THE CANCER LETTER

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NCI To Establish Three Grant Programs Supporting Clinical Cancer Research

NCI plans to establish three grant programs to support clinical cancer research this year, NCI Director Samuel Broder announced this week.

The new programs are designed to expand the options for clinical investigators, Broder said.

"These are meant to complement—and not replace—our extensive array of funding instruments," Broder said to the Div. of Cancer Treatment Board of Scientific Counselors.

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In Brief

Myers, Whang-Peng, Zink Leaving NCI; FDA Hires New Legislative Affairs Chief

CHARLES MYERS, chief of NCI's Clinical Pharmacology Branch, in the Clinical Oncology Program of the Div. of Cancer Treatment, will leave for the Univ. of Virginia, to become head of the cancer center and a professor. Myers, a pharmacologist, began several studies with new agents for prostate cancer, including trials of suramin, genistein, lovastatin and phenyl acetate. **Eddie Reed**, of the Medicine Branch, will become acting chief of the CPB, and the position is expected to be advertised shortly. . . **JACQUELINE WHANG-PENG**, head of the Cytogenetic Oncology Section in DCT's Medicine Branch, will retire after 30 years at NCI. She plans to help establish cancer research training programs for young scientists in Taiwan. . . . **SANDRA ZINK**, a cancer expert in DCT's Radiation Research Program, will retire from NCI in April to operate a ranch in New Mexico. She joined the program in 1985. . . . **DIANE THOMPSON**, former chief of staff for Sen. Barbara Mikulski, has been appointed associate commissioner for legislative affairs at the Food & Drug Administration. Thompson was a partner in the consulting firm of Foreman & Heidepriem in Washington, DC. She was Mikulski's chief of staff from 1987-89, and from 1984-85, she was assistant to the president of the National Organization for Women. . . . **NIH WILL DROP** its attempt to patent human cDNA sequences, the institutes announced last week. NIH will not appeal a rejection by the U.S. Patent & Trademark Office of a patent application and will withdraw another cDNA patent application. The applications were filed on the cDNA sequences developed in the intramural laboratory of Craig Venter. The patent office said the sequences

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Broder: No Excuse If NCI Fails To Receive Grant Applications

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The new programs are:

●**New Investigator Grants for Clinical Cancer Therapy Research.** Approved in concept this week by the DCT board, these new grants will provide $500,000 per award to support new clinical investigators. The board agreed to set aside $1.5 million in FY95 to fund eight four-year awards.

Broder described the program as a step between the current NIH R29 First Independent Research & Support (FIRST) award and a regular R01. NCI's Div. of Cancer Prevention & Control is beginning a similar program in prevention.

●**Small R03 grants for innovative pilot clinical projects.** This program will make available up to $50,000 direct costs per year for up to two years per award.

●**R21 exploratory grants.** This program will allow investigators to request up to $100,000 each in direct costs per year for two years to pursue new ideas in clinical cancer research. The program, suitable for investigators at any stage in their careers, will have three annual application receipt dates. Funding for the program would be outside the traditional research project grant pool.

Special Study Sections Planned

Clinical investigators say the regular NIH review process is biased against clinical research and discourages investigators from applying for grants.

The New Investigator grant applications will be reviewed by a special study section formed by NCI. The institute is seeking clearance from the NIH Div. of Research Grants to form special study sections to review applications for the other two programs.

"Each mechanism will be judged and scored only against others in its own category," Broder said.

While the new programs will fill a void, NCI still would like to see NIH form a clinical research study section, Broder said. The DRG has formed a committee to study the issue.

Applying for grants under the new programs is one way to demonstrate the need for an NIH standing study section, Broder said to the board. DRG officials in the past have said that existing study sections are adequate to handle the relatively low numbers of clinical applications.

"I urge all of you to do what you can to make sure you either send in applications on your own or you induce first-time clinical researchers to send in applications," Broder said. "There really will not be any excuses if there aren't good applications.

"If you are mad that clinical research has not been supported in the past, use this route and help us build the momentum," he said. Later in his talk, he indicated that NCI was going out on a limb with NIH. "I'm going to be in a lot of difficulty if we don't have a lot of good applications," Broder said.

Board Chairman Clara Bloomfield encouraged NCI to widely disseminate information about the new mechanisms.

Enthusiastic Support For New Grants

The DCT board unanimously approved the New Investigator grants program and voted to recommend that NCI reissue the RFA annually over the next three years. The annual reissue requires the support of the NCI Executive Committee.

If NIH decides to create a clinical investigations study section, the New Investigators grants program could be ended, said board member Charles Coltman, of the Southwest Oncology Group. "If that effort fails, this program should be continued into perpetuity," he said.

"This will be the vehicle to boost somebody into R01-land," said Michael Friedman, director of NCI's Cancer Therapy Evaluation Program.

Following is the concept statement. When the RFA is issued, its text will appear in **The Cancer Letter**.

New Investigator Grants for Clinical Cancer Therapy Research. Proposed RFA for R01 grants. First year award $1.5 million, project period four

THE CANCER LETTER

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years, eight awards, planned date of announcement is May 1994, anticipated award date is July 1995.

In the past year, a number of groups have expressed concern over the declining number of young clinical investigators entering and remaining in academic research. Clinical investigators are a critical component in translating new therapeutic agents and modalities from the laboratory into the clinic. They must maintain a broad perspective and knowledge concerning clinical and basic sciences while developing new cancer therapies that are hypothesis driven. They are highly interactive with basic and clinical researchers in related disciplines. This translational clinician is considered distinct from the clinician who has a PhD or equivalent training and concentrates on basic research or the clinician who participates in cancer research by entering patients on clinical trials.

The Clinical Investigations Task Force of the National Cancer Advisory Board and a subcommittee of the American Association of Clinical Oncology have both been addressing the problem of the decreasing number of academic clinical investigators. One of the problems identified is the lack of suitable mechanisms for the training and funding of clinically oriented young investigators involved in translating basic research into new cancer treatments.

There is no specific program available to train the clinical investigators in the design and conduct of clinical trials. The traditional grant mechanisms (R01, R29) are underutilized and often do not fit the needs of young clinical investigators for the support of clinical trials research. The R29 grant mechanism requires the investigator to devote at least 50 percent effort to a 5-year project, and the budget is limited to approximately $70,000. Most pilot clinical studies on new or novel therapies do not require 5 years, and it is impossible to support both the clinical and laboratory components needed within the budget limitations of an R29 grant.

Young clinical investigators do not have the publication or research track record to be competitive for R01 grant support. Thus, very few clinical trial research proposals are submitted by young clinical investigators. DCT would like to reverse this trend and encourage new clinical investigators in the conduct of translational clinical trials research.

Project Description: The Cancer Therapy Evaluation Program and the Biological Response Modifiers Program encourage qualified clinical investigators to develop R01 grant applications for the conduct of clinical trials research on new therapeutic agents and modalities. Grant applications must include clinical trials involving human subjects and designed to ultimately improve cancer survival. The clinical trials must have a strong rationale and be based upon preclinical data generated by the applicant or others that support the underlying hypotheses. New clinical therapeutic trials employing drugs (including differentiating agents), biologics (including monoclonal antibodies), radiation, or surgery, whether used as single agents/modalities or in combination, are appropriate.

The research plan should be focused on the clinical trials proposed. Laboratory studies to monitor patients or to study the mechanism of action of agents should be included.

The principal investigator must be a physician who is working independently but is at the beginning stages of his or her research career. The PI must never have been designated previously as PI on any PHS-supported research project (except R03, R15, or K series awards).

At least 25 percent effort must be committed to the research project by the PI. The direct cost award for the entire 4-year R01 grant period may not exceed $500,000 ($125,000 per year).

The sponsoring institution must acknowledge that the PI is the independent leader of this investigational effort.

The objective of this initiative is to support clinical investigators at the beginning of their research careers in the conduct of clinical trials with new therapeutic approaches for the treatment of cancer. Investigators are urged especially to address the more difficult therapeutic challenges, including the most common malignancies.

NCI To Fund Studies Of MRI For Breast Cancer Staging

Magnetic resonance imaging produces pictures of the breast may times more clear than x-ray mammography and could be used for more definitive staging of breast cancer, a Baylor Univ. expert told the Div. of Cancer Treatment Board of Scientific Counselors this week.

However, as with any new medical device, the technology often becomes widely available before scientific studies are done to determine its best use, said Steven Harms, a professor at Baylor Univ. Medical Center.

To conduct those studies, the DCT board gave concept approval to a new grants program that will establish a multicenter cooperative group for clinical evaluation of MRI in breast cancer. Three to four cooperative agreement awards, for a total of $1.5 million for each of four years, would be funded by the Radiation Research Program. The concept statement appears below.

"We tend to overtreat breast cancer in hopes of eliminating disease that is unseen and create more morbidity than is necessary to cure the disease; however, in some instances, we actually undertreat because of lack of knowledge, and that leads to recurrence of breast treatment failure," Harms told the board.

About half the time, lumpectomy results in inadequate margins and repeat surgery is necessary, Harms said. The MRI technique could better define multifocal and multicentric disease, and better define the extent of disease for lumpectomy. This could potentially save money by reducing unnecessary or unsuccessful surgery, he said.

Goals of MR staging are to improve the sensitivity of imaging diagnosis to prevent inadequate treatment of non-visualized cancer. Three-dimensional resolution is in the order of 1 millimeter, fat must be suppressed, and the procedure must be done in under five minutes. Rotating Delivery of Excitation Off-Resonance (RODEO) is a new pulse sequence Harms and his collaborator, Duane Flamig, have developed that uses a radiofrequency coil to excite water and suppress fat or silicone.

The MR technique can see through dense breasts, fat and silicone, detecting lesions as small as 3 cm (**Cancer Economics**, April 1992). The technique takes 128 3D slices which can be viewed on a computer monitor using image processing technology.

The technique could be used to evaluate therapy by viewing the breast post-treatment.

In a study of 30 patients who had some form of abnormality seen on conventional mammography, Harms found the sensitivity of RODEO was 94 percent compared to 55 percent for conventional mammography. Seventy percent of the patients had multicentric disease that would not have been adequately treated by quadrantectomy. Size of lesions missed by conventional imaging ranged from 3 mm to 12 cm, with the mean diameter 2.5 cm.

The specificity of the technique was 40 percent. However, the false positives were found in lesions that are associated with increased risk for breast cancer: lobular carcinoma in situ, atypical hyperplasia, and fibrocystic change. Biopsy of these lesions are still indicated, Harms said.

Though the technique is not ready for clinical use yet, if validated and refined, it could be used to determine treatment modes and surgical approach to improve breast conservation and reduce morbidity, Harms said.

Following is the unanimously approved concept statement. The RFA is expected to be announced in April, and awards would be made this October:

Multi-institutional Cooperative Group for Clinical Evaluation of Magnetic Resonance Imaging in Breast Cancer. Proposed RFA (cooperative agreements), $1.5 million per year, four years, three to four awards.

Over the last few years, magnetic resonance imaging of the breast has emerged as the most promising clinical tool for staging of breast cancer. Recent studies reported at the Diagnostic Imaging Research Branch, Radiation Research Program workshop "Quantitative Evaluation of Tissue Function," April 1-2, 1993, indicate that breast MRI is more sensitive than conventional x-ray mammography in the detection of early breast cancer. Contrast-enhanced MRI has been shown to be a promising adjunctive diagnostic tool in the following clinical situations: (1) failure of conventional mammography and physical examination to provide diagnosis; (2) detection of small lesions; (3) detection of multifocal and multicentric breast cancer; (4) breast cancer staging (e.g., definition of the anatomic disease extent); and (5) differentiation of dysplasia and scar versus cancer. While the sensitivity of breast MRI appears promising, the specificity of this technique has been reported to be low. However, the recent development of specialized coils and other equipment for MRI-guided biopsy is expected to have an important impact on tissue characterization of the MRI-detected lesions.

On November 27, 1993, DIRB/RRP convened a meeting of the NCI Advisory Group consisting of the leaders of the international academic community and industry in order to discuss the possibility and feasibility of clinical trials in breast MRI at this time and to formulate specific clinical questions that can be answered by such studies. Current results support the hypothesis that MRI (combined with

image-guided biopsy) can improve the early detection and staging accuracy of breast cancer by increasing confidence in unifocal disease and detecting multifocal/multicentric disease. A number of important clinical issues may be addressed by clinical trials in breast MRI:

1. To define clinical indications for breast MRI studies and for MR-guided breast biopsy (which lesions to biopsy, and which not).

2. To define clinical indications for breast MRI versus conventional x-ray mammography versus current ultrasound for detection of multicentric or multifocal breast cancer;

3. To study the sensitivity and specificity of breast MRI in patients who will get pathological confirmation (e.g., mastectomy, lumpectomy);

4. To evaluate whether breast MRI studies would have an impact on treatment decision (if yes, in what percentage of cases?);

4a. To create a patient followup database which would allow addressing of the following future questions: Can breast MRI reduce the number of lumpectomies, with or without radiation? Can MRI assess and affect local recurrence?

5. To explore how small a lesion MRI can detect and how large a lesion MRI can miss.

6. To study the impact of MRI on the cost-effectiveness of breast cancer management (e.g., through possible elimination of repeated lumpectomies, unnecessary radiation treatment, etc.).

Proposed Funding Mechanism: Cooperative agreement in order to facilitate multi-institutional clinical studies (three or four institutions) with centralized, coordinated development of consensus-based experimental study design, statistical data processing, quality control, and cost-effectiveness analysis.

Contract Concept Approved

The DCT board also gave concept approval to the following contract concept, to be issued by the Developmental Therapeutics Program:

Operation of an Animal Diagnostic Laboratory. Recompetition of contracts held by Univ. of Miami and Univ. of Missouri, estimated $174,000 per year, five years (50% Cancer, 50% AIDS).

Quality control is an essential element with the NCI Animal Production Program when rodents are distributed to hundreds of intramural NIH investigators at the Frederick Cancer Research and Development Center and Bethesda, to grantees throughout the US, and to overseas collaborators. Currently, five contracts are used to optimize expertise in quality control. The quality control performed by this effort has been of particular importance with immune-deprived animals (nudes and SCIDs) when serological testing may be of limited value in identifying pathogenic organisms. Animals are submitted from production colonies, contract laboratories, and investigative laboratories when indicated. These animals are tested for ecto- and endoparasites, bacteria, viruses, and nutritional problems. Emphasis is placed on pathological lesions. Diagnostic support has played an essential role in upgrading animal health status from a treatment support status to an exclusion status, wherein investigators can assume that variabilities regarding animal health do not exist. The primary source of contamination is from humans (animal care personnel) to animal, a reversal of a fairly recent time period when such assumptions could not be made.

These two contractors received laboratory animals weekly, as scheduled by the Project Officer, from the DTP animal production contractors and those contractors performing in vivo research activities. This testing confirmed the health status of the production colonies as well as the research colonies that were monitored. Specific contributions were made in two areas during this time. An orphan parvo virus (OPV) was implicated in problems regarding immune suppression of rodents. An improved diagnostic test was developed for this virus, which provided technical information supporting the contention that OPV is ubiquitous in barrier-maintained rodent colonies, but that the rodent is not likely to be the natural host for same. Recent problems with a bacterial infection (Heliobacter) at the FCRDC production facility served to emphasize the importance of pathology support and animal health evaluation. To date, this organism can be identified only through histological techniques.

One award effective December 1, 1995, is expected to be made. Since it is necessary that the in vivo research activities being supported by the NCI Animal Program be done with pathogen-free animals, this diagnostic contract is necessary to confirm the health status. It is anticipated that this effort will be used in concert with other diagnostic support particularly with serological testing, to provide continuing assurance that NCI investigators are provided with pathogen-free, genetically defined animals, which are essential for research purposes.

Howard Temin, Nobel Laureate, NCAB Member, Dead At 59

Nobel laureate and member of the National Cancer Advisory Board Howard Temin died of adenocarcinoma Feb. 9.

Temin, 59, was a researcher at the McArdle Laboratory for Cancer Research at the Univ. of Wisconsin.

Temin won the Nobel Prize in 1975 for his discovery that genetic information in RNA can be transferred to DNA, reversing the usual flow of genetic information. This work led to the discovery of oncogenes and retroviruses.

A nonsmoker who led a lifestyle aimed to minimize the risk of cancer, Temin used the Nobel Prize ceremonies as an opportunity to campaign against smoking. Outraged by seeing several members of the audience light up, Temin declared:

"I am outraged at the lack of measures taken to stop cigarette smoking. To achieve a decrease in cigarette smoking is the most important goal today."

Sources said Temin's recommendation was among the deciding factors in Harold Varmus's appointment to the post of NIH Director.

"Howard Temin was one of the most brilliant scientists of his generation," said HHS Secretary Donna Shalala, a former UW-Madison chancellor. "He was a friend and colleague. We all will miss his leadership of science and his firm commitment to the highest research standards."

Temin began his career in science as a high school student working for a summer at the Jackson Laboratory in Bar Harbor, ME. He graduated from Swarthmore College. At graduate school at the California Institute of Technology, Temin worked under Renato Dulbecco.

Later, Temin, Dulbecco and David Baltimore shared the Nobel Prize in Medicine or Physiology.

In 1960, Temin came to McArdle. At the time of his death, he was the Steenbock Professor of Biological Sciences, the Rusch Professor of Cancer Research and the American Cancer Society Professor of Viral Oncology and Cell Biology.

Temin's cancer was diagnosed in August 1992, two months after he was awarded the National Medal of Science by then President George Bush.

Following the diagnosis, Temin continued to direct the laboratory. Despite aggressive treatment, he published 15 papers and made repeated trips to Bethesda for NCAB meetings. When he was unable to attend in person, Temin participated in meetings through a telephone hookup.

In the final months, Temin's research focused on three areas: the mechanism that generate gene mutations in retroviruses; the use of genetics to study the regions of the virus responsible for making particular proteins; and the development of a new kind of potential vaccine for complex retroviruses, including HIV.

After learning of his diagnosis, Temin had 800 daffodil bulbs planted in his garden, to watch them come into bloom the following spring.

Temin's term on NCAB will end later this year.

He is survived by wife Rayla Greenberg Temin, a faculty member at the UW-Madison Dept. of Genetics; daughters Sarah, of Berkeley, CA, and Miriam of San Francisco; and brothers Michael Temin, a Philadelphia attorney, and Peter Temin, professor of economics at Massachusetts Institute of Technology.

Brigid Leventhal, 58, Pioneer In Pediatric Cancer, Dead

Brigid Leventhal, professor of oncology and pediatrics at Johns Hopkins Univ. School of Medicine, died of cancer Feb. 6. She was 58.

Leventhal was known for her pioneering work in the research and treatment of childhood cancers. She was a founding member of the Pediatric Oncology Group, a member of the NIH Recombinant DNA Advisory Committee, and served on the Boards of Directors of the American Society of Clinical Oncology and the American Assn. for Cancer Research.

She was the first director of the oncology center's Pediatric Oncology Division, from 1976-84.

At the time of her death, she was working with FDA through a grant from the Children's Cancer Foundation to establish post-marketing trials of agents used to treat children with cancer.

Prior to joining Hopkins, Leventhal was chief of NCI's Chemoimmunotherapy Section from 1973-76. She joined NCI in 1965.

Leventhal is survived by her husband, Carl Leventhal, a division director at the National Institute of Neurological Disorders & Stroke, four children, her mother, a brother, and a granddaughter.

Memorial donations may be made to a lectureship at Johns Hopkins Oncology Center, Development Office, 550 North Broadway, Suite 801, Baltimore, MD 21205.

Avon Gives $3 Mil. Expanding Breast, Cervical Screening

Avon Products Inc. has given $3 million to expand the breast and cervical cancer screening program operated jointly by the Centers for Disease Control and Prevention and YWCA.

The program, aimed at women over 50 who belong to the medically underserved populations, will offer culturally targeted breast health education seminars, refer participants to publicly funded screening services and provide exercise and peer support for breast cancer patients.

Since last fall, Avon raised $5 million through sales of "awareness pins," enamel pins shaped as pink ribbons.

The grant allows CDC and YWCA to build on their cooperative agreement to encourage screening through the National Breast and Cervical Cancer Early Detection Program.

Through that agreement, announced last March, YWCA encourages women to obtain screening provided free or at a low cost by state health agencies. CDC has provided grants to 45 states to set up screening programs for the underserved.

Now, the Avon money will allow YWCA to establish a training program for volunteers as well as to develop brochures and video materials. The cosmetics company also said its sales representatives are being encouraged to join the program as volunteers and to distribute materials on breast cancer.

The new YWCA program is called Encore-plus.

"Encore-plus is a non-profit-public-private partnership model that leverages the strengths of each party," said Ann Stallard, YWCA national board president.

"While CDC finances early detection services through state health departments, the YWCA provides the kind of face-to-face, grass roots education and outreach that studies show to be the most effective to promoting access to and use of education and screening services," Stallard said.

YWCA has begun training the volunteers who would, in turn, provide training to others, with the ultimate objective of building a community-based infrastructure that would support the CDC funded breast cancer programs.

The Encore-plus program will include:

- Video materials, including a Spanish-language film.
- Seminars and outreach followed by referral to CDC-funded early detection programs.
- Post-screening support for women who need diagnostic and treatment services.
- Weekly sessions for breast cancer survivors that include peer group support and an exercise program as well as referral to medical and social work specialists for women who have special needs. This component of the program, called Encore, has been available through YWCA for the past 19 years.
- Grants for establishing new programs by YWCA chapters.

YWCA serves two million women in the U.S.

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 to the individual named, Executive Plaza South room number shown, NCI, Bethesda, MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville, MD.

RFP NCI-CN-45594-32
Title: Preclinical evaluation of intermediate endpoints and their modulation by chemopreventive agents
Deadline: Approximately April 23

NCI is seeking contractors qualified to perform animal cancer model studies of biomarkers and intermediate endpoints that might be used in human clinical trials. The work shall be performed to assess, in detail, the biomarker modulating effects of selected chemopreventive compounds. This solicitation is an annual announcement to expand a current pool of master agreement holders qualified to perform this type of work.

Procurement technician: Desiree Sylver-Foust, RCB Executive Plaza South Rm 635, Tel. 301/496-8603.

RFP NCI-CN-45593-32
Title: Phase II clinical trials of new chemopreventive agents
Deadline: Approximately April 22

NCI is seeking contractors to perform phase II clinical trials that are small, short-term, efficient studies to determine the dose of a given chemopreventive agent that exhibits a pharmacodynamic effect on a given endpoint. These studies will also require dose response studies to determine the minimum dose at which a biological effect is observed and confirmation of the maximum safe dose, and the performance of randomized blinded trials in small groups of subjects whose endpoints will be the measurable biological effect of the agent versus a placebo. This solicitation is the annual announcement to expand the pool of master agreement holders.

Procurement technician: Desiree Sylver-Foust, RCB Executive Plaza South Rm 635, Tel. 301/496-8603.

NIH Sets Research Grant Funding Strategies For FY94

NIH last week released a statement designed to guide its institutes and centers in making funding decisions on research project grants in fiscal 1994.

The statement is divided into core principles and funding strategies. Section I, core principles, includes three statements that will be applicable for more than FY 94. Funding strategies, in Section II, may be changed from year to year depending on the appropriation level and associated Congressional directives, the NIH statement said.

I. Core Principles

1. Grants will be awarded on the basis of reasonable and allowable costs, consonant with the principles of sound cost management and in consideration of Institute or Center (I/C) priorities, constraints on the growth of average grant costs, and the availability of funds.

2. The award of noncompeting research project grants at committed levels continues to be the cornerstone of the NIH Financial Management Plan and is the basis of the plan's credibility with the scientific community and Congress.

3. Determination of commitments for future years must take into consideration stability of support for investigators, optimum portfolio balance, and opportunities to address emerging problems.

II. Fiscal Year 1994 Funding Strategies

1. For FY 1994 competing grants, the average increment for the subsequent noncompeting award may not exceed the direct cost level of the previous budget period by more than four percent. NIH staff may make exceptions for specifically justified programmatic requirements and one-time, non-recurring costs such as equipment.

2. Every effort will be made to accommodate shifts in the NIH fiscal situation. If conditions are such that funding at the committed levels is not possible, the I/Cs will consult with the Deputy Director for Extramural Research, NIH, to determine an appropriate resolution.

3. The average total cost of competing grants in the FY 1994 cohort will not increase by more than the Biomedical Research and Development Price Index (BRDPI) (4.19 percent) over the cohort of competing grants in FY 1993, including special initiative small business grants - Small Business Innovative Research (SBIR)/Small Business Technology Transfer (STTR). Given specific appropriation levels, some I/Cs may not be able to provide an increase consonant with the BRDPI.

4. When necessary, budgetary reductions from the requested level will be achieved through implementing a combination of initial review and Council/Board recommendations, staff review for cost allocability, allowability, and reasonableness, and programmatic adjustments to arrive at an appropriate funding level.

5. Based on adjustments to the project, I/C staff, in consultation with the principal investigator, will decide whether or not a new statement of specific aims is required. When reductions are 25 percent or more below the IRG recommended level, staff will obtain a revised statement of specific aims, a revised budget, and/or a revised timetable, as appropriate, for the project, which must be approved and countersigned by the institution and approved by program and grants management staff. To ensure initial review group understanding of the modified scope of a funded project, the approved statement of revised aims should be submitted by the investigator in competing continuation grant applications.

6. For competing continuation grants, one factor in arriving at the award amount will be the level of support in prior years and the extent to which the I/C can permit growth within the existing constraints on average costs.

7. The average length of research project grants will not exceed four years (excluding special initiative small business grants—SBIR/STTR).

8. In making funding decisions, I/Cs should factor in the total costs of a grant, especially at the margin of the funding plan.

In Brief

US Attorney's Office Drops Criminal Probe Of Gallo

(Continued from page 1)

can be determined from information already in the public domain and therefore is not patentable. NIH Director **Harold Varmus** said he believed patenting the sequences would not promote technology development. . . . **US ATTORNEY'S** office in Baltimore last week dropped the remaining federal probe of NCI's **Robert Gallo.** The action ends the federal investigations into the discovery of the AIDS virus. In a Jan. 19 letter to the HHS Inspector General, the prosecutors wrote that the likelihood of winning the case was poor, according to news reports.