THE CANCER LETTER

Vol. 20 No. 34
Sept. 9, 1994

Price $225 Per Year US, Canada
$250 Per Year Elsewhere

P.O. Box 15189 Washington, D.C. 20003 Telephone 202-543-7665

Interim NSABP Leaders Will Not Nominate Chairman, Citing Exec. Committee "Bias"

The interim leadership of the National Surgical Adjuvant Breast & Bowel Project decided not to nominate a candidate for chairman of the cooperative group.

After conducting job interviews with breast cancer surgeons throughout the country, the Univ. of Pittsburgh, which administers the NSABP grant, decided to submit no candidate for consideration of the cooperative group's executive committee.

"In light of the manifest bias and prejudgment that has characterized the approach of at least a substantial part of the executive committee, the Univ. of Pittsburgh has decided not to submit a nominee to the executive committee at this time," NSABP interim chairman Ronald Herberman wrote

(Continued to page 2)

In Brief

FDA Approves Three-Hour Taxol Infusion; Foti Elected President Of NCCR; Luce Retires

TAXOL THREE-HOUR infusion schedule for ovarian cancer that has failed first-line or subsequent therapy has been approved for marketing by FDA. The new dosage and administration section of the drug's package labeling will recommend a dose of 135 mg/m2 or 175 mg/m2 administered intravenously over three hours every three weeks. FDA cleared Taxol in December 1992 for use after failure of chemotherapy for metastatic ovarian cancer, with doses administered over 24 hours. Last April, Taxol was approved as a three-hour infusion at a dose of 175 mg/m2 for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy. . . . **MARGARET FOTI**, executive director of the American Association for Cancer Research, was elected president of the National Coalition for Cancer Research last month, succeeding Robert Day. She will serve a two-year term. Elected members of the NCCR board were: **Anna Barker, James Kitterman, Pearl Moore, John Niederhuber**, and **J. Frank Wilson**. Nineteen national organizations belong to the NCCR. . . . **JAMES LUCE** will retire as interim president and medical director of the Don and Sybil Harrington Cancer Center, Amarillo, TX, on Oct. 1. The center is searching for a permanent director, who should be a leading cancer physician with experience in research, education, patient care, and administration. . . . **SAN ANTONIO** Cancer Institute has won continued funding as an NCI-designated cancer center, receiving a four-year, $6 million grant from NCI.

PCI Files Application For Research Base CCOP . . . Page 2

Eight Applications Received For NSABP Chairman . . . Page 2

Pitt Criticizes NCI Stance On Repayment For Fraud In Trials . . . Page 3

Broder, Herberman Decline To Coauthor Reanalysis Of Data . . . Page 3

"I Can't Permit Destruction Of NSABP," Fisher Writes . . . Page 4

Herberman: Progess Made To Stabilize NSABP . . . Page 7

PCI Files Research Base CCOP Application; 8 Vie For Chair

(Continued from page 1)
in an Aug. 18 letter to Peter Deckers, an executive committee member who heads the search for chairman of the cooperative group.

The NSABP executive committee, along with Bernard Fisher, is a plaintiff in a suit that alleges that the university as well as several individual defendants, including Herberman, acted improperly when they removed Fisher from his leadership roles at NSABP.

On Sept. 20, a US District Court in Pittsburgh will consider the plaintiffs' motion for injunctive relief that seeks the removal of NSABP interim leadership and Fisher's restoration as chairman of the cooperative group.

The parties will first attempt to hammer out a compromise at a Sept. 13 "conciliation conference" before a judge.

Pitt Cancer Institute Files Application For Research Base CCOP

Pittsburgh Cancer Institute last month filed an application for an NCI grant through Community Clinical Oncology Program.

The Univ. of Pittsburgh officials confirmed that the application for a research base CCOP was filed with the Institute, but declined to discuss it in detail.

It is unclear whether the PCI application is related to the dispute with Fisher and the NSABP executive committee. However, a research base CCOP, if approved by NCI, would set up an administrative structure that would be able to perform the same tasks as a cooperative group, sources said.

"We have put in an application for PCI to be a research base for CCOP trials in both cancer prevention and control and treatment trials," Herberman said to **The Cancer Letter**. "We feel that this is a very appropriate step for our cancer center to take, because we have a strong breast cancer program.

"We have strong programs in cancer control and innovative approaches to cancer therapy. Therefore, we think it would be appropriate for us to interact with CCOPs around the country," Herberman said.

Donald Trump, PCI deputy director, clinical investigations, and NSABP interim executive officer, is listed as the principal investigator on the application, Herberman said.

NCI would not be setting a precedent by approving PCI's application. In fact, three other NCI-designated cancer centers operate similar programs. There three are: M.D. Anderson Cancer Center, Wake Forest Univ. and the Univ. of Rochester.

If the Pitt application is to be considered under regular procedures, the application would go to peer review by November, and by the end of the year the applicant would be told the priority scores.

Generally, the institution that runs a research base CCOP receives $350 for every patient accrued, while participating researchers who accrue patients can be expected to be paid $500 per patient for the first year and $200 for every year of follow-up, sources said.

Meanwhile, NSABP Chairman Search Continues, Eight Applications Received

The NSABP Executive Committee has received eight applications for chairman of the cooperative group. The applications deadline was Aug. 31.

The candidates are:

—**Norman Wolmark**, of the Allegheny General Hospital in Pittsburgh, who—if elected—is expected to move the cooperative group to Fox Chase Cancer Center in Philadelphia.

—**Janet Osuch** of Michigan State Univ., Lansing.

—**Roger Foster** of Emory Univ., Atlanta.

—**Blake Cady** of New England Deaconess Hospital, Boston.

—**Donald Morton** of the John Wayne Cancer Center, Santa Monica, CA.

—**Harold Douglass** of Roswell Park Cancer Institute, Buffalo.

—**David Ota** of Ellis Fischel Cancer Center, Columbia, MO.

—**Kirby Bland** of Rhode Island Hospital in Providence.

THE CANCER LETTER

Editors: **Kirsten Boyd Goldberg**
Paul Goldberg
Founder & Contributing Editor: **Jerry D. Boyd**

P.O. Box 15189, Washington, D.C. 20003
Tel. (202) 543-7665 Fax: (202) 543-6879

Subscription $225 per year North America, $250 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter.

According to a letter from Deckers to NCI Div. of Cancer Treatment Director Bruce Chabner, by mid-September the NSABP search committee will narrow down the field to "several candidates" and interview them on Sept. 17, 18 and 19.

In the letter, dated Sept. 1, Deckers invited an NCI representative to take part in the interviews.

By the end of the month, the search committee will submit one or two names for a vote by the full executive committee. "My hope is to have this completely accomplished no later than mid-October," Deckers wrote.

The letter also indicates that the NSABP executive committee expected the Univ. of Pittsburgh to pay the travel expenses. Pitt appears to be reluctant to reimburse those expenses. In an earlier memo to Deckers, Herberman wrote that the request for funds "raises issues of law." "We will attempt to secure a clear answer and will let you know when we do," Herberman wrote in the memorandum dated Aug. 31.

Herberman's response did not satisfy Deckers, who wrote to Chabner that Pitt's stance would slow the executive committee's search for chairman.

"I strongly believe that the Univ. of Pittsburgh, as the custodian of NSABP funds awarded by the NCI, has an obligation to cover all expenses for the [search] subcommittee and for the candidates we interview," Deckers wrote to Chabner.

"I believe Dr. Herberman's obligation to fund this activity is a direct mandate which the executive committee of the NSABP received from NCI. I, therefore, would appreciate it considerably if you would direct Dr. Herberman to provide appropriate expenses... so that we [could] conduct our business in as timely a fashion as possible," Deckers wrote.

Chabner was out of the country and could not be reached for comment by **The Cancer Letter**.

Pitt Criticizes NCI Stance on Repayment, Memo States Institutions Become Insurers

According to an internal memorandum drafted by attorneys for the Univ. of Pittsburgh, no legal authority exists for imposing consequential damages liability on grantees for the scientific institutions they are charged with monitoring. A copy of the document was obtained by **The Cancer Letter**.

"By its nature, research fraud is a secret, complex and often subtle phenomenon whose presence is difficult to document even when it is suspected," the memorandum states.

"Indeed, even the full investigative powers of [Office of Research Integrity], concentrated with great intensity and expense on a single incident after the possibility of research fraud is raised, sometimes fail to produce clear answers to all relevant questions related to the incident.

"It is too much to expect, therefore, that a system of random audits or monitoring, no matter how diligently carried out, will necessarily uncover fraud that its perpetrators have carefully contrived to conceal.

"Even where a monitoring institution's audit procedures do not fully conform to NCI's requirements, moreover, it is not necessarily reasonable to assume that better auditing would have detected or prevented the misconduct in question.

"Although it will often be relatively easy for NCI to speculate after the fact that a better audit 'could have' detected the misconduct, fairness demands that liability for the misconduct of others be based on more than mere speculation.

"NCI's proposed provision, however, does not even require NCI to speculate as to whether better monitoring would have detected the misconduct in question.

"Under NCI's proposed provision there is no requirement that NCI establish any causal link between perceived monitoring deficiencies and the occurrence of research misconduct.

"To justify a repayment demand, it is sufficient for NCI to show: (a) scientific misconduct at a monitored institution, and (b) monitoring procedures that have not been 'carried out to the satisfaction of NCI.'

"Under this highly elastic standard, any monitoring institution where auditing procedures are not letter perfect in every respect, or not 'satisfactory' in NCI's subjective judgment, will be subjected to a repayment demand with respect to any research fraud that occurred on its 'watch,' whether or not it could have prevented the fraud by reasonable diligence.

"In effect, therefore, the proposed provision makes monitoring institution the insurers of the research purity of all institutions for which they are responsible."

Broder, Herberman Decline To Coauthor Reanalysis Of NSABP Data In NEJM

The New England Journal of Medicine last month requested that NCI Director Samuel Broder as well as NSABP interim leaders appear among the coauthors of papers reanalizing the results of the B-

06, B-13 and B-14 trials.

Responding to the request, Herberman wrote that he and Broder had no interest in becoming coauthors of the papers.

The reanalysis of two of the three trials is expected to be submitted by Oct. 1.

In an Aug. 25 letter to Herberman, NEJM editor-in-chief Jerome Kassirer wrote that NCI Director Samuel Broder should be among the authors of the article. The letter also appears to assume that Herberman would be among the authors.

A copy of the letter was obtained by **The Cancer Letter**.

"Dr. Broder informed me last week that he is planning to turn over the results of the audit of B-06 and B-13 to the leadership of the NSABP, and as soon as those results are available, the reanalysis should be submitted to the New England Journal of Medicine for publication," Kassirer wrote.

The audit of the B-14 study, taken over by FDA, remains incomplete, which would mean the reanalysis of that study would be published separately, the letter said.

"The reanalysis should take into account all of the findings of the NCI audit, as well as findings of the ORI," Kassirer's letter continued. "The general format of the original reanalysis submitted by Dr. Fisher was satisfactory, but I ask you to summarize the results as briefly as possible.

"Ideally, the reanalysis should be co-authored by all of the original authors of both studies, but I appreciate that it might not be possible to include those no longer under the NSABP umbrella.

"Nonetheless, a major effort must be made to include nearly all the authors. In as much as the audit was performed under the aegis of the NCI, I hope that Dr. Broder would also be a co-author.

"The authors should be made to understand that the National Cancer Institute has the authority to make their participation a condition of their continued involvement in the NSABP, and I am told that the NCI is prepared to exercise this authority," Kassirer wrote.

Responding to Kassirer's letter, Herberman pledged to "provide the needed resources and support to facilitate" the reanalysis and to review the draft of the manuscript for accuracy and completeness prior to submission to NCI or the journal.

"However, neither Dr. Trump or I have any interest in becoming co-authors of this manuscript, and we believe it would be most appropriate to remain in the hands of the original authors," Herberman wrote in a letter dated Sept. 6. A copy of the letter was obtained by **The Cancer Letter**.

"Regarding the inclusion of the results of the recent audits, we certainly agree that this is an important component, and I have discussed this matter with Dr. Broder," Herberman wrote. "He has assured me that the results of the audits will be provided and we will make these immediately available to the authors for their inclusion in the manuscript.

"I also discussed with Dr. Broder the issue that you raised about inclusion [of] NCI personnel as possible coauthors, and he has indicated that he does not see any desirability for that," Herberman wrote.

"I Can't Permit Destruction Of NSABP," Fisher Writes To Group Members

"I can no longer sit idly by and watch as political maneuvering and media frenzy not only continue to discredit NSABP studies but, by innuendo, all clinical trials, particularly those related to breast cancer," Bernard Fisher wrote in a letter to the cooperative group investigators.

The letter, written in the defiant tone characteristic of Fisher's previous statements, represents the final distillation of the surgeon's account of the events that led to his downfall as chairman and principal investigator of the cooperative group.

The excerpted text of the letter follows:

I feel that what has taken place to discredit me can happen to any scientist who is engaged in clinical research, or, for that matter, to those in basic research as well.

Scientists must have the freedom to initiate, conduct, and publish research, as well as the right to due process when required. This is particularly important for those whose academic careers are in their infancy.

One such individual who has written to me has succinctly stated that the entire affair has, "...made me question whether an academic career is as virtuous as I once thought it was."

Most important, I can no longer permit further destruction of the NSABP, an organization that has been responsible for providing most of the advances in breast cancer treatment in this century.

I urge you to remember that these accusations against me have also been aimed at other NSABP headquarters personnel and they relate to the investigators who have participated so grandly over

the years in that they intimate that those who participate in clinical trials must be carefully "policed" since there is less than full trust in their integrity and their ability to do "the right thing."

I find this perception totally abhorrent.

Even more important for you, as many of you have learned from Dr. Peter Deckers, on July 20, the NSABP Executive Committee voted to join in the lawsuit against the Univ. of Pittsburgh so that the [university] be restrained from unlawful interference in the governance, projects, and independence of the NSABP.

The Executive Committee took this action in an attempt to remedy the damage that has already occurred to the goals and objectives of the NSABP; to rapidly implement the scientific mission of the NSABP; and to recognize the authority of the Executive Committee of the NSABP to appoint a chairperson.

Now permit me to comment about some of the issues that have been raised:

Falsifications at St. Luc Hospital: NSABP staff discovered the falsifications, and, within 24 hours after it was certain that they existed, the NCI was notified and the investigator, Dr. Roger Poisson, was suspended... The assertion that there was a delay in reporting such falsifications is untrue.

The Office of Scientific Integrity, which later became the Office of Research integrity, began a two-year investigation; during that time we were embargoed from discussing the matter.

With permission of the ORI, the Executive Committee was notified of the falsifications in February 1992. During the embargo, the NSABP Biostatistical Center performed multiple reanalyses of the data in all 22 protocols to which Dr. Poisson contributed patients.

All of the reanalyses demonstrated that removal of St. Luc patients failed to alter either the outcome or conclusions of the original findings. Most important, members of the NCI, NIH, and ORI were aware of the findings and agreed that no public health problem had occurred as a result of the falsifications.

Publication of Findings from Reanalyses: A decision had been made by NSABP headquarters staff to publish the results of our reanalyses in a peer-reviewed journal and to prepare a technical report containing those findings.

Because the results of the reanalyses confirmed our original findings, and because the NSABP, ORI, NIH, and NCI agreed that there was no public health problem, there did not appear to be any urgency to publish such a report.

In retrospect, in view of the reaction to the delay in publication, a reaction created by the media, we would have made a different judgment. It must be emphasized, however, that we did have a definite plan for presentation to the membership and for publication. That plan was presented to and accepted by the NCI.

It must also be emphasized that the NCI's purported "insistence" that we publish the paper is misleading, since reference to publication of the reanalyzed data is mentioned, in passing, in only two letters to us in which other matters were presented.

We assure you that any delay in publishing a paper presenting reanalyses of data was not a "cover-up," since there was absolutely nothing to hide. Moreover, if the NCI and ORI had perceived that such delay in publication was harmful, they had full authority to disregard our plan and "get their message out" to physicians and the public.

I can also assure you that, if the reanalyses had demonstrated that the results and conclusions of our previous studies had changed, you and everyone else would have been notified at once.

Publications with Data from St. Luc Included: We had no prior direct or indirect experience with fraudulent data, and we knew of no guidelines for handling such data.

Initially, because of the embargo, we could not discuss issues of data exclusion with scientific journals. During that time, NSABP Biostatistical Center staff had concluded that, for scientific and ethical reasons, the St. Luc data should not be excluded because of the strong justification for using the "intent-to-treat" principle when performing reanalyses.

That approach is a widely accepted and acclaimed biostatistical principle. Moreover, the exclusion of St. Luc patients from follow-up and analysis after they had been treated would have resulted both in failure to report toxicities or long-term adverse effects that had already occurred among patients and in failure to detect and report such events that might occur in the future.

Finally, we emphasize that there was absolutely no intent on our part to deceive by including data from St. Luc Hospital, and we can conceive of no reason for wanting to do so.

The decisions regarding what was done were part of an interactive process between NSABP

biostatisticians who provide to NSABP medical personnel data that they deem appropriate for publication.

Despite the strong conviction for using the intent-to-treat principle, we did comply-but did not agree-with the NCI's notification in January 1993 that data from St. Luc Hospital be excluded in papers reporting studies from which no data had been previously published.

For you to put into appropriate perspective the likelihood of the St. Luc findings affecting the results and conclusions of the NSABP studies, it is important for you to realize that a total of 1,511 of the 33,885 patients entered into 22 NSABP trials were from St. Luc Hospital and that 99 of the 1511 patient records were found by the ORI to include falsified data. Almost all falsifications related to eligibility criteria and occurred prior to randomization.

All patients existed, all were treated as stipulated by the protocol, they were followed, and their outcomes were recorded. Thus, the issue of whether all patients should be excluded, or included by the intent-to-treat principle, or whether only the falsified data should be removed remains an important consideration.

Most statisticians subscribe to the intent-to-treat principle; some, however, would advocate removal of only those patients with falsified data.

Reporting of Deaths from Endometrial Cancer: We have been accused of delaying reporting of deaths from endometrial cancer in breast cancer patients treated with tamoxifen.

I assure you that we reported the four deaths that we knew about as soon as we knew that they were due to endometrial cancer. Once again, we had no vested interest in the use of tamoxifen or in the conduct of the prevention trial, only insofar as to determine the truth about the worth of tamoxifen in the treatment and prevention of breast cancer.

It is slanderous to indicate otherwise. It is necessary for you to understand that this is a complex subject difficult for many to comprehend.

It is often hard to know with certainty that death in a breast cancer patient is caused by endometrial cancer.

When a death occurs in a woman who had breast cancer and who later developed an endometrial cancer, it is extremely difficult to be sure which cancer caused the death. It cannot be assumed that the death occurred as a result of the endometrial cancer.

The woman may have died of breast cancer. The important issue here is whether a woman who had breast cancer and received tamoxifen died with endometrial cancer or died of endometrial cancer. This is a very difficult call for physicians, pathologists, and oncologists to make.

As soon as we had information about a woman in protocol B-14 who had breast cancer, and who died, and were reasonably sure that she died of — and not with—endometrial cancer, we immediately reported this to the proper authorities, i.e., the drug manufacturer and the NCI.

Only by conducting ongoing medical review and re-review and by obtaining difficult-to-get information can one be sure which cancer caused the death.

Such medical "detective" work takes a long time. Some have viewed this meticulous effort to obtain precise information as a "delay" in determining and reporting a cause of death. Delay in obtaining information about deaths can occur because patients move, go to different hospitals, change physicians, miss follow-up examinations, or because families fail to notify physicians about a death.

These delayed responses can result in a delay in confirming the cause of death. Death certificates can be ambiguous or inaccurate and not readily obtainable. Autopsies are infrequently performed and often fail to aid in determining cause of death.

Frequently it is impossible to determine whether the extensive metastases that kill a patient arise from the initial breast cancer, from the subsequent endometrial cancer, or even from some other cancer, such as that of the lung or colon.

In summary, I can tell you that, once a death was shown conclusively to be from endometrial cancer in a patient receiving tamoxifen, the NSABP followed the reporting mechanisms that had been established. There is no substance to the accusation that the NSABP delayed in providing information about deaths from endometrial cancer in patients treated with tamoxifen.

Audit Procedures: There has been criticism about NSABP data auditing procedures.

I emphasize that, while there were some delays in submitting audit reports to the NCI and to some investigators, none of the problems with audits, to the best of our knowledge, affected the outcome of our studies; certainly, none of the problems were so severe as to justify the kind of action taken by the NCI and by the press.

All of the problems were readily "fixable" and

were being taken care of at the time the studies were suspended. According to the reviewers of our 1991 grant renewal application, our audit program was "exemplary."

During the fourth audit cycle, which comprised the years 1991-1993, all institutional audits scheduled were conducted and had biostatistical and medical reports generated.

The on-site part of the quality-assurance program was interrupted in April 1993 to permit us to implement and test in the prevention trial revised audit procedures in accordance with recommendations by the NCI. On-site audits in the treatment trials were to resume using the new system just at the time when the suspension occurred.

The new audit program had been thoroughly tested in the BCPT. and was found to be not only appropriate but capable of permitting more audits in a shorter period of time.

Consequently, the hiatus in the treatment trial audits did not preclude all institutions being audited in a three-year cycle. The new audit system, when implemented in the treatment trials, would permit a "catching-up." Even though on-site audits had been halted for treatment trials, source data material continued to be received and reviewed by headquarters' staff.

Thus, the quality-assurance program was continued during that interval.

In summary, there was some tardiness in submitting audit reports to the NCI. We do not deny that. This happened because of a variety of human circumstances related mainly to personnel who had retired or changed jobs.

It was also due, in part, to the relocation of the operations center office and to the massive increase in the number of women who entered our trials and in the number of data forms submitted within the last two years. (The number of patients being followed in NSABP studies increased from 25,000 in 1991 to 41,000 in 1993, and the number of data forms processed expanded from 225,000 in 1991 to 413,000 in 1993.)

Again I emphasize that the "serious" deficiencies of the audit program, as portrayed in the media, were readily correctable and did not affect the outcome of studies.

It is of interest to point out that, using the revised audit system that we were ready to implement in the treatment trials, the interim leadership of the NSABP declared that they had corrected the problem within six to eight weeks. We could probably have done this in less time!

St. Mary's Hospital. The accusation has been made that I was aware for six months of a data discrepancy found at St. Mary's Hospital (Montreal) in September 1993 and I did not notify the NCI.

This was given as reason for my being removed from the chair of NSABP. The statement that I "sat on" such information is not true. I was not notified of this problem until March 22, 1994, at which time I immediately notified a university lawyer. It is my understanding that, to this date, the issue as to whether the data irregularity is a falsification remains unresolved.

Lack of Cooperation: The accusation that the NSABP headquarters failed to "cooperate" relative to reporting or to responding to requests is nonsense.

For 25 years, the NSABP's relationship with officials of the NCI was based upon mutual respect and cooperation. That relationship was apparent in frequent memos, letters, meetings, and phone conversations until the day it was terminated by the NCI. Until then, from our perspective, our relationship was continuously interactive, productive, and mutually supportive.

Comments: I remain troubled by the abrupt suspension of all NSABP clinical trials in progress and by the postponement in the development and start of new studies. These events could affect the lives of thousands of breast cancer patients in years to come. I believe that this was a dangerous and ill-advised action for which there must be accountability.

The integrity of the NSABP and its 37-year dedication to using the scientific method for clinical problem solving in the treatment and prevention of breast and colorectal cancer is being destroyed.

"Much Progress Made To Stabilize Group," Herberman Writes To NSABP Members

In a letter to NSABP members, the cooperative group's interim chairman Ronald Herberman wrote that while some of the group's "inherited" problems remain to be resolved, "much progress has already been made to stabilize the group, correct deficiencies, restore public and patient confidence, and most importantly, get the NSABP back on track and operating again."

"While the road to full operations is rather bumpy, we are taking the steps necessary to reach our research objectives," Herberman wrote in the Aug. 11 letter.

"Understandably, there is considerable support

and loyalty for Dr. Bernard Fisher, and as you know there are certain legal proceedings related to his role in the NSABP. While these will be resolved in an appropriate way, we all need to continue to work closely together and keep in mind our central objective to help women and men with breast or bowel cancer," Herberman wrote.

The letter offered an overview of the state of the group:

—Last June, NCI gave NSABP approval to begin accruals to treatment trials that were open. The only open trials are R-03 and B-23, which were accruing slowly prior to the group's problems. "Changes have been made in the R-03 protocol, to relax entry constraints, and in the near future we expect to obtain approval of these changes and transmit the revised protocol to participating institutions," he wrote.

—As of Aug. 11, NCI had granted permission to resume accrual at 202 sites. There are 140 sites that still need to meet the Institute's criteria, which include satisfactory completion of a clinical trials audit within three years, and completion of necessary notification of patients on tamoxifen trials.

—NSABP headquarters is seeking volunteers to help conduct audits. "One major impediment to resumption of accrual continues to be a lack of satisfactory, recent audits for many institutions. Unfortunately, there is a very extensive backlog of audits. Until now, the burden has been handled by staff from NSABP headquarters, buttressed by coordinators and faculty from PCI. To address this serious limitation more aggressively, we have developed a plan to get considerably more assistance with audits, both from non-NSABP auditors and from many NSABP investigators and clinical study associates."

—"In April, NCI considered transferring responsibility for [the Breast Cancer Prevention Trial] to another cooperative group. Because we convinced the NCI that the NSABP will have the ability to perform this important study with a very high level of quality assurance, the BCPT will resume under the auspices of the NSABP."

—Draft revisions to the BCPT protocol have been submitted to Endpoint Review, Safety Monitoring, and Advisory Committee; the Steering Committee; the Gynecology Committee, as well as to NCI.

—As of Aug. 11, 183 sites have been certified as having adequate consents for the BCPT and are permitted to submit risk assessment forms. Altogether, 119 sites remain to be certified.

—Investigators are planning a study of some current and prospective BCPT participants to develop strategies to overcome barriers to participation or compliance.

—NCI has approved the revised B-26 protocol, and the revisions were sent to treatment sites. Until more NSABP protocols are approved investigators could contribute to intergroup protocols for breast and colorectal cancer. An intergroup protocol for adjuvant treatment of colon cancer is expected to be distributed to sites shortly.

— "Currently under development are protocols involving a somatostatin analog, Taxol or Taxotere, and Navelbine. These protocols now require final statistical input. We have made arrangements to obtain increased biostatistical manpower and to expedite this critical step."

—Development of the prototype computer system is proceeding at Univ. of Pittsburgh and Jewish General Hospital, Montreal, with the assistance of the Westinghouse Science and Technology Center and the Carnegie Group Inc. The pilot phase should be completed by the end of September and after evaluation, the system would be extended as quickly as possible to other NSABP institutions.

PCI Receives NCI Breast Cancer Research Funds

PCI investigators were awarded two NCI grants to support breast cancer research programs.

—One of the grants, for $620,000, to be paid out over two years, will support the development of a Breast Cancer Research Program that will emphasize the study of interactions of genetic, endocrine and environmental factors that affect the growth and other characteristics of breast cancer tissue.

Much of the work is designed to pinpoint variations in breast cancer cells that correlate with prognosis in the clinic. The BCRP also emphasizes biobehavioral research that includes studies of how various interventions, including exercise, biofeedback and counseling, affect breast cancer survivors.

—Another grant, for $90,000 will fund the purchase of a multi-mode microscope and computer software. The microscope will be bought from Biological Detection Systems, a Pittsburgh-based biotechnology company.

"We are very impressed with the leadership of the Pittsburgh Cancer Institute," NCI Director Samuel Broder said in a statement. "The people of Western Pennsylvania have one of the finest programs in breast cancer in the nation right at their doorstep."