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House Expected To Eliminate Earmarks, Give NCI $2 Billion For FY94, A $40 Million Increase

The House Labor, HHS Appropriations Subcommittee is expected to report an appropriations bill that will contain a 5.3 percent increase for all NIH institutes, Capitol Hill sources said.

The bill, which was expected to be reported to the House Appropriations Committee June 22, contains no earmarks and eliminates the out-year spending for breast cancer research, sources said.

Under the bill, the NCI budget was expected to be $2.082 billion,

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In Brief

Gene Therapy For ADA Deficiency Moves Forward With Stem Cell Treatment In Calif. And At NIH

GENE THERAPY of adenosine deaminase deficiency moved forward recently when two newborn boys in California were injected with healthy copies of the defective ADA gene in blood stem cells. **Donald Kohn**, Childrens Hospital, Los Angeles, and **Diane Wara**, Univ. of California, San Francisco, are the principal investigators. They used placental blood as a stem-cell source. During the same week, NCI investigator **Michael Blaese** and consultant **Kenneth Culver** treated a girl, one of the first two gene therapy patients, with stem cell therapy. The second girl on their original ADA protocol will be treated later this summer. . . . **STEPHEN RUBIN** joined Univ. of Pennsylvania Medical Center as director, Div. of Gynecologic Oncology, succeeding **John Mikuta**, head of the division since 1962. Rubin was program director, gynecologic oncology fellowship, Memorial Sloan-Kettering Cancer Center. Mikuta will remain active in patient care and teaching. . . . **MELVYN GOLDBERG** joined Fox Chase Cancer Center as chief, thoracic surgery. Goldberg was director, esophageal-function laboratory, Mount Sinai Hospital, Toronto. . . . **U.S. ARMY** Medical Research & Development Command will release the solicitation for research proposals for the $210 million FY93-94 breast cancer program as soon as approval comes from the Dept. of Defense Secretary, Army sources said. Deadline for proposals will be Oct. 1. . . **CORRECTION:** The story in the June 11 issue of **The Cancer Letter** about Rhone-Poulenc Rorer and the drug Taxotere contained an erroneous description of the materials currently used to produce the competing drug, Taxol. According to Bristol-Myers Squibb Co., the maker of Taxol, all commercially available Taxol currently is made from the bark of the Pacific yew tree. The company said it has developed a process to manufacture Taxol derived from renewable sources (yew needles) and is seeking FDA approval for that process.

Capitol Notes

House Likely To Cut Earmarks, Give NCI $40 Mil. Over FY93

(Continued from page 1)

which amounts to a $40 million increase over fiscal 1993.

The subcommittee is said to have eliminated the three-year appropriations for breast cancer research contained in the President's budget. Early in the appropriations process, these funds, which had been transferred into NIH from the Dept. of Defense, quickly became known as "funny money" on Capitol Hill.

"If the reports we have heard are correct, [Appropriations Committtee and Labor, HHS Subcommittee] Chairman William Natcher (D-KY) and Rep. John Porter (R-IL) in very tough times have sent a message to the cancer community, both survivors and researchers, that a balanced approach to cancer is indeed a priority," said Terry Lierman, executive director of the National Coalition for Cancer Research.

The bill expected to be reported by the subcommittee would be consistent with the remarks by the subcommittee members as they heard testimony from NCI Director Samuel Broder earlier this month (**The Cancer Letter**, May 21).

The subcommittee's version of the budget would reverse President Clinton's "funny money" arithmetic under which NCI was to receive $2.142 billion, an $8.1 percent increase over fiscal 1993.

However, the funds that NCI could not spend in fiscal 1994 accounted for 5 percent of the increase. Thus, with the outyear funds excluded, the increase proposed by Clinton amounted to 3.1 percent.

Most of all, the subcommittee bill would be good news for the nine of the 17 NIH institutes or centers that faced budget cuts under Clinton's budget proposal.

THE CANCER LETTER

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President Clinton earlier this week signed the **NIH reauthorization bill**, ending four years of debate over the legislation.

The law authorizes an appropriation of $2.78 billion for NCI (**The Cancer Letter**, May 28).

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Sen. Tom Harkin (D-IA), chairman of the Senate Appropriations Committee, is preparing a hearing June 24 on the progress of the **NIH study of unconventional medicine**.

Sources said Harkin, whose amendment to the appropriations bill created the NIH Office of Alternative Medicine, appeared intent on conducting the hearing despite NIH requests for a delay.

The office has no advisory committee. Several individuals have been informed that they would be appointed to the panel. However, the official explanation holds that the advisory group has not begun to function since NIH is trying to comply with President Clinton's executive order mandating cuts in the number of such committees.

Earlier this spring, informal advisors to the office were expected to produce a report to describe the areas of unconventional medicine and guide the activities of the office. However, sections of the report varied in length and objectivity, with some lines resembling stanzas from a political manifesto. As a result, the deadline for the report's completion has been moved up to late June, sources said.

The political battle lines among the office's constituents have been drawn between the proponents of the "cures" for catastrophic diseases including cancer and the proponents of palliative treatments (**The Cancer Letter**, Feb. 26). The Request for Apllications recently issued by the office leaned toward homeopathy and acupuncture, neither of which is curative (**The Cancer Letter**, April 9).

Last year, NCI benefited from the slow start of the NIH alternative medicine venture. The Institute received about $1 million from the program, because of its planned phase 2 trial of "antineoplaston," a substance invented by the unconventional practitioner Stanislaw Burzinski and administered at his Houston clinic (**The Cancer Letter**, June 5, 1992). Institute sources said the trial is yet to begin.

Meanwhile, Harkin appears to be persistent. Recently, at an appropriations hearing he grilled NCI Director Samuel Broder on the subject of shark cartillage and NCI's reluctance to accept studies of the substance, conducted in Cuba.

The NCI position is that the data on shark cartillage do not warrant clinical trials. However, NIH

has awarded grants to support the study of the chemical composition of the substance and, possibly, animal studies.

ACS Initiates Change In Approach To Alternative Methods Study

The American Cancer Society has moved toward playing a stronger role in responding to claims made for unconventional methods of cancer treatment.

The ACS Medical Affairs Committee approved a recommendation by its Subcommittee on Questionable Methods of Cancer Management calling for a multidisciplinary study to define the role of ACS in responding to issues involved in unconventional methods. The action was taken at the Society's board meeting earlier this month.

In essence, the Society has adopted plan of action suggested by Barrie Cassileth, a psychosocial oncologist who serves on the questionable methods subcommittee and is expected to be appointed to the advisory board of the NIH Office of Alternative Medicine.

The Society plans to develop a mechanism for a proactive, immediate response to media reports on cancer treatments and diagnoses. "These [news reports] are well-promoted, publicly and in advance, giving us adequate lead time for action," Cassileth wrote in a letter that was circulated to the group.

Typically, in days after such news splashes, physicians, hospitals, NCI and ACS find themselves innundated with calls from people seeking access to the "cures."

"Examples are the shark cartillage 'cure,' much of the Bill Moyers TV series, including the message that acupuncture permits patients to speak during brain surgery, and the March 9, 1993, full page 'New York Times' ad for the 'Penthouse' expose about the medical establishment's withholding of hydrazine sulfate which arrests cachexia and can 'shrink and ... eradicate tumors,'" Cassileth wrote in the letter.

To develop the responses, ACS would have to keep track of all NCI studies involving unconventional therapies and establish a cooperative relationship with Canada's Health Protection Branch.

"What we're witnessing in the country today is a new interest in alternative methods for treating everything," said Helene Brown, a member of the questionable methods subcommittee.

"The health care reform movement is looking for inexpensive ways to treat many diseases. The eventual product will be greater inclusion of treatment with alternative methods, greater than any ever seen," Brown said.

"Any statement from the American Cancer Society should be carefully worked out, based on evidence. We should take the view that we should look at [the adjunctive treatments in question], and review the evidence carefully before we spend money on clinical trials. We need to keep an eye on the NIH office [of Alternative Medicine]. I'm afraid it will get bigger and bigger budgets as the number of alternative methods increases," Brown said.

Subcommittee member David Wellisch said that after 20 million people watched the "60 Minutes" segment on shark cartillage, ACS and NCI information offices were deluged with calls. "The public needs to know more of what we know," he said.

"Who is going to track this?" asked William Jarvis, president of the National Council Against Health Fraud and a member of the ACS subcommittee. "Maybe we need to fund someone to do that." Jarvis said the Canadian health plan provides a clearing-house or coordinating body for reimbursement.

"They have up to date information on all this in Canada, and they don't think much of it. They go along with reimbursement to some extent," Jarvis said.

Brown suggested that the ACS committee, or whatever body the Society establishes to study the problem, needs to be adquately funded, and it should look at the larger context of alternative and complementary treatments.

DCT Advisors Ok New RFAs In HIV, Surgery, Breast Cancer, Radiation

Advisors to NCI's Div. of Cancer Treatment have given concept approval to three new Requests for Proposals for cooperative agreement (U01) grants in minimal access surgery, tissue and fluids bank in HIV, and breast cancer therapies.

The DCT Board of Scientific Counselors last week agreed to set aside $4.75 million for first-year funding for as many as 16 awards in the three grant programs proposed by the Cancer Therapy Evaluation Program.

The board also gave concept approval to a new RFA to establish a Positron Emission Tomography Diagnostic Oncology Group. Also approved were three concepts for program announcements to be issued by the Biological Response Modifiers Program.

Following are excerpts of the concept statements:

Development and Evaluation of Minimal Access Surgery in Cancer Treatment. Proposed RFA (cooperative agreements), first year award $750,000, five to six awards, three years. Cancer Therapy Evaluation Program.

Minimal access surgery has been proposed to decrease the trauma of surgical access without limiting exposure of the

operative field. Approaches used include laparoscopic, thorascopic, endoluminal, and perivisceral. Many pelvic, abdominal, and thoracic surgical procedures have been modified to permit minimal access surgery. Recent reports have documented the use of minimal access surgery in cancers of the lung, stomach, liver, pancreas, gallbladder, colon, ovary, endometrium, and cervix.

Advantages to minimal access surgery include accelerated recovery and convalescence, with a corresponding decrease in length of hospital stay and hospital expenses, as well as a quicker return to normal activity. Wound complications, including infections, are also decreased. Potential benefits include a decreased incidence of postoperative pneumonia, deep vein thrombosis, and adhesion formation.

In oncology, minimal access surgery may be useful to obtain adequate tissue for accurate diagnosis of malignancy, to ascertain the degree of spread, to stage the disease, and to assess operability. Definitive cancer surgery may be performed using minimal access techniques. Minimal access surgery has not been prospectively compared with standard surgery in the care of cancer patients in terms of accuracy of staging, cost-effectiveness, efficacy of treatment, safety, survival, and quality of life.

The project will use the cooperative agreement mechanism (U01) to fund large multi-institutional consortia or consortia of cooperative groups to perform Phase III evaluation of minimal access surgery in the care of cancer patients. Each consortium should have the capacity for statistical and surgical data management. It is anticipated that a single trial will be funded in each organ site selected. Among the selection criteria will be the speed with which the trial can be successfully completed, plans to evaluate quality of life and cost, and investigator experience with minimal access surgery. Cancers in which such a trial might be appropriate include colon and gynecological malignancies.

Grantees will be funded via individual cooperative agreements, assistance mechanisms that retain the decision-rnaking prerogatives of the principal investigator and his/her colleagues, but at the same time perrnit the active participation of NCI and other Public Health Service agencies in awardees' activities. Participation by NCI and other Public Health Service agencies through the Program Director will provide assistance in the nature of information on institute priorities and ongoing efforts elsewhere within the scientific cornmunity, as well as oversight, through the protocol review process, of methodology, feasibility, patient safety, and adherence to regulatory requirements.

Tissue and Biological Fluids Bank of HIV-Related Malignancies. Proposed RFA (cooperative agreements), first year award $2 million, three to four awards, four years. Cancer Therapy Evaluation Program.

Research into the pathogenesis of HIV-associated malignancies has been hampered by the lack of large amounts of well-characterized tumor tissue and longitudinal specimens of biological fluids, such as blood, that could be examined for the effects of therapy on cytokine production, HIV replication, other viral cofactors (such as human papillomavirus in the anogenital dysplasias and cancer, Epstein-Barr virus in primary central nervous system lymphomas) and oncogene expression. The laboratory investigations could offer insight into the pathogenesis of the malignancies that arise in HIV-infected individuals and potentially have an impact on the development of effective therapies. The need to obtain tumor tissue for research was recognized at the conference on AIDS-lymphomas convened in May 1992 by the Cancer Immunology Branch, Div. of Cancer Biology, Diagnosis & Centers.

The Cancer Therapy Evaluation Program has been investigating methods to develop and utilize tissue and clinical data banks. The most efficient method would be to take advantage of the meticulous followup and monitoring of patients in the context of clinical trials in the institutions involved in the care of patients with HIV-associated malignancies. It is felt that the success of attaining specimens will be directly correlated with the degree to which the investigators donating such specimens will be involved in determining research priorities.

The project will use the cooperative agreement mechanism (U01) to fund a consortia of institutions to design and develop a tissue and biological fluids bank of HIV-associated malignancies. Investigators should document the number of HIV-infected patients seen at their institutions and provide a discussion section on how those patients who develop malignancies would be referred to their participating oncologists. Tissues and fluids to be included should come from groups of patients treated uniformly on standard therapeutic regimens or clinical trials where clinical and outcome data are available.

The awardees will provide tissue and fluids for high-priority research studies as identified by a committee selected by the awardees, the Research Evaluation and Decision Panel (REDP), and agree to participate as part of a coordinating committee. The prioritization of research studies will be made by a REDP according to criteria established by their coordinating committee. NCI will help coordinate this process through membership in the REDP. Funding for pilot studies will be provided to obtain sufficient data to form the foundation for R01 research grant applications. The pilot studies would help identify new research areas where additional investigations should be pursued.

Examples of such studies could include, but are not limited to, the following: prospectively comparing the response to therapy in patients with different molecular characteristics (i.e., immunoglobulin rearrangements, oncogene rearrangements), occurrence and configuration of EBV DNA, and histologic subsets of non-Hodgkin's lymphoma treated uniformly on a therapeutic regimen; determining the cytokine expression that might be etiologically involved in the development of Kaposi's sarcoma (by tumor or by peripheral cells within the microenvironment) and the effect on such expression by therapy; evaluating the interaction of HIV and HPV in anogenital dysplasias and cancers and the effects of therapy (i.e., retinoids, interferon) on the tumor, the viruses individually, or their interaction; assessing the impact of therapy both on viral burden and on tumor response; and establishing new cell lines and xenograft models for in vitro or in vivo testing of novel compounds in HIV-related rnalignancies.

New Therapeutic Approaches for the Treatment of Breast Cancer. Proposed RFA (cooperative agreements), first year award $2 million, five to six awards, four years. Cancer Therapy Evaluation Program.

The incidence of breast cancer has been increasing and

now accounts for 32 percent of all carcinomas in women. It is estimated that there will be a total of 46,300 deaths from breast cancer and 183,000 breast cancers diagnosed in 1993. Treatment during the past decade has concentrated on attempts to optimize conventional chemotherapeutic agents by varying drug dosage, schedule, and intensity. Although there have been treatment advances, 5-year relative survival rates increased only three to four percentage points in the 1980s over that observed for patients diagnosed in the 1970s. With the dramatic increase in the diagnosis of in situ tumors in the 1980s and 1990s, new opportunities exist for the early treatment of breast cancer. For patients with the most advanced stages of cancer, mortality rates have not improved, and new therapeutic strategies to treat such tumors are needed. Therefore, this [proposed] RFA focuses on novel approaches to breast cancer treatment.

Recent advances in understanding the pathobiology of breast cancer have furthered the development of a wide range of novel anticancer therapeutic agents that will soon require clinical testing. These agents include new classes of cytotoxic agents derived from natural products, as well as genetically engineered agents to act via immune-stimulatory effects, or which are targeted specifically to novel cancer cell targets, including surface receptors, signal transduction molecules, transcriptional factors, and particular DNA and RNA sequences. Furthermore, mechanisms of action of these new anticancer agents available for clinical study include not only the mediation of anticancer effects through cytotoxic and immunologic mechanisms, but also through growth inhibition by interruption of specific oncogene-associated biochemical functions, inhibition of protein synthesis through targeted toxins, biochemical reversal of drug resistance, induction of differentiation and/or programmed cell death (apoptosis), and through inhibition of tumor angiogenesis. In addition, new strategies to overcome resistance to conventional cancer therapeutic approaches are also of interest.

CTEP proposes to create a mechanism by which innovative investigator-initiated approaches may be fostered to evaluate new agents or therapeutic strategies in Phase I/II breast cancer clinical trials. Collaborative interactions between clinicians and laboratory scientists will be essential features of these investigations. Proposals are expected to be multidisciplinary and may include preclinical evaluation in in vitro or in vivo models. Pilot clinical studies and relevant laboratory studies needed to better understand the mechanism of action of the therapeutic agents will be a necessary part of the proposal.

CTEP is proposing to stimulate clinical research relevant to breast cancer through the support of multidisciplinary teams of basic and clinical investigators interested in performing Phase II trials of innovative therapeutic strategies and in conducting laboratory studies relevant to the clinical development of the agents. Scientific approaches should reflect the creativity and capabilities of the investigators.

Each team of investigators will be referred to as a Breast Cancer Treatment Group. Each BCTG should be composed of a principal investigator, who will provide scientific leadership for the group, and one or more co-investigators responsible for the clinical or laboratory programs within the application. We anticipate that participation in BCTGs will include academic, nonprofit, and/or commercial institutions. The multi-institutional approach may provide access to a wide range of expertise.

Applications should be focused on integrating clinical goals with laboratory research areas. A clinical program and one or more laboratory programs should be included. Preclinical studies that are necessary for the clinical development of the new therapeutic agents or therapeutic strategies may be proposed. Pilot clinical trials may be included with the goal of initiating Phase I/II evaluation of the therapy within the funding period. Correlative laboratory programs designed to elucidate the mechanism of action of the proposed therapeutic strategies or to create and provide new monitoring techniques for patients on the study are appropriate.

Clinical studies should be designed to evaluate new therapeutic agents or new therapeutic strategies for breast cancer. Examples of new clinical trials include (1) differentiating agent or apoptosis; (2) novel growth factor or hormone-based therapies utilizing new agents; (3) gene therapy and new therapies involving antisense or ribozymes; (4) immunomodulatory approaches to breast cancer treatment (such as vaccines); (5) targeted therapies including monoclonal antibody therapy, radioimmunobiology, and the use of new immunotoxins; (6) biologics in combination with drug or radiation regimens; (7) new therapies combining endocrine manipulations with chemotherapeutic agents; (8) treatrnent strategies for overcorning hormone-, drug- or radiation-resistance of breast cancer; and (9) treatment strategies based on novel mechanisms of action of defined therapeutic agents (e.g., interference with signal transduction, induction of immune response).

Clinical Trials of the Treatment of HIV-Related Malignancies with Biological Response Modifiers. Proposed Program Announcement. Biological Response Modifiers Program.

The purpose of this [proposed] program announcement is to stimulate Phase I clinical research in the area of treatment of AIDS-associated malignancies with BRMs (initially defined as "agents or approaches that will modify the relationship between tumor and host by modifying a host's biological response to tumor cells, with resultant therapeutic benefit," Biological Response Modifiers: Subcommittee Report, 1983).

This program will be supported through the traditional investigator-initiated research project grant mechanism, which includes R01, R29, and P01 applications. The proposed trials, which should be based on sound preliminary data, should be hypothesis-driven studies that include laboratory evaluations focusing on potential mechanism(s) of action of the agent(s) proposed for study, with particular ernphasis on studies of host/tumor interactions. Evaluation of the effects of the therapeutic approach on HIV infection (e.g., viremia, p24 antigenemia, effects on latent infection) should be included, as scientifically appropriate. Clinical endpoints (toxicity, antitumor response) should not be the only objectives of the proposed trials.

Examples of areas of study include, but are not limited to, cytokines and differentiating agents; cytokine and growth factor antagonists; targeting agents (e.g., antibodies, ligand toxin constructs) directed at tumor-associated antigens (e.g., idiotype of B-cell lymphoma) or unique receptors; use of combinations of colony-stimulating factors with cytotoxic therapy; adoptive immunotherapy; use of cytokine gene-transfected cells or other constructs as cancer vaccines; and use of agents to induce apoptosis in tumors or to prevent apoptosis of CD4+ cells early in HIV infections in order to prevent the development of malignancies.

Applications would be invited for early clinical trials of new BRM agents or approaches. Applicants are encouraged to propose trials of promising agents or approaches currently in preclinical development and should include evidence that patient accrual may begin promptly after award (e.g., access to the proposed agents, an IND already filed or soon to be filed). A detailed clinical protocol should be part of the application.

Clinical Trials of the Treatment of Breast Cancer with Biological Response Modifiers. Proposed Program Announcement. Biological Response Modifiers Program.

Rapid developments in basic immunology, molecular biology, and protein engineering continue to give rise to new biological response modifiers available for clinical trials in breast cancer and other malignancies. BRMs currently being studied in clinical trials in breast cancer include IL-2 gene-transfected tumor cells used as a vaccine; monoclonal antibodies (murine, chimeric, and humanized) directed against breast cancer antigens and used to deliver radioactive isotopes or to mediate toxicity in association with complement or immune effector cells; hematologic growth factors used to attenuate the myelotoxicity of high-dose chemotherapy; bispecific monoclonal antibodies that target breast cancer antigens together with triggering molecules on immune effector cells; and interferons in combination with cyclosporin A to induce autologous graft-versus-host disease following autologous bone marrow transplantation in patients with breast cancer.

The proposed program announcement would stimulate Phase I clinical research with BRMs in the treatment of breast cancer. This program will be supported through the traditional investigator-initiated research project grant mechanism, which includes R01, R29, and P01 applications. The proposed trials, which should be based on sound preliminary data, should be hypothesis-driven studies that include laboratory investigations focusing on potential mechanism(s) of action of the agent(s) proposed for study, with particular emphasis on studies of host/tumor interactions. Clinical endpoints (toxicity, antitumor response) should not be the only objectives of the proposed trials. Examples of potential studies include, but are not limited to, trials of new targeting agents, where the goal is to improve a specific biologic effect (tumor infiltration by effector cells, agent localization to tumor, reduction in host immune response); trials of combinations of hematologic growth factors, with correlative studies of hematologic progenitor cells; and trials of tumor vaccines, with correlative studies of cellular and humoral immune response, including studies of specific T-cell responses.

Applications for early clinical studies of new BRM agents or approaches would be invited. Applicants are encouraged to propose trials of promising agents or approaches currently in preclinical development and should include evidence that patient accrual may begin promptly after award (e.g., access to the proposed agents, an IND already filed or soon to be filed). A detailed clinical protocol should be part of the application.

Laboratory Studies of the Treatment of AIDs-Related Malignancies with Biological Response Modifiers. Proposed Program Announcement. Biological Response Modifiers Program.

The purpose of this proposed program announcement is to stimulate novel laboratory research in the area of treatment of AIDS-associated malignancies with BRMs. This program will be supported through the traditional investigator-initiated research project grant mechanism. Examples of areas of study include, but are not limited to, monoclonal antibody therapy specifically targeting antigens on AIDs-associated tumors (e.g., anti-idiotype targeting of B-cell lymphomas), targeting of unique receptors (e.g., Oncostatin M receptor) by antibody or ligand-toxin constructs, synergistic use of combinations of agents (e.g., colony-stimulating factors and interferons with or without antiviral therapy), use of agents to augment the immune system without activating latent HIV, use of antisense oligonucleotides to inhibit the transcription or translation of oncogenes, establishment of appropriate animal models in which to study AIDS-related tumors, adoptive immunotherapy strategies, immune augmentation followed by tumor vaccination, use of agents to induce apoptosis in turnors or to prevent apoptosis of CD4+ cells early in HIV infection in order to prevent the development of malignancies, and strategies involving gene therapy.

The proposed studies should take into account the unique problems involved in the treatment of AIDS-related cancers such as the immunocompromised state of the host, in many cases, and the potential for activation of latent virus(es). If possible, the unique biology and physiology of the tumor cell should be related to the mechanism of action of the BRM proposed for study.

Positron Emission Tomography Diagnostic Oncology Group (PETDOG). Proposed RFA (cooperative agreements), annual budget $800,000, four years.

While currently used clinical diagnostic imaging modalities, such as magnetic resonance imaging and x-ray computed tomography, provide predominantly anatomic information, positron emission tomography (PET) reflects tissue physiology and metabolism. Although CT and conventional MRI provide information about the location and the local extent of tumors, these techniques frequently cannot differentiate invasive lesions from treatment-induced edema and/or necrosis. PET, on the other hand, can be used to localize and characterize tumors by providing a measure of metabolic activity. A variety of clinical reports over the last several years have suggested that PET imaging has wide potential applicability to cancer management. In November 1992, the Diagnostic Imaging Research Branch convened a conference to discuss the current status and future potential of PET as a clinical tool in oncology. The panel concluded that sufficient preliminary data existed to justify prospective clinical trials assessing the ability of PET-FDG to stage newly diagnosed primary breast cancer and lung cancer in multi-institutional, centrally coordinated trials. The panel felt strongly that the clinical and cost-effectiveness evaluation of PET is critical at this stage, before wide dissemination of this technology takes place.

PETDOG Specific Research Goals for Breast and Lung Cancer:

1) To detect tumor extent and to characterize its metabolic activity; 2) To detect regional lymph node involvement; 3) To detect systemic metastases; 4) To assess tumor response to treatment; 5) To correlate PET data with other imaging modalities and clinical outcome.

Cooperative agreement (three or four institutions) with the

establishment of the headquarters for centralized, coordinated development of consensus-based experimental study design, statistical data processing, quality control, and cost-effectiveness studies.

NCI Roundup

DCT Board Urges Continued Payment Of Patient Costs In Clinical Trials

Advisors to NCI's Div. of Cancer Treatment have sent a letter to HHS Secretary Donna Shalala urging that reimbursement for routine patient care costs associated with clinical trials continue to be paid under any proposed health care reform package.

"In the ongoing discussions of health care reform, we realize that there is a need to limit expenditures for costly and ineffective therapies," the DCT Board of Scientific Counselors said in the June 8 letter. "Only through clinical research can more effective therapies be identified. Clinical research also results in the elimination of ineffective approaches and often the development of less costly therapies.

"However, often health insurance companies have frequently disallowed coverage for patients on clinical trials as a way of cost cutting. We believe this is unwise, and in the long run, counterproductive. We strongly urge that you consider the following issues before specific legislation or plans for changes in the health care system are formulated.

"1. For patients with life-threatening illnesses, routine patient-care costs incurred during the course of clinical trials that have undergone peer review, such as those sponsored by the NIH, should be covered by third-party carriers or by government-sponsored reimbursement systems such as Medicare.

"2. Experimental protocols not properly peer-reviewed in the manner of those supported by NIH should not be covered.

"3. The financial impact of the foregoing policy will be relatively small for the health care system but the policy will have a great impact by promoting effective, less toxic and more cost-efficient therapy for many patients with life-threatening diseases.

"4. The results of the clinical research provide rational guidelines for the therapy of these diseases.

"We strongly urge you to create a public dialogue in this area." The board asked to meet with Shalala or her staff to discuss the issue.

NCI Prepares Statement

NCI will send a statement of its position on clinical research costs to Shalala, based on a memo written by Michael Friedman, director of NCI's Cancer Therapy Evaluation Program.

Following is Friedman's memo, titled "Considerations for the Support of Federally Sponsored Medical Clinical Investigation."

"Currently, for nearly every disease, standard therapies are insufficiently effective, too toxic or too expensive. Additionally, the excellence of the health research of academic institutions and the vigor of the biotech industries mean that there will be an increasing need for high quality clinical research in order to identify better prevention, treatment, and rehabilitation technologies and products.

"Financially, there are two components of this clinical investigation--the research costs (special tests, data collection, statistical analysis, etc.) and the clinical care costs (routine care appropriate for that condition). The former costs should be borne by the research sponsor (such as the National Institutes of Health), the latter costs have traditionally been reimbursed by third party payers. But, since Federally sponsored clinical research utilizes tax dollars and aims to benefit the health of all citizens, it is essential that consideration be given to how payment for the clinical care costs of such research can be incorporated into a new, comprehensive, health care plan.

"It is assumed that in the future only legitimate clinical services would be convered, ineffective approaches would not be funded, and unproven interventions would be carefully scrutinized rather than not automatically excluded. Also, it is assumed that Federally sponsored research would continue to be scrupulously peer reviewed and quality assured so that optimal care would be provided, the best scientific questions pursued and ethical standards upheld. Although such research addresses broad biologic, medical outcomes and cost-effectiveness issues, the overall scope of this effort would remain small (predictably less than 5% of all patients).

"Possible options for covering these clinical care costs include:

"1) No reimbursement whatever would be permitted. Only wealthy, motivated patients could participate in such research--very little research would occur and access to the benefits of participation would be inequitable. Research progress would be slow.

"2) The sponsor could begin paying for all clinical costs as well as research costs; these costs would be enormous and could not be accommodated in the present appropriations. Specifically, a vast increase in the [Dept. of Health & Human Services] research budget would be required for Federally sponsored clinical research projects (from NIH, Centers for Disease Control, etc.).

"3) Permit reimbursement (consistent with coverage guidelines) for clinical care costs for patients participating in appropriately defined clinical trials.

"While clinical investigation is a relatively small component of the health care package, it is crucial. It would be most in accord with the national scientific and societal goals to exercise either the second or third option (or some variant). Otherwise, advances in relieving the suffering and premature disability and death of citizens will not continue to be realized."

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Hiring freeze at NIH is making it difficult for NCI's Div. of Cancer Treatment to expand, particularly in breast cancer and AIDS, DCT Director Bruce Chabner told the division Board of Scientific Counselors last week.

"For every six people who leave, we can hire one new person," Chabner said. In the past year, DCT hired three people.

FDA Simplifies Reporting System For Adverse Events, Product Defects

The Food and Drug Administration has announced a program to improve the safety of drugs, biologics, medical devices, dietary supplements, medical foods, infant formulas and other regulated products by encouraging health professionals to report serious adverse events and product defects.

The program, called MEDWatch, is designed to bring information on post-marketing safety and efficacy to FDA's attention as soon as it is gathered by health professionals.

"MEDWatch is not just a new FDA system; it is a way of making reporting of adverse events and product problems a part of the culture of health care providers," FDA Commissioner David Kessler said. "Physicians, nurses and others who care for patients are the first to know when a drug or medical device does not perform as it should. The sooner they report it to FDA, the faster the agency can analyze the problem and take corrective action."

As part of MEDWatch, the agency has developed several ways to make it easier for health professionals to report adverse events involving almost all regulated products. Concerns with vaccines will continue to be reported separately through the Vaccine Adverse Events Reporting System.

The major change is a simplified reporting form that replaces five other forms previously issued for the same products.

The one-page form, which can be folded and mailed postage-free, will be made widely available, FDA said.

The American Medical Assn., Pharmaceutical Manufacturers Assn., Public Citizen Health Research Group and more than 50 other organizations agreed to promote the program to their members.

FDA also established a 24-hour, seven-day-a-week toll-free telephone hotline for adverse event information.

FDA said adverse events that should be reported include the patient's death, life-threatening illness or injury, hospitalization, disability, congenital anomaly and experiences that required intervention to prevent permanent impairment of health.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD.

RFP NCI-CM-47001-64

Title: Clinical trials of biological response modifiers

Deadline: Approximately July 27

NCI plans to award five-year incrementally funded contracts for the performance of multiple clinical trials of biological response modifiers. Offerors will be required to demonstrate their capability to perform, within appropriate timeframes, Phase I clinical trials of biological response modifiers. Emphasis should be on excellent patient accrual, trial design, and conduct of laboratory studies of biological correlates. A theoretical (sample) laboratory and clinical protocol will be required with the proposal. The contractors will design, write, and develop clinical protocols for the biological response modifiers identified for study. NCI will supply agents for clinical trials and hold the investigational new drugs. All contract clinical protocols will require NCI approval. Contract clinical trials will be monitored by NCI's Clinical Trials Monitoring Services. These trials will focus on initial Phase Ia/Ib studies of new biological response modifiers and on studies specifically related to issues of mechanism of action. Each contractor will perform up to three clinical trials per year. Up to three awards are planned. At least one award will be devoted to monoclonal antibodies and targeting agents, and at least one award will focus on biological response modifiers such cytokines and growth/differentiation factors. Beginning with each contract protocol, the contractor will submit data to Clinical Trials Monitoring Service biweekly using NCI Case Report Forms or electronic data transfer.

Contract specialist: Carl Newman, RCB Executive Plaza South Rm 603, Tel. 301/496-8620.

Availability Of Program Project Guidelines

NCI announces the availability of updated guidelines for program project (P01) applications that are likely to be assigned to the NCI for review and funding.

Investigators may obtain copies of the guidelines and referrals for information regarding programmatic interests from: Referral Office, Div. of Extramural Activities, NCI, Executive Plaza North Rm 636, Bethesda, MD 20892, Tel. 301/496-3428, Fax 301/402-0275.