THE CANCER LETTER

Vol. 17 No. 27
July 5, 1991

Price $205 Per Year US, Canada.
$230 Per Year Elsewhere

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

NCI Develops Plan For Specialized Centers, But Funding $67.5M Program Depends On New $$

NCI, long frustrated by the lack of financial growth in the Cancer Centers Program, has planned a $67.5 million program that it hopes will attract "new money" from Congress to support institutions that would specialize in research on breast, prostate, and lung cancer. The "Specialized Program of Research Excellence," or SPORE, as it is called, was given concept approval by the Div. of Cancer Biology, Diagnosis &

(Continued to page 2)

In Brief

Frei Retires As Dana-Farber Director, Successor Is David Livingston; Benacerraf Plans Departure

EMIL (TOM) FREI has stepped down as director and physician in chief of Dana-Farber Cancer Institute, a position he held for 19 years. Frei will become physician in chief emeritus and will continue as chief of cancer pharmacology. **David Livingston** has been selected as the institute's new director and physician in chief. The change took place July 1. Frei, a legendary figure in clinical oncology, developed the first successful chemotherapy regimen for treatment of leukemia, at NCI in collaboration with Emil (Jay) Freireich. Frei came to NCI in 1955 and left for M.D. Anderson Cancer Center 10 years later. He went to Dana-Farber in 1972. Frei discussed his work and the evolution of chemotherapy at an NIH symposium last year. He and Freireich were presented the first NIH Distinguished Alumni Award (**The Cancer Letter,** Sept. 14, 1990), and shared the Albert Lasker Award in 1972 and the General Motors Research Foundation's Charles Kettering Prize in 1983. Frei was twice chairman of the Cancer & Leukemia Group B, and chairman of the Southwest Oncology Group. Livingson, a professor of medicine at Harvard Medical School, is an expert in the study of genes that regulate cell growth. He will continue as chief of the institute's Div. of Neoplastic Disease Mechanisms. . . . **BARUJ BENACERRAF,** president of Dana-Farber Cancer Institute, reportedly will leave the post he has held since 1980 this month. The institute's board is expected to consider the selection of **Christopher Walsh** as its new president. Walsh is chairman of the biological chemistry and molecular pharmacology department at Harvard Medical School. . . . **STANLEY ORDER,** professor and chairman of the radiation oncology department at Johns Hopkins Univ. Medical School, will leave on Aug. 1 to take the position of director of the Institute for Systemic Radiation Therapy in the radiation oncology department of Cooper Hospital/University Medical Center, Robert Wood Johnson Medical School at Camden.

NCI Plans Specialized Cancer Centers Contingent On New $ In Centers Line

(Continued from page 1)

Centers Board of Scientific Counselors last week. The board committed $22.5 million in maximum total costs for the first year of the program to fund nine centers ($2.5 million each per year), or a total of $67.5 million for three years. The centers would recompete for five year grants.

Funding for the program is planned under the P50 grant mechanism, which has not been used by NCI in at least the past 20 years.

NCI Director Samuel Broder told cancer center directors attending a recent NCI workshop in Baltimore that the program would be funded with "new money added to the cancer centers line." The funds would not come out of the research project grant pool or from the existing cancer centers program.

The three diseases were selected because they are the most common, Broder said. For breast cancer, there is a need to translate molecular research to the area of treatment; new approaches are needed for prostate cancer; and for lung cancer, "We need innovative responses other than smoking cessation," Broder said.

Broder briefly discussed the new program at a House hearing on the NCI budget earlier this year (**The Cancer Letter,** April 19). The House Appropriations Committee mentioned the program in its report on the FY 1992 Labor, HHS, Education appropriations bill.

Cancer centers with existing support grants (P30s) would be eligible to apply, but they will not be allowed to duplicate the shared resources funded by their P30.

THE CANCER LETTER

Editor: **Kirsten Boyd Goldberg**
Associate Editor: **Lisa M. O'Rourke**
Contributing Editor: Jerry D. Boyd

Editorial/Subscriptions Office
PO Box 15189, Washington, DC 20003
Tel: (202) 543-7665 Fax: (202) 543-6879

Subscription rate $205 per year North America, $230 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter and AIDS Update.

Following are the concept statements; language that was duplicated in each concept has been edited:

Specialized Program of Research Excellence in Breast Cancer. Three awards at maximum total cost per year of $2.5 million per individual SPORE or total annual cost of $7.5 million. Initial funding for three years ($22.5 million total). Renewal for five years subject to successful recompetition.

The objective of this initiative is to establish three Specialized Programs of Research Excellence (SPORE) in Breast Cancer at institutions that will make a strong institutional commitment to the organization and conduct of these programs. Each SPORE must be dedicated to research on prevention, diagnosis and treatment of human breast cancer and the translation of basic research finding into more applied, innovative research settings involving patients and populations; the SPORE could be used in rehabilitation and quality of life research. Each SPORE must provide career development opportunities for new, independent investigators who wish to pursue active research careers in translational breast cancer research; develop human breast cancer tissue resources that will benefit translational research; develop extended collaborations in critical areas of research need with laboratory scientists and physician scientists within the institution and in other institutions; and participate with other SPORES on an annual basis to share information, assess scientific progress in the field and identify new research opportunities that may have an impact in reducing breast cancer incidence and mortality. It is expected that each SPORE will support a mix of basic and clinical research. The SPORE mechanism is not intended to support basic research to the exclusion of clinical or applied research.

Breast cancer is the most common cancer among U.S. females, is the highest incidence cancer in the U.S., and is the second leading cause of cancer death among women. Since 1980, breast cancer incidence has increased dramatically in both pre- and postmenopausal women at a rate approximately 2 percent per year. During this time, the scientific information base for breast cancer has expanded significantly; however, application of this scientific base to clinical and preventive activities has not been commensurate with this expansion. There is thus a need to encourage translational research that would require interdependence between basic and clinical investigators in both the planning and implementation of research and would emphasize clinical application of basic research findings with patients and populations. There exists significant scientific and clinical expertise in breast cancer in NCI designated cancer centers and other institutions throughout the country. A concerted effort to mobilize this expertise through SPOREs can accelerate advances in the management and ultimately prevention of this disease. The recent NCI sponsored workshop "Emerging Concepts and Strategies in Breast Cancer" indicated a number of areas where such interdisciplinary applications could prove fruitful. Experts from many disciplines addressed growth factors, oncogenes and suppressor genes, new technologies relevant to the field and resistance to drugs and hormones. Interdisciplinary groups considered the science presented at the workshop with specific focus on its relevance for incidence, diagnosis, treatment and prevention.

Special requirements of SPORES: The institutions selected for award of SPOREs must assemble a critical mass of basic and clinical scientists dedicated to the translation of basic findings into more applied, innovative research settings involving patients and populations with the ultimate objective of reducing incidence and mortality to the disease. Each SPORE must include the following elements:

1. A strong **institutional commitment.** Institutions receiving

these awards must incorporate the SPORE into its institutional priorities. It must provide a plan which addresses how the institutional commitment will be maintained and sustained and how it will maintain accountability for promoting scientific progress. A SPORE application can originate from an institution with or without an existing P30 core grant. If a P30 already exists, lines of authority should be clearly indicated such that the SPORE does not interfere with the P30 chain of authority.

2. A qualified **program leader**. A leader must be selected as the principal investigator who can oversee, conduct planning activities and provide direction to SPORE with a translational research emphasis.

3. A substantive breast cancer **patient population.** Each SPORE must be a recognized leader in the treatment of breast cancer and have access to a patient population that can participate in and benefit from the innovative applied clinical and population research activities of the SPORE.

4. **Research projects.** Research projects must be headed by independent investigators and oriented toward translational research activities using human materials and human subjects which address new, innovative possibilities in breast cancer research.

5. **Specialized resources.** Each SPORE must have a dedicated activity to human breast cancer tissue collection. This resource must benefit the specific research activities of the SPORE as well as the research activities of other scientists within and outside of the parent institutions who are concentrating on translational research issues. A plan must be proposed for prioritizing distribution of tissues to SPORE scientists and others. The development of other resources of special significance to translational breast cancer research is also encouraged.

If the SPORE is part of an NCI designated cancer center, the development of resources should not duplicate resources already provided by the center on an existing cancer center support grant (P30). The applicant should show that the P50 will effectively and synergistically interact with an existing P30 where this is applicable.

6. **Career development.** The SPORE must demonstrate an increased commitment to career development. A minimum of $100,000 in direct costs per year must be dedicated to the salaries and research activities of new, independent investigators who wish to pursue translational research careers on breast cancer and who would be expected to leave the SPORE with the necessary research experience to develop independent breast cancer research programs within or outside of the parent institution.

7. **Developmental research funds.** Each SPORE must allocate a significant proportion of its budget and efforts to the conduct of pilot projects that continually explore new, innovative ideas in collaboration with scientists within the institution and with other institutions. It is important that SPOREs use developmental funds to stimulate projects that take maximum advantage of new research opportunities.

8. **Annual meeting** of SPORE. Breast cancer SPOREs will be expected to participate in an annual meeting with the Organ Systems Coordinating Branch of NCI to share data, assess progress, identify new research opportunities, and establishing priorities relative to the most effective approaches for reducing incidence and mortality.

If a SPORE is located in an institution that is already an NCI designated cancer center, the program director of the SPORE must be a senior leader in the cancer center and the SPORE must be a major programmatic element. However, there must be a separate and distinctive commitment of the institution to breast cancer research.

The P50 grant mechanism differs from program project grants in that they are usually developed in response to an announcement of the programmatic needs of an institute or division and subsequently receive attention from its staff and are more complex and flexibly in terms of the activities that can be funded.

Recognizing that the initial funding period may be too short for substantive scientific accomplishments, the recompetition would evaluate progress toward accomplishment rather than accomplishment itself. This would include, for example, progress toward planning, developing, and implementing new research programs, progress toward developing the careers of new scientists, progress toward procuring and distributing tissue specimens, progress toward developing substantive collaborative interactions, etc.

Specialized Program of Research Excellence in prostate cancer. Three awards. Each SPORE must conduct state of the art research in biology, prevention, diagnosis, and treatment of prostate cancer; rehabilitation and quality of life research may also be pursued. The SPORE must foster basic/clinical research collaborations; develop resources specialized for prostate cancer research; provide career development opportunities for new, independent investigators who wish to pursue basic and/or clinical research careers in prostate cancer research; and participate with other SPORES on an annual basis in sharing information and assessing scientific progress. In addition to promoting interdisciplinary research on prostate cancer within the institution, each SPORE will be encouraged to develop extended collaborations and interactions with scientists and clinicians in other institutions.

Prostate cancer is now the most common cancer in U.S. males and the second leading cause of cancer death in men. Mortality due to prostate cancer is two fold higher in U.S. blacks than U.S. whites. At present, this disease costs more than $1 billion annually, requires a quarter of a million hospitalizations and results in more than 30,000 deaths. Prostate cancer has lagged far behind research in other major forms of cancer and there has been a lack of new investigators entering the field. In part, this has been due to lack of accessibility to human prostate tissues and lack of suitable in vitro and in vivo models. Effective reduction of incidence and mortality to prostate cancer will require a special effort to expand the scientific information base. This was reinforced at the recent "NCI Roundtable on Prostate Cancer" ("Cancer Research," 51: 2498, 1991) which defined areas of research that could advance our understanding and management of prostate cancer. Studies of molecular analysis and mechanisms of growth control of the prostate cell are critically needed. The development of androgen independence in the transformation to malignancy is poorly understood. The capability of identifying which latent prostate cancers will become clinically aggressive does not exist. There is no effective screening for prostate cancer and the risk factors for this disease are unknown.

SPORES must address the weaknesses in the scientific information base and provide focal points for sustaining and maintaining state of the art research that will contribute to improved detection, diagnosis, treatment and prevention of prostate cancer. SPORES will not only be expected to conduct a wide spectrum of research activities, but also to contribute significantly to the development of specialized research resources, career development of new investigators, the development of improved research model systems and the expansion of the research base through collaborative research with scientists and clinicians in other institutions locally and nationwide.

Special requirements of SPORES: see above.

1. **Institutional commitment.** See 1 above.

2. **Program leader.** See 2 above.

3. **Research projects.** See 4 above.

4. **Specialized resources.** Each SPORE must dedicate itself to the development of model systems for research and to the implementation of human cancer tissue bank for research. A prioritized plan to make model systems and tissues available to investigators within and outside the SPORE should be proposed. The development of other resources of special significance to prostate cancer research is also encouraged.

5. **Career development.** See 6 above.

6. **Developmental research funds.** See 7 above, adding: Each SPORE would also be encouraged to conduct innovative pilot projects within the SPORE that might have a more immediate and significant impact on improving the diagnosis, detection, treatment, and prevention of prostate cancer.

7. **Annual sharing of data/priority setting.** SPORES in prostate cancer will be expected to participate in annual workshops with the Organ Systems Coordinating Branch of NCI in sharing data, assessing progress, and identifying new research opportunities.

Specialized Program of Research Excellence in Lung Cancer. Three awards. Each SPORE must conduct state of the art research in prevention, diagnosis, and treatment, and could be used in rehabilitation and quality of life research. The SPORE must foster basic/clinical research collaborations; provide career development for new, independent investigators who wish to pursue basic and/or clinical research careers in lung cancer research; and participate with other lung SPOREs on an annual basis in sharing information and assessing scientific progress. In addition to promoting interdisciplinary research on lung cancer within the institution, each SPORE will be encouraged to develop extended collaborations and interactions with scientists and clinicians in other institutions.

Lung cancer, by far, is the leading cause of cancer deaths in the U.S., with an estimated 143,000 deaths in 1991. However, the incidence rate for lung cancer has begun to decline in men from a high in 1984. In women, the rate continues to increase. Since 1987, more women have died yearly of lung cancer than of breast cancer. The scientific information base for lung cancer continues to expand significantly; however, its application to the clinical and preventive activities is languid and is incommensurate with research advances. Thus, there is a need to encourage translational research that would require interdependence between basic and clinical investigators in the planning and implementation of research. An emphasis in translational research would intensify the application of basic research findings to clinical patients and to populations. There exists significant research and clinical expertise in lung cancer NCI designated cancer centers and in other institutions throughout the country. A concerted effort to mobilize this expertise through SPOREs could accelerate advances in the management and prevention of this disease. The recent NCI workshop "Investigational Strategies for Detection and Intervention in Early Lung Cancer" indicated areas where such interdisciplinary applications could prove fruitful. Experts from many disciplines addressed growth factors, oncogenes and suppressor genes, and new technologies relevant to the field.

Special requirements of SPORES: see above. 1, 2, 3, 5, 6, and 7 are same as prostate cancer concept above.

4. **Specialized resources.** Each SPORE must dedicate itself to the development of model systems for research and to the implementation of human cancer tissue bank for research. A prioritized plan to make model systems and tissues available to investigators within and outside of the SPORE should be proposed. The development of other resources of special significance to lung cancer research is also encouraged.

Andrew Chiarodo, chief of the Organ Systems Coordinating Branch, which will direct the SPORE program, said NCI hopes to issue RFAs this fall and make awards in the fall of 1992.

DCBDC Board member Vittorio Defendi questioned Chiarodo about the cost of the program. Chiarodo said the cost was based on the cost of program project grants, plus the requirement for developmental funds and $100,000 in career awards. "Where will the money come from?" Defendi asked.

"All I know is where it's not coming from--RPGs and centers. It is my understanding that Dr. Broder is going to seek new money for this," Chiarodo said.

DCBDC Director Alan Rabson noted that the House budget markup (**The Cancer Letter,** June 28) gives NCI an FY92 increase of $116 million over FY91, and that NIH Director Bernadine Healy also will receive an increase in discretionary funds. "That's $116 million we didn't have in '91," Rabson said. The Institute also could start the program by funding only one or two, rather than three, SPOREs per site, he said.

Other board members questioned the requirement for expenditure of $100,000 per year for career development. "The intention is to seed the field, so to speak, with new investigators," Chiarodo said. Board member Albert Owens, who made the motion to approve the concepts, spoke against specifying an amount for career awards. "I wouldn't try to micromanage or tie the hands of the investigators," he said. "In our institution [Johns Hopkins Oncology Center], one could argue for more than $200,000 in the beginning. I just don't want to see a pronouncement for a floor or a ceiling."

The board voted on the three SPORE concepts as a group and unanimously approved them. After the vote, board member Ross McIntyre said he wanted to add a "postscript" to the discussion, in regard to the lung cancer SPORE concept: "The way to deal with lung cancer is to deal with why people smoke. Research on nicotine addiction may be as useful as research on lung cancer treatment," McIntyre said.

Bristol-Myers Holds Taxol Briefings, Outlines Timetable For Development

Opposition from environmentalists over expanded harvesting of the Pacific yew tree failed to materialize at meetings held last week specifically to explain to them the recently signed cooperative agreements between Bristol-Myers Squibb and the two federal agencies who control most of the forests involved.

Representatives of those agencies, Bristol-Myers Squibb, and NCI held briefings for environmentalists

and other members of the public in Washington DC and in Portland, OR.

Under the agreements, BMS will attempt to harvest enough yew tree bark to provide sufficient taxol for clinical trials sponsored by the company and NCI. An estimated 750,000 pounds of bark, taken from about 38,000 trees, will be needed to supply enough taxol for 12,000 patients. NCI hopes that will be enough to supply the current and planned clinical trials plus some for compassionate distribution to some patients not enrolled in those trials.

The U.S. Forest Service and the Bureau of Land Management control most of the federally owned land in the Pacific Northwest areas where the yew is most frequently found. The agreements permit BMS to carry out the harvest under carefully controlled conditions which the agencies said will protect the forests and the wildlife there and will guard against depletion of the yew. The agencies estimated there are about 30 million yew trees on their property in Oregon and Washington, and another 13 million on state and private lands.

The yew is also found in other Pacific Northwest states, in Northern California, and British Columbia. BMS is exploring prospects of extending its harvest into those areas.

BMS has subcontracted with Hauser Northwest Inc., a subsidiary of Hauser Chemical Research Inc., to collect the bark through local independent workers and processors. Hauser also will process the bark for extracting and purifying taxol. Currently, the Hauser process is the only large scale operation capable of doing that job that meets the good manufacturing practice standards of FDA.

Representatives of Resources for the Future, Environmental Defense Fund, and the U.S. Forestry Assn. who were at the meeting in Washington asked only perfunctory questions about environmental impact statements. Government representatives said there would be no harvesting in areas where that would be deemed harmful to the environment and to wildlife such as the spotted owl. In any event, the process of selectively harvesting trees would not normally destroy nor adversely modify the spotted owl's critical habitat, BMS said.

At the Portland meeting, local interests and environmentalists had similar responses to the agreements. However, Oregon Congressman Ron Wyden indicated he will call a hearing on the issues involved, scheduled for July 29.

Z.P. Horovitz, vice president for licensing of Bristol-Myers Squibb, described the effort the company is planning under the cooperative research and development agreement (CRADA) with NCI. He also laid out a timetable for development of other taxol sources which calls for ending reliance on harvesting of wild trees by 1998, and possibly sooner.

The taxol molecule is exceedingly complicated, making total synthesis very difficult. Nevertheless, BMS hopes that total synthesis through commercially feasible methods can be achieved in six or seven years. In the meantime, NCI and the company are pursuing other methods:

Biomass--This refers to the renewable parts of the yew, such as leaves and twigs. "Ideally these would be used to extract taxol, but their yield probably would not be sufficient as a major source of the compound," a company position paper says. "Bristol-Myers Squibb is negotiating with a number of research laboratories and universities to support research on enhancing the process of extraction and identifying other yew species from which taxol or related compounds could be extracted."

Semi and total synthesis--"In the future, taxol might be produced by extracting an intermediate, or incomplete, taxol molecule from the leaves of readily available members of the yew family such as ornamental hedge plans. When a laboratory made side chain is added to the intermediate, taxol results. This advanced technology is being actively pursued in Bristol-Myers Squibb's new laboratories, and by research laboratories with which the company has agreements, including Florida State Univ. The research necessary to devise a wholly synthetic form of taxol is being negotiated between Bristol-Myers Squibb and a number of major university research facilities."

Plant cell culture--"Bristol-Myers Squibb scientists are working to produce taxol from the cells of fast growing parts of the yew tree, such as its roots and leaves. Small samples of tissue from several species of yew are grown in cultures of hormones and growth factors. These cell explants, which may be grown by a number of methods including a fermentation type process, may produce taxol under well defined laboratory conditions. Much more research and engineering will be necessary to obtain taxol in large quantities from plant cell culture. Agreements for additional cell culture work are being negotiated with researchers at several universities and various industrial concerns."

Plantations--"Bristol-Myers Squibb is currently investigating the feasibility of developing yew plantations which would be stocked with a variety of yew species. In this feasibility study, yews yielding the highest content of taxol would be identified as well as the best conditions for growth and taxol production.

The high producers would be densely planted and grown under controlled conditions. Their harvest is expected to provide large quantities of the natural compound or a useful intermediate."

The time table Horovitz described calls for development of biomass and semisynthesis products in two to five years; plantation farming and plant cell culture in four to eight years; and total synthesis in six or more years.

Saul Schepartz, special assistant to Director Michael Grever of NCI's Developmental Therapeutics Program, said that 61 proposals had been received in response to an RFA for research and development of alternative sources. Nine to 12 will be funded, he said.

Taxol is the first of a new class of antitumor compounds with a novel mechanism of action distinct from other cytotoxic agents. It is an antimicrotubule agent, blocking the microtubule proteins essential in cell growth and development. Investigators are excited about its potential use in combination with other drugs with different mechanisms of action. Clinical trials of some of those combinations have begun.

Taxol has consistently obtained 30 to 35 percent responses in advanced refractory ovarian cancer and 50 percent responses in advanced refractory breast cancer. If those rates continue, and if similar responses are seen in some of the trials against other tumors that are under way, the demand for taxol will be several times that of the 12,000 patients who will receive it this year.

To stop illegal harvesting of yew bark from trees on government land, the Forest Service is offering a reward of $10,000 for information leading to the apprehension of thieves.

Grace Monaco, Washington attorney and a founder of the Candlelighters, suggested that stolen yew bark might turn up in the "quackery market." With the publicity taxol is getting as a potentially powerful anticancer agent, so called health food stores could peddle it as "taxol tea," Monaco said.

Schepartz noted that 60 pounds of bark is required for extraction of enough taxol for one treatment. Any effort to make a health food claim for it would bring reaction from FDA, he said.

A small California company said last week that it had developed a cell tissue culture technique that should enable it to produce taxol in commercial quantities within two years.

ESCAgenetics Corp., based in San Carlos, announced that development at a meeting of the International Biotechnology Partnering Conference. The company said that expression of taxol in tissue culture, using the firm's proprietary "phytoproduction tissue culture technology," was confirmed by independent mass spectroscopic analysis by researchers at the Univ. of California (Berkeley).

Raymond Moshy, president and chief executive officer of ESCAgenetics, said that the expression of taxol was obtained less than nine months after the firm started its taxol program.

A company spokesman confirmed to **The Cancer Letter** that ESCAgenetics has discussed with Bristol-Myers Squibb the prospects of a collaborative effort. "We need a pharmaceutical house with the resources for marketing anticancer agents," he said. He added that ESCAgenetics could scale up to produce large quantities of taxol, but did not rule out licensing the process to others if that becomes necessary.

ESCAgenetics was founded in 1987 and is engaged in producing new food products, new seeds, and botanically derived pharmaceuticals. The company employs 50 persons and grossed $4.4 million in 1990, $2.5 million so far this year. It is a public company, traded on the American Stock Exchange (ESN).

Proposed New CIS Regions Draw Mostly Support, Some Objections

The proposed distribution of Cancer Information Service offices as drawn up by NCI CIS and Office of Cancer Communications staff appeared acceptable to directors of most of the current offices but drew opposition from some of those who will be pitted against each other in the new recompetition.

CIS provides free phone consultation for those who call for information on cancer (1-800-4-CANCER). More than 500,000 calls were received last year.

CIS representatives met with NCI staff in Bethesda last month to take a look at the proposal for 18 regional offices, which will replace the present system of 22 offices plus the national office (**The Cancer Letter**, May 17).

Kate Duffy, chief of the Cancer Information Service Section in OCC, said that the regions were drawn up without considering the existing offices. The primary consideration is to spread the workload more evenly by funding a CIS entity in each region, with the regions grouped in similar population sizes. NCI hopes that this will increase the level of service to some areas and help reduce the busy signal rate (now 58%), along with the addition of more phone lines. Geographical factors and the cancer resources available also were taken into consideration, Duffy said. "To some extent, the boundaries were arbitrary," she added.

Duffy, OCC Director Paul Van Nevel, and Reports & Inquiries Branch Chief Eleanor Nealon insisted that a final decision on the new regional boundaries had not been made and that suggestions from those at the meeting would be considered in arriving at the final makeup of the regions. They previously had invited written comments, with a June 28 deadline.

An RFP will be issued, possibly in August, which will delineate the final regional boundaries. NCI hopes that the new contracts will be for a 10 year period, longer than nearly all contracts NIH has ever awarded. Whether NIH and the department will go along remains to be seen.

One of the 18 regional offices will be selected as the "super office" to handle calls after 10 p.m. in each of the regions.

The offices also will have a certain amount of outreach responsibility, most likely in working with cancer centers in their regions. The scope of those efforts, and NCI's expectations, were questioned at the meeting. NCI staff was asked to clarify that issue in the RFP. Here's how NCI drew up the regions (some changes are almost certain):

Region 1--Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut. Region 2--New York City and Long Island. Region 3--The rest of New York state and Western Pennsylvania. Region 4--Eastern Pennsylvania, Delaware, New Jersey. Region 5--Maryland, District of Columbia, Virginia, West Virginia. Region 6--North Carolina, South Carolina, Georgia. Region 7--Florida, Puerto Rico. Region 8--Alabama, Mississippi, Louisiana. Region 9--Kentucky, Tennessee, Arkansas. Region 10--Ohio, Michigan. Region 11--Minnesota, South Dakota, North Dakota, Iowa, Wisconsin. Region 12--Illinois, Indiana. Region 13--Missouri, Kansas, Nebraska, Oklahoma. Region 14--Texas. Region 15--Alaska, Washington, Idaho, Montana, Oregon. Region 16--Wyoming, Colorado, New Mexico, Nevada, Utah, Arizona. Region 17--Hawaii, Northern California. Region 18--Southern California.

Among the objections and suggestions for altering boundaries were:

--New York City CIS representatives would like to add seven counties north of the city and sections of northern and central New Jersey.

--CIS directors in Philadelphia and Pittsburgh would like to have Pennsylvania in one region.

--Representatives of Washington Hospital Center, who are planning to compete for one of the offices, requested that the DC metropolitan area, including areas of Maryland and Virginia, be designated as a region.

--The Maryland CIS, at Johns Hopkins, and the West Virginia CIS are two of the strongest current offices, and NCI regretted putting them into the same region. Hopkins suggested dropping West Virginia; the latter would not mind Maryland and DC going somewhere else but argued that its close partnership with Virginia should be continued. West Virginia also suggested that Tennessee, Kentucky, and Ohio could be added to that group.

--The Louisiana CIS asked that Arkansas be added to its region because of the current relationships, and suggested that Alabama would be more logically placed in another group.

--Ohio and Michigan representatives agreed the two states should not be in the same region. Ohio suggested it would be better off with Indiana and/or West Virginia and that Michigan could be grouped with Wisconsin. Michigan agreed that it "shares 50 miles of state line" with Ohio "and not much else," but suggested it would be better off with Indiana than Wisconsin.

--Jane Henney, Univ. of Kansas, suggested that Missouri, Kansas, Nebraska, and Iowa, which make up a Public Health Service region, be grouped as a CIS region.

--Rocky Mountain CIS representatives suggested realigning states in regions 15 and 16, grouping Alaska, Washington, and Oregon in one and splitting the others into two other regions. NCI staff did not rule out the addition of a region.

--Hawaii representatives made a strong pitch for an office exclusively for that state, citing the time differential with the mainland, slower mail service, travel costs, and various cultural differences.

--North California CIS staff suggested that Northern Nevada could be added to its region because of referral patterns.

--Southern California CIS asked that Santa Barbara, San Louis Obispo, and Kern counties, designated in the proposal for Region 17, be given to Region 18 because of referral patterns and other ties. Southern California would accept Las Vegas for those reasons.

Henney and Helene Brown, UCLA, expressed concern about the requirements for outreach activities. "The number of FTEs [proposed for each office] is small for that purpose," Henney said. "I'm not sure it can be done well. This needs a significant investment, perhaps with matching or joint funding."

"It would be an extremely difficult matter, in a population of 15 to 19 million, for one or two people to make a dent in outreach," Brown said.

Gilbert Fridell, Kentucky, said that "you have to make more explicit the function you expect of CIS. It

seems that the direction you are taking is to pick up some of the activities [supported by] the Div. of Cancer Prevention & Control."

House Still Sees Deficiencies In NIH Financial Management

The House Appropriations Committee has directed NIH to remove caps on the size of grant awards and discontinue across the board cuts on grants, in its report on the FY 1992 Labor, HHS, Education appropriations bill.

The bill was passed by the full House last week; the Senate Appropriations Committee is scheduled to consider its bill on July 11. The House bill contains a last-minute amendment, sponsored by Rep. John Porter (R-IL), that would block enforcement of a regulation that prohibits federally funded abortion clinics from counseling women on abortion. President Bush has threatened to veto the bill.

The House approved an NIH appropriation of $8.824 billion, $50 million above the President's request and $548 million above the FY91 operating level, for a 6.6 percent increase. The committee expects that amount to fund 6,000 new research project grants and a total of 22,248 competing and noncompeting grants.

The committee gave "the highest priority" to women's health issues, which received more than one third of the increases over the President's budget. That amount included funding for additional staff for the NIH Office of Women's Health to initiate or expand research in AIDS, reproductive health, links between oral contraceptives and breast cancer, and osteoporosis.

The growth in women's health programs will come at the expense of other areas. The committee said NIH expects to save $55 million by implementing indirect cost reforms. The human genome project was limited to 7 percent growth, and the committee decided to defer modernization of the NIH Clinical Center. The committee added $195 million to the NIH FY92 budget over the President's request, and made cuts of $145.6 million, resulting in a net increase of $50 million.

The committee said it is "pleased" that NIH has mostly implemented the financial management plan outlined in last year's committee report, and said it was encouraged that the President's request is "the largest increase ever presented by a president for NIH." The plan directed NIH to limit the average cost of grants, projected at $224,000 in 1992, to rise at the rate of the biomedical research price index, and to control the average cost through "specific cost management strategies."

However, in its FY92 report, the committee said that researchers testified that many Institutes have imposed artificial caps on the size of awards and continue to use across the board percentage cuts. "If downward negotiation is to be eliminated, NIH will have to play a more aggressive role in analyzing the reasons for cost increases, in setting guidelines and policies about appropriate funding levels for certain types of expenditures, and in reviewing the budgets submitted by potential grantees.

The committee also criticized the shift in NIH use of "award rates" to "success rates." Congress had noted that 95 percent of NIH grant applications were being approved, though only 40 to 50 percent were considered "scientifically strong." The committee said the success rate method "indicates the proportion of all grants submitted, good or poor, which were, or could be, funded." That method "does not tell either Congress or NIH what portion of the applications which are deserving of support can actually be funded," the report says.

In an extremely rare move, the committee appropriated less for two institutes than the President requested. The National Heart, Lung & Blood Institute would get $1.2 billion, a decrease of $7.5 million under the President's budget. That amount is $75.4 million over the FY91 appropriation. The National Institute of Allergy & Infectious Diseases would receive $972.8 million, a decrease of $3.88 million from the President's request, but $65.5 million over FY91.

For the trans-NIH Women's Health Study, the committee proposed an increase of $25 million over the President's request for the NIH Office of the Director to support the first year of the trial.

In AIDS, the committee proposed a total of $1.9 billion for research, education and other activities conducted by NIH and the Centers for Disease Control. The committee called for greater research efforts on women and HIV infection, especially research on the "new chemical and physical barriers to HIV infections that might address these concerns."

Funding by Institute in the House bill: NCI, $1.83 billion; NHLBI, $1.2 billion; Dental Research, $161 million; Diabetes, Digestive & Kidney Diseases, $667 million; Neurological Disorders & Stroke, $583 million; Allergy & Infectious Diseases, $972.8 million; General Medical Sciences, $820 million; Child Health & Human Development, $524 million; Eye Institute, $272 million; Environmental Health Sciences, $254.9 million; Aging, $362.5 million; Arthritis & Musculoskeletal & Skin Diseases, $204.9 million; Deafness & Other Communication Disorders, $114 million; Center for Research Resources, $309 million; Nursing Research, $43 million; Human Genome Research, $93 million; Fogarty International Center, $19.9 million; National Library of Medicine, $99.5 million; Office of the Director, $149 million; buildings & facilities, $108 million.