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NSABP Agrees To Three-Month Search For Chairman Candidates, Review Of Plans

The new chairman of the National Surgical Adjuvant Breast & Bowel Project will be elected following a three-month search for candidates and a thorough review of their platforms, the NCI and the cooperative group agreed.

In a letter to the NSABP executive committee, a senior NCI official said the acceptance of a plan to screen and elect candidates would be a prerequisite for the Institute's nod for resumption of patient accrual.

"If this is agreeable to you, I believe we can begin to accrue new

(Continued to page 2)

In Brief

Kalt Named Director, NCI Extramural Div.; Browning Is Deputy; Other DEA Staff Changes

MARVIN KALT has been named director of the NCI Div. of Extramural Activities. Kalt, acting director since the retirement of Barbara Bynum last January, has been deputy director of the division for the past four years. Prior to joining NCI in 1990, Kalt oversaw peer review as chief of the Scientific Review Office of the National Institute on Aging. Before that he was a faculty member in the Dept. of Anatomy at the Univ. of Connecticut Health Center. . . . **ROBERT BROWNING**, chief of the Grants Review Branch, has been appointed acting deputy director of DEA. Other changes in the Div. of Extramural Activities: **David Irwin**, head of the Research Program Review Section, has been appointed acting chief of the Grants Review Branch. **Lemuel Evans**, director of the Comprehensive Minority Biomedical Program, is on detail tot he NIH Office of Research on Minority Health. **Lester Gorelic** is the acting program director. **Paulette Gray**, chief of the Review Logistics Branch, is on detail to the HHS Office of the Deputy Assistant Secretary for Women's Health. **Ray Bramhall** is the acting branch chief. **Kevin Washington**, deputy chief of the Administrative Management and Planning Branch, is on detail to the NIH Office of Technology Transfer. **Rosemary Cuddy**, acting chief of the Research Analysis and Evaluation Branch, has been named branch chief. . . . **SOPHY A. GOLDBERG**, mother of **Cancer Letter** editor Paul Goldberg, died of ovarian cancer June 8. She was 57. We thank everyone who was involved in her care. Next week's edition of **The Cancer Letter** will be published two days late. The May issue of **Cancer Economics** will be combined with the June issue, after which the normal publication schedule will resume.

Accrual Of Treatment Trials Resumes At 100 NSABP Sites

(Continued from page 1)
patients and begin the process of restoring NSABP to its proud reputation," Bruce Chabner, director of the NCI Div. of Cancer Treatment wrote in a letter to a member of the NSABP executive committee.

A copy of the letter, dated June 2 and addressed to Peter Deckers of the Univ. of Connecticut Health Center, was obtained by **The Cancer Letter**.

Since the NSABP's 23-member executive committee accepted the NCI conditions, accrual for treatment trials was restarted at about 100 of the group's 485 sites, including NCI designated cancer centers, institutions involved in the Community Clinical Oncology Program and other sites that have passed the NCI audit. Accrual for the treatment trials began on June 7.

The Breast Cancer Prevention Trial, too, is being brought closer to resumption, as institutions are being asked to provide documentation of institutional review board approval of the latest revision in consent forms and of completion of the reconsenting process.

Funds To Be Disbursed

Moreover, NCI gave a nod to the cooperative group to begin disbursement of funds for patient followup.

The authority of the cooperative group's interim leadership was challenged last month, when the executive committee came close to nominating Pittsburgh surgeon and NSABP official Norman Wolmark to the post of chairman of the group. However, the executive committee later reversed itself, deciding to endorse no candidate until a later date (**The Cancer Letter,** May 27).

"We urge that enough time be allowed so that candidates and their specific written plans would be made available for discussion and review," Chabner wrote to Deckers. "In order to provide the fairest and most effective process, perhaps we could agree to conduct the search and election in the period up to Sept. 1."

Wolmark: Will Comply

Though the NCI's demand and its acceptance by the NSABP executive committee constitute a setback to his campaign, Wolmark remains the only declared candidate to succeed the ousted Bernard Fisher as chairman of the cooperative group.

"Whether I personally agree with the time allocation, I will certainly comply with the NCI recommendation," Wolmark said to **The Cancer Letter.** Wolmark, NSABP's deputy director for medical affairs, plans to move NSABP to Fox Chase Cancer Center.

NSABP's interim leaders said they are committed to keeping the cooperative group in Pittsburgh.

"We are pleased that the executive committee agreed to follow a very careful and thoughtful process about this critical step," Ronald Herberman, the group's interim chairman, said to **The Cancer Letter**.

In another agreement that is likely to enhance stability of the group's leadership, NCI agreed to recompete the NSABP grants no earlier than the fall of 1995, which would give the group a full year to test its newly developed administrative structure and to submit its bid for the grant.

Recompetition In Fall 1995

"We will be recompeting the various operations at the Univ. of Pittsburgh ahead of schedule," Chabner said in a letter to Deckers. "Our plan is to make an announcement and request applications, providing enough time for all groups and individuals who may wish to compete for the NSABP grant(s) to do so on a level playing field.

"Perhaps the discussions of new leadership for the NSABP should be coordinated with these steps," Chabner wrote.

NCI is likely to play a crucial role in selection of the cooperative group's chairman, sources said. The NSABP executive committee will consult the Institute as it identifies candidates and screens their platforms.

After a candidate is identified, NCI would have

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to approve the placement of his or her name on the ballot. Only one name is expected to be placed on the ballot, with cooperative group members being asked to vote Yes or No, sources said.

At the NSABP membership meeting in Nashville June 13, the group's investigators are expected to be asked to ratify changes in the group's constitution.

Coalition Was Started By Eight Univ. of Pittsburgh Employees

The mysterious coalition that attempted to trigger a letter-writing campaign in support of Bernard Fisher consisted of eight employees of the Univ. of Pittsburgh, according to internal documents obtained by **The Cancer Letter**.

A memorandum by the Univ. of Pittsburgh Internal Audit office states that the group, which identified itself as the Coalition in Support of Breast Cancer Research included three physicians affiliated with the National Surgical Adjuvant Breast & Bowel Project, four employees of the therapy center and one data management employee.

The coalition existed for only eight days, during which it sent out 408 packages which urged NSABP principal investigators to write to Congress and the Administration to demand Fisher's reinstatement to his post as NSABP chairman and further demanding the investigation of his firing by NCI.

According to a memorandum dated May 13 and addressed to Lewis Popper, general counsel for the university, three senior NSABP staff members admitted to being members of the Coalition in Support of Breast Cancer Research.

Used $100 Of University Resources

"They indicated that in their minds CSBCR started March 31 and ended with the April 7 mailing," the document states. "However, due to its fluid form, they believed that some lower level staff members felt that CSBCR lived on and exists to this day."

Subsequently, letters of reprimand were placed in the files of several members of the coalition (**The Cancer Letter,** May 13).

According to the memorandum, the coalition used about $100 in university resources, mostly through the use of copying equipment for which the coalition bought paper.

One group member used a personal check to pay for the mailing to NSABP investigators. Group members also appeared to have negotiated a bulk discount with UPS, the memorandum said. The document also said UPS was informed that the coalition's mailing was separate from university business and made a business decision to provide the group with a discount rate of $5 for its overnight mailings.

According to the memorandum, one member of the coalition asked her staff member to take vacation time to contact patients and urge them to write letters in support of Fisher.

The subordinate declined, stating that "she felt uncomfortable doing this in light of the university directive that the NSABP employees speak to no one outside the university about the events of the previous days," the document said.

Following that incident, no calls to patients were made by NSABP employees, the memorandum said.

NCI To Require Adverse Drug Reaction Reports From Trials

NCI will require principal investigators to notify the Institute and all participating physicians of adverse drug reactions that occur in the course of clinical trials.

Food and Drug Administration regulations that require the principal investigator to inform the holder of the Investigational New Drug Application of adverse drug reactions. The IND holder in turn notifies FDA.

NCI will revise the cooperative agreement (U10) grants that support the clinical trials cooperative groups to make an additional requirement, Bruce Chabner, director of the NCI Div. of Cancer Treatment, said. The principal investigator will be required to notify the NCI project officer of adverse drug reactions. The group headquarters will be responsible for informing all participating investigators and cancer patients of the adverse reactions.

Responsibility Of Investigators

The requirement is a reaction to criticism that the National Surgical Adjuvant Breast & Bowel Project did not quickly notify physicians or patients involved in tamoxifen trials of the risk of death from endometrial cancer.

"All parties involved will be notified immediately, including NCI, investigators, and the sponsoring drug

company," Chabner said to the National Cancer Advisory Board last week. "This will be the responsibility of all participating investigators."

Chabner provided the board with an overview of the NSABP controversy, and changes made to the cooperative group awards as a result. While this information has been previously reported in **The Cancer Letter,** Chabner's slides are reprinted as a summary of events.

Fraud Investigation at St. Luc Hospital

June 1990	Initial discovery by NSABP staff
Sept. 1990	NSABP audit confirms fabrication additional cases found
Jan. 1991	Repeat audit; additional cases found
Feb. 1991	NSABP reports findings to NCI; NCI notifies OSI and FDA investigation begun
May 1991	Poisson admits fabrication to OSI and FDA
July 1991	NCI told B06 trial results not changed
March 1992	B06 reanalysis presented to OSI NCI and OSI recommend publication of reanalysis
April 1993	ORI (OSI) completes investigation report published in ORI newsletter
June 1993	ORI report published in Federal Register

NCI Requests for Reanalysis of NSABP Trials

July 1991	Verbal request to Carol Redmond
March 1992	Verbal requests to Bernard Fisher and Redmond
June 1992	Verbal request to Fisher
Jan. 1993	Written request to Fisher
Oct. 1993	Written request to Fisher

Revised Terms of Award for Cooperative Groups

●Establish auditing timelines and guidelines. Routine reports must be submitted to NCI within six weeks.

●In cases of serious data irregularities, notify Clinical Trials Monitoring Branch in NCI Cancer Therapy Evaluation Program within 24 hours.

●In cases of scientific misconduct, NCI requires:

—Notification of the group's data safety and monitoring committee, NCI, collaborators, institutional review boards, and funding sponsors.

—Immediate notification of journals.

—Reanalysis of results after deleting falsified or suspect data within 90 days.

—Submit reanalyzed results to original journal within 90 days.

—NCI may distribute published reanalysis as broadly as necessary.

—Data files shall be made available to NCI upon request.

●NCI retains the right to reanalyze data affected by scientific misconduct or data integrity or affecting patient safety.

●Under consideration: Notification of all involved parties (NCI, all participating investigators) of any adverse drug reaction, not just the IND holder.

Deficiencies in NSABP Operations

●Failure to publish St. Luc fraud case and reanalysis of important breast cancer trials.

●Failure to notify NSABP membership of fraud at St. Luc Hospital.

●Failure to expunge St. Luc data from NSABP data files.

●Failure to exclude St. Luc data from publications, 1991-1994.

●Failure to reanalyze and submit for publication all previously published major trials containing St. Luc data.

●Failure to establish required data safety and monitoring board (Dec. 1992).

●Suspension of all treatment trials audits (April 1993).

●Failure to provide NCI with requested audit schedule (1993).

●Six-month delay in reporting evidence of second fraud case to NCI (3/25/94).

●Six-month delay in reporting problem audit in New Orleans.

●Failure to report audit results of prevention trial (1993-1994).

Deficiencies in NCI Operations

●Failure to compel publication of reanalyses.

●Failure to compel compliance in auditing and reporting.

●Lack of standard procedures to guide response to fraud.

—Immediate notification of journals

—Immediate notification of public

—Recovery of funds

—Expunge all data from central protocol files

—Reanalysis of previously published trials and publication of reanalysis results

NSABP Probation March 30: Required Actions

- Group administrative/executive officer.
- Improved on-site monitoring and quality assurance.

—Improved audit procedures for verification of data and protocol compliance.

—Written standards for audit reports and limits of noncompliance.

—Monthly audit schedule to be provided to NCI.

—Must catch up on backlog of audits since April 1993.

—Notification of NCI of any and all problems within 24 hours.

—Six-week limit for reports of non-problem audits to NCI.

- Establishment of independent data safety and monitoring board.
- Reanalyze all reported trials containing data from St. Luc Hospital.
- Submit all manuscripts to NCI for approval.

Broder: Groups 'Tightly Woven Throughout Fabric' Of NCI

The clinical trials cooperative groups are an NCI creation, and the groups used to be headed by NCI staff, the Institute's director said last week.

Responding to criticism of NCI's asserting authority over the groups during the crisis involving the National Surgical Adjuvant Breast & Bowel Project, NCI Director Samuel Broder recounted the historical beginnings of the groups in remarks to the National Cancer Advisory Board last week.

"The cooperative groups are tightly woven throughout the fabric of the NCI, and there will be no change in this fact," Broder said. "Where there are strengths in our clinical trials program, we must make sure they are identified and disseminated widely. By the same token, where there are problems, we should identify them and take steps to correct them clearly and non-defensively."

The Institute's clinical trials program was begun by NCI officials, Broder said.

"Gordon Zubrod [director of the Div. of Cancer Treatment until 1974] saw the need for multi-institutional clinical trials back in the 1950s and helped create the administrative support for the forerunners of our modern cooperative groups," Broder said. "At one time, Zubrod was in effect the chairman of [the Eastern Cooperative Oncology Group], and Paul Carbone and many others at NCI and continued the tradition."

Emil (Tom) Frei headed the Cancer & Leukemia Group B while he was a branch chief in DCT, Broder said. Frei also chaired the Southwest Oncology Group, he said.

The funding mechanism for the groups was changed from a grant to a cooperative agreement in 1979 (**The Cancer Letter,** Nov. 9, 1979).

"The essence of our clinical trials process is that primary responsibility and accountability must reside with the grantee," Broder said. "The principal investigator on every NCI grant, including the U10 grants that support clinical trials, must forthrightly accept responsibility and accountability for the performance of the grant."

Clinical trials are a "foundationstone" of the National Cancer Program, Broder said.

"It is important that we all acknowledge, whether we are basic scientists or clinicians, the importance of our clinical trials programs," he said. "It is also important that we do more than just talk. Talk is cheap, and we cannot pay for clinical trials with words."

Since 1981, there has been a 57 percent growth in funding for the clinical trials support mechanism, while NCI as a whole has experienced 28 percent growth in funding, Broder said.

"I cannot tell you the clinical trials budget is adequate," he said. "However, we are making a substantial commitment to our clinical trials process, for prevention, diagnosis and treatment."

Avon, NABCO Award 18 Grants In Breast Health Education

Avon Products Inc. and the National Alliance of Breast Cancer Organizations announced that NABCO has awarded $370,000 in grants to 18 organizations in 14 states whose programs improve women's access to breast health education and early detection services.

The programs were funded through Avon's Breast Cancer Awareness Crusade, begun in October 1993.

Cancer Center Planning Grants Approved For Recompetition

The NCI Div. of Cancer Biology, Diagnosis & Centers has been given concept approval to recompete the planning and development grants for cancer centers.

The program three years ago funded 14 institutions developing a research base to be able to compete for NCI designation as clinical, basic or comprehensive cancer centers.

The concept statement for the program was approved by the division's Board of Scientific Counselors at a meeting this week.

The board also gave concept approval to an RFA for small research grants to historically Black colleges and universities.

The concept statements follow.

Planning and Development Grants for Prospective Cancer Centers in Underserved Geographic Areas. RFA, $1 million total, three years, three to five awards. Cancer Centers Branch.

The purpose of this program initiative is to announce the availability of planning and development grant funds to assist eligible institutions to develop the organizational capability that will lead to the formation and/or development of cancer research centers of excellence. The goal of the initiative is to continue to encourage development of clinical cancer research centers in geographic areas that are currently not served by existing NCI-designated clinical or comprehensive cancer centers, and to encourage research in these areas targeted to minorities and under-represented populations. In addition to basic cancer research, these new centers should plan to emphasize clinical and prevention/control research that will ultimately impact on the populations in their regions, especially minorities and other underserved populations. It is anticipated that after completion of these planning and development grants, recipient institutions will be in a position to provide to their region state of the art care coupled with research that will ultimately have an impact on reducing cancer incidence and mortality.

The Cancer Centers Program of NCI currently supports 53 multidisciplinary cancer research centers through Cancer Center Support Grants using the P30 grant mechanism.

However, since the passage of the National Cancer Act in 1971, Congress has emphasized in legislative language the need for better geographic distribution of NCI-designated cancer centers around the US. A majority of funded NCI-designated comprehensive, clinical and consortium cancer centers are located on the East and West coasts and around the Great Lakes reflecting both US population density and the locations of medical research centers. There are, however, medical institutions existing in currently under-represented areas that have sufficient peer reviewed cancer research or could develop the research base to become NCI cancer centers. In 1991, the RFA titled Planning Grants for Prospective Cancer Centers was issued. It was designed to encourage qualified institutions to make the investment necessary to establish a cancer center. Twelve awards using the P20 mechanism were made. In 1993, two other planning awards were made to institutions which complied with the original intent of the RFA and which received competitive peer review.

The 14 institutions receiving these P20 awards reflected the entire spectrum of development. Some institutions were at later stages of development and others were at very early stages in their development. In order to provide another opportunity for institutions to develop cancer centers in underserved areas, this initiative is for institutions that have not previously had planning grants or for institutions that are currently funded by planning grants and wish to renew these grants in order to complete the planning process.

Institutions in states which currently have no NCI-funded clinical or comprehensive cancer center are eligible to apply, although exceptions to this rule will be considered by NCI under very special circumstances. Institutions which received P20 awards in FY 1992 are eligible to reapply if they do not yet meet the $1.5 million research base requirement as noted in the 1992 CCSG guidelines, or if they can demonstrate a need to build greater size and breadth into the research base in order to perform as an effective cancer research center.

Specialized Small Research Grants Program for Historically Black Colleges and Universities. RFA for R03 awards of up to $85,000 direct costs per year; total $1 million per year for three years, eight to 10 grants. Cancer Biology Branch, Cheryl Marks, program director.

This program would promote research by faculty at HBCUs. As research areas that are appropriate for this RFA, NCI supports basic research, in vitro and in vivo, on: the cellular and molecular biology of malignant cells, the role of the immune system in tumor growth and progression, the transfer of basic research findings to improve the diagnosis and prognosis of cancer, the mechanisms of cancer induction and promotion by chemicals, viruses, and environmental agents, drug discovery and synthesis of new anticancer agents, the biochemical and molecular mechanisms of antitumor drug action, the pharmacology and toxicology of antitumor agents, identification and evaluation of agents that prevent carcinogenesis, identification of biologycal markers of risk or exposure, the role of nutrition in cancer. These are but a few possible areas of inquiry.

Foundation Seeks Applicants For Smoking Cessation Grants

The Robert Wood Johnson Foundation intends to make $3 million available for grants to researchers to develop smoking cessation interventions for women of reproductive age.

The new program, Smoke-Free Families: Innovations to Stop Smoking During and Beyond Pregnancy, will fund up to 15 two-year pilot projects with grants averaging $200,000 per project.

About 25 percent of expectant mothers in the US smoke throughout their pregnancies, according to the 1990 Surgeon General's report. Around the time of pregnancy, women may be receptive to smoking cessation efforts, the foundation said.

The new program is designed to stimulate the next generation of smoking-cessation interventions for women of reproductive age. The foundation is especially interested in novel smoking cessation approaches that have not been described or evaluated previously. The pilot projects are intended to be precursors for clinical trials.

Letters of intent may be sent to: H. Pennington Whiteside Jr., deputy director, Smoke-Free Families, National Program Office, Dept. of Obstetrics & Gynecology, Univ. of Alabama at Birmingham, Birmingham, AL 35233-7333, Tel: 205/975-8951.

RFP Available

RFP NCI-CP-50512-60

Title: Support for Research on Retroviral Pathogenesis, Treatment and Prevention

Deadline: Approximately Aug. 1

NCI is soliciting proposals from offerors with the capability to (Task A) culture, detect, characterize and provide human and animal retroviruses, to analyze sera for retroviral antibodies, to provide monoclonal and polyclonal antibodies and purified and characterized biologically active viral and cellular proteins, and to evaluate protein effects on cell growth and angiogenesis, and/or (Task B) provide stem cell cultures and to assess and evaluate in vtro and in vivo stem cells with inserted genes. A four-year award for each task is estimated. Offeror must demonstrate the ability to: 1) establish, prior to contract award, biocontainment facilities (P2) with (P3) capability to carry out the work with human and nonhuman primate retroviruses (HIV-1, HIV-2, HTLV and HIV) and 2) provide, prior to contract award, facilities from the freshly prepared specimens can be delivered to the NIH, Bethesda, MD, within one hour after harvest or collection.

Contract specialist: Barbara Birnman, RCB Cancer Etiology Contracts Section, 6120 Executive Blvd., Room 620, Bethesda, MD 20892, Tel: 301/496-8611.

RFAs Available

RFA CA-94-016

Title: **Community Clinical Oncology Program**

Letter of Intent Receipt Date: July 1

Application Receipt Date: Aug. 25

The NCI Div. of Cancer Prevention and Control invites applications from domestic institutions for cooperative agreements to the Community Clinical Oncology Program (CCOP). New community and research base applicants and currently funded programs are invited to respond to this RFA as described below.

This issuance of the CCOP RFA seeks to build on the strength and demonstrated success of the CCOP over the past ten years by continuing the program to support community participation in cancer treatment and cancer prevention and control clinical trials through research bases (clinical cooperative groups and cancer centers supported by NCI) and utilizing the CCOP network for conducting NCI-assisted cancer prevention and control research.

New applicants and currently funded programs are eligible as described below. Two types of grantees are eligible to apply: community programs and research bases. Community applicants may be a hospital, a clinic, a group of practicing physicians, a health maintenance organization (HMO) or a consortium of these. Community programs (CCOPs) will be required to enter patients onto NCI-approved treatment and cancer prevention and control clinical trials through the research base(s) with which each CCOP is affiliated.

Research base applicants must be either an NCI-funded clinical trials cooperative group or cancer center. Research bases will be required to provide clinical research treatment and cancer prevention and control protocols, monitor the quality research and follow CCOP accrual.

Support will be through the Cooperative Agreement (U10). Total project period for applications submitted in response to this RFA may not exceed three years for new applicants and five years for applicants currently supported under this program. Currently supported applicants will be funded for three, four, or five years depending upon priority score/percentile, review committee recommendations, and programmatic considerations.

It is anticipated that up to $5 million in total costs per year for five years will be committed to specifically fund applications that are submitted in response to this RFA. Approximately two research base awards and up to 15 CCOP awards will be made.