilot projects, development and testing of new methodologies, secondary data analyzes, or innovative projects that provide a basis for more extended research.

New investigators in relevant fields and disciplines (e.g., medicine, public health, health promotion, health communications and informatics, epidemiology, anthropology, social work, nursing research, nutrition, health policy, health services research, and behavioral sciences, such as psychology, health education, and sociology) may apply for small grants to test ideas or do pilot studies.

This Program Announcement (PA) replaces and supersedes PAR-95-091, which was published in the NIH Guide, Volume 24, Number 33, September 22, 1995.

Eligible applicants include new investigators who have not previously been Principal Investigator (PI) on a NCI-funded cancer control research grant (R03, R01, P01), or established scientists refocusing their research interests to behavioral research in cancer. Predoctoral investigators currently enrolled in an accredited doctoral degree program also are eligible to apply. All applicants should identify a mentor or sponsor from whom they will receive guidance regarding the proposed research.

Support will be through the NIH Small Research Grant (R03) mechanism. The total project period may not exceed two years. The total budget must not exceed

$100,000 in direct costs for the entire project period. The direct costs in any one year must not exceed $50,000. The small grant award is not renewable.

This program is designed to encourage investigators from a variety of academic, scientific, and public health disciplines to apply their skills to behavioral research investigations in cancer prevention and control. The research may occur in a variety of settings, such as universities, cancer centers, communities, schools, health departments and worksites.

Investigators may choose any of the full range of scientific approaches to their work. Studies may contribute to the design, implementation or evaluation of future phase III-V studies, e.g., descriptive baseline surveys, testing, modification and validation of surveys or program materials for use in the proposed population groups, testing of recruitment, intervention or compliance procedures for participants, etc. Proposals should include justification of study design, methods, and sample size, including any relevant theoretical concepts which underlie the research, as well as clearly indicate the significance of the research and where it will lead.

Inquiries: Helen I. Meissner, Sc.M., DCCPS, NCI, Executive Plaza North, Room 232, MSC 7330, Bethesda, MD 20892-7330, phone: 301-435-2836, fax: 301-480-6637, email: hm36d@nih.gov

In Brief:

BMS Experiments In Space

(Continued from page 1)

possible to produce greater quantities of existing medicines and even see if we can discover completely new drugs," said **Salvatore Forenza**, executive director, lead discovery, at the BMS Pharmaceutical Research Institute. Since 1996, the company has collaborated with BioServe Space Technologies, a NASA-funded, nonprofit company affiliated with the University of Colorado's Aerospace Engineering Sciences Department, to design and conduct experiments aboard three previous shuttle missions in the areas of fungal and bacterial fermentation, medicinal plant growth, and X-ray crystallography. . . . **LYNNETTE JOHNSON WILLIAMS** was appointed deputy assistant secretary for public affairs/policy and strategy in the Department of Health and Human Services. Since 1994, Williams has been a public affairs executive at Powell Tate. Prior to joining the public relations firm, she served as press secretary for Sen. Carol Moseley-Braun (D-IL). . . . **WOMEN'S HEALTH INITIATIVE**, a 15-year study begun in 1991 by NIH and administered by the National Heart, Lung, and Blood Institute, has reached its recruitment goal of 68,000 women for the clinical trial component of the initiative. The trial explores long-term effects of estrogen and progestin on coronary heart disease, osteoporosis, and breast cancer; examines the effect of a low-fat, high-fiber diet in preventing breast and colorectal cancers and heart disease; and tests the ability of calcium and vitamin D supplements to prevent fractures and reduce the risk of colorectal cancer. Besides the clinical trial, the initiative includes an observational study and a community prevention study. The initiative is seeking additional minority women for the observational study looking at the relation between lifestyle factors and health. Information is available at the WHI website at http://www.nhlbi.nih.gov/nhlbi/whi1. ***Suzanne Hurd*** is the WHI acting director and **Jacques Rossouw** is the WHI lead project officer. . . . **NATIONAL LIBRARY OF MEDICINE** announced 24 contract awards totaling $2.3 million to medical institutions and companies to develop innovative medical projects that demonstrate the use of the capabilities of the Next Generation Internet. Among the NGI capabilities expected to be available are improved security and medical data privacy, "nomadic" computing, network management, and infrastructure technology for "collaboratories." "If we are to benefit from the fruits of modern medical science we must be able to transfer massive amounts of data—instantaneously, accurately, and securely," said NLM Director **Donald Lindberg**. "These projects are an important step in that direction." Among the funded contracts are a "telemammography" project at the University of Pennsylvania, a remote radiation oncology treatment planning project by the Johns Hopkins University Applied Physics Laboratory, and a pathology image database system by Yale University. Information about the NGI and telemedicine on the NLM website at http://www.nlm.nih.gov. . . . **BUILDING 37** on the NIH campus, which houses NCI laboratories, is being renovated floor by floor over the next eight years. Work began last June to modernize the 30-year-old building. The project is estimated to cost more than $80 million, according to the NIH Record (http://www.nih.gov/news/NIH-Record/10_20_98/story02.htm). . . . **NAME CHANGE** for the National Institute of Dental Research at NIH, on the occasion of the Institute's 50th year. The new name, National Institute of Dental and Craniofacial Research, more accurately reflects the research base supported by the Institute, NIH officials said.