THE CANCER LETTER

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NIH Alternative Medicine Office Under Fire For Proposed RFA In Homeopathy, Acupuncture

Following a confidential discussion of a $1 million concept for a Request for Applications on acupuncture and homeopathy earlier this month, the NIH Office of Alternative Medicine has found itself under fire from two directions: the advocates of unconventional cancer treatment and the advocates of mainstream science.

The former say the proposal to use half of the OAM budget to fund 25 studies in homeopathy and acupuncture would de-emphasize the study of unconventional cancer therapy. The latter say the RFA concept,

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In Brief

NCCR Presents Gold Medal To Sen. Harkin; DCT Recruits Okunieff For Radiation Oncology

SEN. TOM HARKIN (D-IA) was presented a gold medal Congressional Award by the National Coalition for Cancer Research at its board meeting last week. NCCR President **Robert Day** thanked Harkin for his leadership last year to increase spending on cancer research, "which will enable critical priorities and gaps in our National Cancer Program to be addressed as it enters the next decade, keeping the vision of hope alive for millions of Americans." The award commemorates the 20th anniversary of the National Cancer Act of 1971. Said Harkin: "I'm deeply committed to furthering the control of cancer through the continuing emphasis on research and making those results widely known to improve the lives of the 8 million cancer survivors in this country, and to emphasize the very great importance of cancer prevention in the overall attack on this disease." . . . . **PAUL OKUNIEFF**, Massachusetts General Hospital, has accepted the position of chief of NCI's intramural Radiation Oncology Branch, Div. of Cancer Treatment Director **Bruce Chabner** said. The post has been filled by acting chief **James Mitchell** following the departure of **Eli Glatstein** one year ago. . . . **DEE WEST** was named executive director of the Northern California Cancer Center by the center's board of trustees. West has been serving as deputy director of the center since 1991 and as acting director since last July. . . . **RAYMOND WARRELL**, Memorial Sloan-Kettering Cancer Center, received the Public Health Service Award for Exceptional Achievement in Orphan Products Development this week in recognition of his critical role in the development of two orphan products, gallium nitrate and all-trans retinoic acid. He was nominated by **Marvin Jaffe**, president of the R.W. Johnson Pharmaceutical Research Institute.

NIH Office Criticized Over RFA On Acupuncture, Homeopathy

(Continued from page 1)

as well as the manner in which the new office conducts business, deviate substantially from the NIH practice.

"Acupuncture and homeopathy are certainly important modalities, but they have little direct preventative or curative impact on cancer or other major killers," Ralph Moss, a proponent of unconventional cancer treatment, wrote to OAM after taking part in the Feb. 4 telephone conference discussing the RFA concept.

A copy of his memo was obtained by **The Cancer Letter.**

"What they are doing is certainly not what we know to be the usual practice," said Helene Brown, member of the Board of Scientific Counselors of the NCI Div. of Prevention & Control and a member of the American Cancer Society's Committee on Questionable Methods of Cancer Management.

"I am just flabbergasted at a group who are acting on behalf of the government, not being fully chartered yet, yet talking about the use of government funds for an RFA," Brown said.

The ACS committee was scheduled to meet with OAM Director Joseph Jacobs later this week.

Critics on both sides say the office appears to be forging too far ahead before NIH formally approves its charter and appoints a permanent board of advisors. For now, the office is consulting with a group drawn from the 125 participants of a conference it convened last September.

The ad hoc panel with which the OAM staff discussed the RFA concept consisted of the 19 "co-chairs" of committees of participants of the September meeting. Since that meeting was organized by an NIH contractor, its participants were not required to file conflict of interest statements.

In an interview with **The Cancer Letter**, Jacobs said that he, too, was eagerly awaiting the chartering of an advisory committee, which is mandated by the legislation authorizing the office. However, the chartering has taken longer than he anticipated, Jacobs said. "We didn't realize the bureaucratic process we had to go through," he said. "We had to have the approval from [NIH Director Bernadine] Healy. We had to submit a charter, a cover memo; there had to be a publication in 'The Federal Register.'"

The charter and the list of advisors are expected to be approved in a matter of weeks, Jacobs said.

"What we do here is going to be above board, consistent with the NIH rules," Jacobs said. "If people don't like it, either they have to live with it, or I will leave."

According to Jacobs, the proposed RFA is consistent with the mission of his office.

"If this office were to focus on alternative cancer therapy, we would have been put in the NCI, and we are in the office of the Director of the NIH," he said. As it is, "cancer accounts for 20 percent of our activity and takes up 80 percent of my time.

"We will focus on the palliation, not the cures, in cancer," Jacobs said. "It's clear that there are a lot of patients that may feel better as a result of alternative therapies. I think we need to get away from certain rhetoric about the cures and ask, 'How is the patient benefited by this?'"

In the past, Jacobs and NIH deputy director Jay Moskowitz have gone to great lengths to retain the support of the proponents of unconventional cancer therapy, including former Rep. Berkley Bedell, whose lobbying had convinced his fellow Iowa Democrat, Sen. Tom Harkin, to appropriate funds for the office.

"Not the Usual Practice"

"What I see is two separate tracks," Brown said to **The Cancer Letter.** "There is a code of conduct for the Office of Alternative Medicine and a code of conduct for everyone else. As an NCI advisor, I had to fill out conflict of interest papers an inch thick."

The issues expected to be brought up at the ACS meeting with Jacobs included:

▶Indications that Jacobs and Moskowitz held at least one private meeting with the proponents of unconventional treatments. "I don't suppose there is anything wrong with it, if what they are doing is talking about the weather or their concerns as individuals," Brown said. "There is nothing wrong,

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unless what follows gets fashioned to be less than good science."

▶Questions about the wisdom of funding research in acupuncture and homeopathy.

Some at ACS as well as the self-described "quack-busters" say they would like to see NIH fund studies of palliative treatments, including those provided by acupuncturists and homeopaths.

However, one critic, Barrie Cassileth, a member of the OAM ad hoc panel of advisors and consulting professor of community and family medicine at Duke Univ., contends that an RFA for the study of homeopathy and acupuncture would deviate from established procedures at NIH.

"RFAs generally address scientific problems or issues, not methods," Cassileth wrote to OAM in a memo a copy of which was obtained by **The Cancer Letter.** "In line with that traditional route, OAM would issue an RFA to study specified diseases, symptoms, etc. It would not request applications that apply particular methods.

"There is good reason for this tradition, and none that I see to ignore it," wrote Cassileth. It would be more appropriate for the committee, as opposed to the OAM staff, to select the research topics and that peer review procedures would need to be in place before an RFA could be issued, Cassileth wrote.

"We are putting out an RFA. If Ralph Moss doesn't like it, I am sorry," Jacobs said to **The Cancer Letter.** He declined to discuss Cassileth's criticism of the RFA. "I don't want to discuss the merits of an RFA in the press that hasn't been released yet," Jacobs said.

The RFA Concept

In a Jan. 26 memo to the ad hoc panel, OAM's Deputy Director Daniel Eskinazi wrote that acupuncture and homeopathy were chosen as subjects for an RFA because these practices are "among the most commonly used in alternative medicine."

"They are also areas in which substantial research has been conducted, and some promising evidence of efficacy has been accumulating...

"The office would also be interested in proposals dealing with unconventional, multifaceted cancer and AIDS treatments that include acupuncture and homeopathy."

According to the memo, the RFA would have the following features:

▶"Invitation of all practitioners and/or researchers interested in alternative medicine to apply (provided that they are affiliated with an eligible institution prior to funding, rather than prior to applying);

▶"Postponement of the requirement for approval for human subjects research until after review (but prior to funding);

▶"Feedback from reviewers to improve proposal;

▶"Help and monitoring of research progress by Office staff."

In an interview with **The Cancer Letter,** Jacobs said the majority of those consulted by his office agreed with the RFA concept.

The Separate Meeting

Following the discussion of the RFA concept at a telephone conference, Moss fired off a memo to Eskinazi.

In the memo, Moss questioned the staff decision to proceed with the RFA prior to appointment of a chartered advisory panel.

"I have heard that this telephone panel is 'representative' of the full panel," Moss wrote. "But, as you know, at least one prominent member of the advisory process, Berkley Bedell, was not on the list of telephone participants. Doesn't his voice count in making crucial decisions of this office?"

Bedell is not among the 19 "co-chairs" consulted by OAM.

The memo also referred to a separate meeting involving Jacobs and Moskowitz and the proponents of unconventional cancer treatment:

"My conception of the office, which Frank Wiewel, Gar Hildenbrand, Berkley Bedell and I agreed on with Joe Jacobs and Jay Moskowitz on Jan. 7-9, is that the focus of OAM should be patient outcomes research (field investigations) of currently existing treatments." Wiewel is the president of People Against Cancer, an advocacy group, and Hildenbrand is executive director of Gerson Institute, a California-based alternative care provider that operates a clinic in Mexico.

Asked by **The Cancer Letter** to describe the meeting, Moss said, "My memory is failing me, because I am having a hard time separating all the meetings we've had in Washington."

"There have been no secret agreements. To the best of my recollection, immediately after that meeting there was a meeting of the entire group, where the same concerns were discussed."

Wiewel, too, said he could not recall whether the meeting took place.

"I am assuming [Moss] is referring to one of the meetings at which we discussed the issues we would like to address," Wiewel said. "We've had many meetings with Jay, and they were just meetings between concerned citizens and a public official."

Jacobs said no private meeting took place in January, saying that there were at least 10 people in

the room during the workshop held on the date mentioned by Moss. However, one such meeting took place a month earlier, Jacobs said.

"They wanted to have a meeting with me and Jay," Jacobs said. "It was Jay's desire to meet with the entire group present, but in the end we thought it would be better to meet with them."

Asked to describe what happened at the meeting, Jacobs said, "they were complaining and making recommendations about program direction, and we basically explained some things to them that they seemed to understand."

In Congress

NCCR To Seek $380 Million Increase For NCI In FY94 As Step To Bypass

The National Coalition for Cancer Research, which includes the major specialty groups and several key patient lobbies, plans to seek an FY1994 appropriation $380 million above the FY1993 budget of $1.991 billion for NCI.

"The coalition has embarked on a three-year campaign to get the NCI funding up to the bypass level, and the $380 million increase is but the first step in that campaign," said Terry Lierman, president of Capitol Associates Inc., the coalition's lobbying group.

The NCI FY1994 bypass budget is $3.2 billion.

"It's important to note that the NCCR budget is a balanced research program which includes prevention, early detection, basic research, clinical trials, cancer centers, training and rehabilitation and survivorship programs," Lierman said to **The Cancer Letter.** "The coalition feels very strongly that the whole cancer program can only survive and thrive by adequately addressing each piece of the picture."

The $380 million increase would be distributed in the following manner:

--$60 million for cancer prevention and control, above the current budget of $105 million,

--$155 million for basic research, above the current budget estimate of $960 million,

--$56 million for clinical research, above the current budget estimate of more than $300 million,

--$37 million for the cancer centers, above the current budget of $144 million,

--$5 million for rehabilitation and survivorship, above the current estimate of $15 million,

--$33 million for construction, above the current budget of $8 million,

--$34 million for research training and education, above the current budget of $60 million.

NCI's Revised Drug Screen Tests, Selects New Agents Against Cancer

NCI's Developmental Therapeutics Program is screening 400 compounds a week for activity against human tumor cell lines, and late last year incorporated eight human breast cancer cell lines into the drug screen.

NCI revised the drug screening process in 1990 to test drugs against about 60 human cell lines for seven types of cancer, rather than against in vivo animal tumor models. The old system relied heavily on mouse leukemias, and even after the introduction of animal solid tumors in the late 1970s and early 1980s, the program required new compounds to show activity against the mouse leukemias before further testing.

In the past two years, the program has screened 25,000 agents, referred 1,617 for further testing, identified 434 of those as high priority, and has made 80 agents available for preliminary clinical research, according to DTP Director Michael Grever.

Last year, the program filed Investigational New Drug applications with the Food and Drug Administration for seven new agents. The program plans to file INDs for 10 to 15 new agents this year, Grever said to the Div. of Cancer Treatment Board of Scientific Counselors this week.

The latest development in the program is the incorporation of human breast cancer cell lines into the screen. In December 1992, the program tested 1,166 agents against the breast cancer cell lines, referred 97 for further testing, and narrowed to 36 agents to be evaluated.

The program also is testing agents against a prostate cancer assay developed by Stanford Univ. researcher Donna Peehl. DTP sent Peehl 1,083 compounds for testing, and selected 75 for evaluation in vivo.

Some of the new agents expected to be available for clinical trials are: bryostatin-1, temozolomide, the camptothecin derivative CPT-11, rhizoxin, and clomesone. Later this year, the program is planning IND submissions for bizelesin, penclomedine, O^6-benzylguanine, glendanamycin derivative (showing strong activity against prostate cancer), and a brefeldin prodrug.

A year and a half ago, the program also began to look for agents active against AIDS-related lymphoma; 528 compounds have been screened by in vitro assay, and 48 were tested in a SCID mouse model. Some agents will be ready to take into the clinic soon, Grever said.

Agents identified in the new screening process also

are tested against the old P388 murine leukemia system to provide solid data on whether the new system is more effective, Grever told the board.

The program is trying to reduce the number of animals needed for in vivo testing. DTP's Melinda Hollingshead developed a method that enables testing of three agents simultaneously in one mouse by implantation under the skin of three hollow fibers containing tumors.

Grever said the new screening process seems to be cost effective. Compared to the old system, the new process requires smaller quantities of agents, conserves the number of animals needed, and agents can be assessed in two weeks time.

Over the past four years, the contract budget for the program has decreased, and in FY93, the Developmental Therapeutics Program's budget will drop from the FY92 amount of $137.5 million to $129 million, a 6 percent cut.

Recompetition Of Contracts Approved

The board this week gave concept approval to recompetition of four large contracts that support the screening program, together worth $2.475 million a year. Following are the concept statements:

Development and manufacture of oral dosage forms. Recompetition of contracts held by Applied Analytical Industries Inc. and Univ. of Iowa. Estimated $500,000 per year, five years (25% AIDS funding, 75% cancer).

This contract effort provides pharmaceutical development and production of oral dosage forms for AIDS and cancer drugs for clinical trials, as well as oral formulations for animal toxicology and pharmacology studies. The effort originally consisted of three contracts, which provided latitude for specific formulation development and the ability to perform multiple tasks simultaneously and quickly.

The number of organizations with the specialized equipment as well as expertise to handle cytotoxic and AIDS compounds is extremely limited. Special gowning, personal air supply apparatus, clean-up, and disposal procedures need to be in place and validated. Special rooms equipped with negative air pressure plenums, gowning facilities, showering facilities, and air handling/filtration systems are required.

There are several oral dosage forms of cancer and AIDS drugs currently on the NCI inventory including tablets, capsules, oral powders, and oral solutions. This project furnishes the essential services, personnel, materials, equipment, and facilities to develop and manufacture oral drug dosage forms suitable for human use. These dosage forms include tablets, soft and hard gelatin capsules, oral liquids, and oral powders. The contractors are also responsible for inventory and testing of all raw materials as well as finished dosage forms produced in accordance with the FDA's GMP. The contractors are responsible for labeling, packaging, storing, and shipping these products in accordance with the FDA's GMP.

Several important new drugs have been produced under the contracts. Notable among these is a candidate entering clinical trials in this country. Temozolomide (NSC-362856) has undergone Phase I and limited Phase II clinical trials in Europe and has shown dramatic responses in patients with glioma. The European operation for the production of the capsules is very small and has not been able to keep up with the demand. The capsules made in Europe were hand filled. We anticipated large trials in this country, and contractors have developed temozolomide formulations suitable for machine filling. Using formulations, our contractors have manufactured several batches of 10,000 capsules each of two different capsule strengths. We anticipate producing batches of up to 50,000 capsules to meet the demand for this drug.

A newly developed antimetastatic agent, CAI (NSC-609974), has undergone pharmacokinetic evaluation in Phase I trials. It is anticipated that the trials will be expanded. The current formulation is an oral solution in PEG 400. To meet the future demand for this drug, contractors are producing liquid-filled soft gelatin capsules in several strengths. These formulations will mask the taste and allow for patient convenience in chronic therapy.

2'-B-fluoro-ddA, a clinical candidate currently under development for AIDS treatment, shows activity similar to that of ddI and is also orally active. While ddI is unstable in stomach acid, 2'-B-fluoro-ddA is totally resistant to stomach acid. The major disadvantage of both the buffered tablets and the oral powder formulation of ddI is the large amount of buffers required to minimize drug hydrolysis in the stomach. Common side effects with both ddI formulations are GI irritations and diarrhea. Since AIDS patients are already predisposed to diarrhea, this problem is significant. 2'-B-fluoro-ddA tablets of equal activity and more reliable oral bioavailability would also be much smaller and, therefore, more appealing to pediatric patients. There is a great deal of enthusiasm for this drug in the NCI clinical community involved in treating pediatric patients. Small batches of 2'-B-fluoro-ddA have been developed and manufactured by contractors for pharmacology and toxicology studies.

The contractors produced coated and uncoated tablets of KNI-272, a protease inhibitor (NSC 651714), for use in toxicology and pharmacology studies. The oral bioavailability of this novel agent has placed it at the forefront of our anti-HIV drug development program. Iowa also completed a formulation of 0.5 mg ddC tablets (NSC-606170). These contracts also produce buffered formulations of ddI for clinical AIDS trials. HMBA, uridine, hydrazine sulfate and matching placebo, semustine, and other orally active cancer drugs would be manufactured under these contracts also.

Penclomedine (NSC-338720) has been under development for several years as an injectable emulsion. This promising agent has shown reproducible preclinical activity in breast cancer. Recent pharmacology studies indicate that the drug is also orally active. These contractors will, therefore, develop and produce oral formulations of this new agent, which is quickly approaching Phase I clinical trials.

Future Plans: NCI plans to recompete these contracts as a combined effort for both AIDS and cancer oral dosage form production. This is the only effort under which the NCI has the capacity to develop and produce oral AIDS and cancer drugs under GMP conditions and with proper attention to the safety of personnel performing the tasks. Historically, NCI developed only a few drugs for oral use in cancer therapy. This approach has dramatically changed and oral bioavailability studies are now added as part of preclinical pharmacological studies. As a result, several potential candidates for oral dosage form production are currently in the pipeline.

These include Penclomedine, an agent with potential activity in breast cancer; 9-aminocamptothecin, an agent active against colon cancer in preclinical models, and a new flavinoid with in vivo activity against prostate cell lines.

Maintenance of a rodent production center. Recompetition of a contract held by Taconic Farms. Estimated $270,000 per year, three years (100% cancer funding).

To meet the need for athymic nude mice, the Biological Testing Branch has used a rodent production center contract at a level of 2,000 cages maintained under maximum barrier conditions capable of producing such mice free of pathogenic contamination. Immune-deprived mice are also produced at other supplier facilities including Simonsen Laboratories (California), Charles River Laboratories (Raleigh, NC), and the Frederick Cancer Research and Development Center (FCRDC, Frederick, MD). Total production of athymic mice is approximately 4,500 per week at an annualized value of slightly over $3 million.

In addition to internal DCT usage, animals from this production center are delivered to intramural investigators (NCI/NIH) and to grantees throughout the USA. DCT receives reimbursement from all outside users. The overall reimbursement support provides funding to the extent that DCT funding is needed to support DCT usage only. Approximately 1,200 nude mice are shipped weekly from this 2,000-cage contract.

Preparation of radiolabeled materials. Recompetition of contracts held by Research Triangle Institute. Estimated $450,000 per year for cancer, $450,000 per year for AIDS, five years.

These contracts are devoted to the preparation of new radiolabeled synthetics and natural products needed by various programs of DCT. The compounds scheduled for synthesis are not available from commercial sources and involve a variety of chemical structures. All new radiolabeled syntheses are initiated upon DN IIA approval. In rare instances, syntheses of compounds have been initiated prior to Decision Network review upon approval by the Associate Director. In select cases, resyntheses are performed to meet the needs of grantees, extramural and intramural researchers. These contracts also provide for the procurement of a very small number of radiolabeled materials or their intermediates that are available from commercial sources.

To date, 12 compounds labeled with ^{3}H and nine compounds labeled with ^{14}C in amounts ranging from 6 mCi to 300 mCi have been synthesized under these contracts. Five of these were prepared under the AIDS contract and 16 under the cancer contract. Some recent examples of radiolabeled compounds are: penclomidine; dolastatin-10; taxol; Uniroyal Jr.; and pyrazoloacridine. A total of 145 shipments have been made to intramural and extramural researchers. The majority of these have been recipients of research grants.

New synthesis assignments include: ^{14}C-Cosalane, ^{14}C-combretastatin-A_4 monophosphate disodium salt, subunit A of crotoxin, the ^{14}C-Hoechst flavone, michellamine B, and calanolide A. In the planning stage are Halomon, UCN-01, and geldanamycin.

Previously, two separate contracts were utilized, one for cancer and one for AIDS. To increase the flexibility of project assignments, it is proposed to combine the resources into a generic workscope, possibly with multiple awards.

Resynthesis of compounds for screening. Recompetition of contracts held by Research Triangle Institute, Starks Associates, and New Mexico State Univ. Estimated $805,000 per year, five years (50% cancer, 50% AIDS).

The Drug Synthesis and Chemistry Branch is engaged in a worldwide effort to acquire selected novel synthetic compounds and fully characterized natural products for evaluation as anticancer and anti-AIDS agents. These compounds are generally supplied in milligram amounts for testing in the Developmental Therapeutics Program's in vitro antitumor and anti-AIDS screens. Once a compound is found to be active in a screen, additional quantities may be required for in vitro confirmation or secondary in vivo evaluation. Larger amounts of compounds are not always available from the original source for a variety of reasons.

A variety of organic and inorganic compounds of varying complexities are synthesized, including heterocycles, carbocycles, nucleosides, organometallics, and peptides. About 150 compounds per year may be assigned to the contractors for resynthesis. The scale of resynthesis ranges fron 100 mg to 5 grams. Three contracts will be awarded.

[Reports on concept reviews by the boards of scientific counselors of NCI divisions provide readers with advance notice of the Institute's spending plans. Proposals need not be submitted until notices of Requests for Proposals, Requests for Applications, or Program Announcements are published in ***The Cancer Letter.****]*

NCI News Roundup

DCT Plans Cuts In Several Programs To Fund Research In Four Cancers

NCI's Div. of Cancer Treatment will decrease funding for drug development, clinical trials and exceptional grant funding in fiscal 1993 to increase spending for research in breast, ovarian, prostate and cervical cancer, and NCI official said this week.

"There is no doubt that the new Administration, and the country at large, has made a number of new issues matters of high priority, and we cancer researchers, as beneficiaries of government support, will have to address their concerns," DCT Director Bruce Chabner said to the DCT Board of Scientific Counselors this week.

"The appropriations language for this fiscal year requires that we significantly increase our spending for breast cancer, ovarian cancer, prostate cancer, and cervical cancer," Chabner said. "This will have to be done at the expense of other areas of research, since the overall increase in [NCI's] appropriation is only $33 million, while the earmarked increases for these four areas of research alone total approximately $90 million."

For NCI overall, money earmarked for breast cancer research will be used for expanding research project grants in imaging, prevention research, vaccine research, more funding for breast cancer Special Programs of Research Excellence (SPOREs); and, in DCT, drug screening has begun using breast cancer cell lines, Chabner said. In the Cancer Therapy Evaluation Program, treatment research in breast cancer will receive greater emphasis.

The redirection also will be important for grants that fall below the payline and compete with others for "exception" funding. The NCI Executive Committee will be more amenable to funding grants that address the four critical cancer sites, Chabner said.

DCT By Mechanism

DCT will spend $293.4 million on cancer research

project grants, a 4 percent drop from last year; and $4.3 million on AIDS research project grants, a 7.3 percent increase.

Funding for the clinical cooperative groups will fall from $77 million to $74.5 million in FY93, a 3.3 percent drop.

Research and development contracts for cancer will be cut by more than 20 percent, for an estimated $37.3 million in FY93. Contracts for AIDS will be cut by 4.2 percent, for $22.8 million. The overall decrease is $10 million. These amounts include funding for Small Business Innovation Research contracts.

DCT intramural research will get an estimated $99.8 million total, a 1.1 percent cut overall. Within that, however, funding for cancer intramural research will fall 4.6 percent, for an estimated total of $67.9 million, while funding for intramural AIDS research will increase by 7 percent to $31.9 million.

DCT's estimated FY93 budget is $532.4 million, compared to nearly $535 million last year.

DCT By Program

Chabner cut the budget of his own office by 11.5 percent, or $724,000, as part of the redirection. The savings comes from a decrease in research and development contracts funded by the office.

Funding for the Radiation Research Program will increase from $108 million to $114 million, about 5.6 percent.

The Biological Response Modifiers Program will get $56.7 million, a .6 percent cut from last year.

The Cancer Therapy Evaluation Program will receive $172 million, a 2.3 percent increase from last year's amount of $168 million.

Funding for the Clinical Oncology Program will fall by nearly 4 percent, from $53 million to $51 million.

The Developmental Therapeutics Program will take a 6.2 percent cut, from $137 million last year to $129 million this year.

DCT will spend $1.97 million on drugs provided by contract, down by 33 percent, and funding for SBIR contracts will remain at $950 million.

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Grants funding for FY93: NCI's Div. of Cancer Treatment expects to fund only 12 percent of new R01 grant applications and 29 percent of renewal applications this year, Div. Director Bruce Chabner told the division's Board of Scientific Counselors this week.

DCT funded 25 percent of new R01s and 47 percent of renewal R01s last year.

In contrast, the funding rate for new and renewal P01s will improve, from 31 percent for new applications last year to 36 percent, and from 56 percent for renewal applications last year to 66 percent this year.

DCT expects to fund 113 new and competing R01s this year, compared to 189 last year. Twenty-two P01s will be funded, compared to 33 last year. The division also expects to fund:

--2 Outstanding Investigator Grants; 17 were funded last year (NCI is phasing out the program).

--89 Small Business Innovation Research grants, versus 112 last year.

--9 RFAs, 8 MERIT awards, 24 FIRST awards, 50 cooperative agreements, and 24 conference grants.

FY92 was a good year to submit a new SBIR grant application to DCT, since 90 percent were funded. This year, DCT expects to fund 52 percent of new SBIR grants submitted, and 60 percent of renewals. This program is required by law to provide 1.25 percent of the Institute's extramural research budget to small companies (see story in this month's **Cancer Economics.**)

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Struggles over the shrinking dollar were evident at the DCT board meeting this week.

▶Board member Philip Greenberg said he was concerned about DCT's spending on grants solicited by Requests for Applications.

NCI policy is to spend no more than 8 percent of funds for competing grant applications on grants solicited by RFAs, Chabner said. "I've expressed concern that we are relying heavily on RFAs," he told the board this week. "On the other hand, we are getting Congressional demands to fund research in certain areas and one way of doing that is to encourage research through RFAs."

▶Board member Clara Bloomfield said money for breast cancer research should be added to the budgets for the cooperative groups, some of which are being funded at 59 percent of the peer review recommended level. "Clearly, this is breast cancer related research, peer reviewed, investigator-initiated," she said.

"We've made that point with the Institute," Cancer Therapy Evaluation Program Director Michael Friedman replied.

▶Board member Lester Peters commented on the "rollercoaster payline" over the past three years for new and renewal R01s: 18 percent in FY91, 23 percent in FY92, and now about 14 percent in FY93.

"It's almost a lottery when your grant comes up for renewal; it's not fair," Peters said. "What can you do to have a consistent payline year to year?"

"Unfortunately, there is nothing we can do," since the amount of money available for R01s is determined by Congress, Chabner said. "I don't see any cure for the problem."

NCI Advisory Group, Other Cancer Meetings For March, April, Future

NIH Recombinant DNA Advisory Committee--March 1-2, NIH Bldg. 31 Conference Rm 6, open 8:30 a.m.

National Meeting for State Cancer Pain Initiatives--March 4-7, Charleston, SC. Contact Sarah Aslakson, phone 608/263-2856.

Stem Cell Factor & Related Cytokines in Bone Marrow Congenital Dysplasias--March 8-9, Cattolica, Italy. Contact Marina Minzoni, Studio ER Congressi, Via Riva Reno 47, 40122 Bologna, Italy, phone 39-51-235-293.

International Conference on the Adjuvant Therapy of Cancer--March 10-13, 1993, Tucson, AZ. Contact Nancy Rzewuski, Arizona Cancer Center, phone 602/626-2276, fax 602/626-2284.

International Yew Resources Conference--March 12-13, Berkeley, CA. Contact Univ. of California at Berkeley Forest Products Laboratory, phone 510/231-9456.

Society of Toxicology Annual Meeting--March 14-18, New Orleans, LA. Contact Society of Toxicology, phone 202/371-1090.

Mechanisms of Action of Retinoids, Vitamin D, and Steroid Hormones--March 15-20, Banff, Alberta, Canada. Contact American Assn. for Cancer Research, phone 215/440-9300.

Assn. of Community Cancer Centers National Meeting--March 17-20, Washington, DC. Contact ACCC, phone 301/984-9496.

Monoclonal Antibody Immunoconjugates for Cancer--March 18-20, San Diego, CA. Contact Professional Conference Management, phone 619/565-9921.

Society for Surgical Oncology--March 18-21, Los Angeles, CA. Contact SSO, phone 708/359-4605.

Cancer Center Support Grant Review Committee--March 25-26, Chevy Chase, MD. Holiday Inn. Open 7-8 p.m. March 25..

NCI Div. of Cancer Etiology Board of Scientific Counselors--March 25-26, NIH Bldg. 31 Conf. Rm 6. Open 1 p.m.-recess March 25 and 9 a.m.-adjournment March 26.

Diagnosis & Treatment of Neoplastic Disorders, Medical, Surgical & Radiotherapeutic Aspects--April 1-2, Baltimore, MD. Contact Johns Hopkins Office of Continuing Education, phone 410/955-2959.

European Assn. for Cancer Research Biennial Meeting--April 4-7, Brussels, Belgium. Contact Prof. M. Roberfroid, tel. 32-2-764-73-69; fax 32-10-45-40-99.

Reconstructive Surgery & Microsurgery for Cancer Patients--April 12-16, Keystone, CO. Contact Conference Services, M.D. Anderson Cancer Center, phone 713/792-2222.

Anticarcinogenesis & Radiation Protection--April 18-23, 1993, Baltimore, MD. Contact Dr. J. Corn, phone 410/955-9334.

Loss of Genomic Integrity in Neoplasia--April 21-23, Chapel Hill, NC. Contact Vickie McNeil, UNC Lineberger Comprehensive Cancer Center, phone 919/966-3036.

Mechanisms of Carcinogenesis--April 23, Memphis, TN. Contact Dr. James Hamner, Univ. of Tennessee, phone 901/528-6354.

American Radium Society Annual Meeting--April 24-28, Aruba. Contact Office of the Secretariat, phone 215/574-3179.

American Roentgen Ray Society Annual Meeting--April 25-30, San Francisco, CA. Contact ARRS, phone 703/648-8992.

Breast Cancer Research: Current Issues, Future Directions--April 25-28, Atlanta, GA. Contact Continuing Medical Education, Emory Univ. School of Medicine, fax 404/727-5667.

International Assn. for Breast Cancer Research--April 25-28, Alberta, Canada. Contact Continuing Medical Education, Univ. of Calgary, phone 403/220-7240, fax 403/270-2330.

International Cancer Chemoprevention Conference--April 28-30, 1993, Berlin, Germany. Contact Dr. Waun Ki Hong, M.D. Anderson Cancer Center, 1515 Holcombe Blvd Box 080, Houston, TX 77030, phone 713/792-6363.

RFAs Available

RFA CA-93-19

Title: **Cooperative breast cancer tissue registry**

Letter of Intent Receipt Date: March 15

Application Receipt Date: April 29

The Cancer Diagnosis Branch of NCI's Div. of Cancer Biology, Diagnosis and Centers invites applications for cooperative agreements from organizations (individual institutions or consortia) capable of and interested in participating in a network of organizations working together as the Cooperative Breast Cancer Tissue Registry.

The purpose of the Registry is to stimulate cooperative efforts to identify and improve access to archival breast cancer tissue and other appropriate breast specimens and associated clinical and outcome data for the evaluation of predictive and diagnostic markers. The goal is to improve access to breast cancer tissue specimens for the evaluation of predictive markers.

The Registry will provide resources to enable participating organizations to inventory their tissue collections and to establish a database for existing associated clinical and outcome data. It will also provide resources to identify, obtain and provide tissues and patient data to investigators for predictive marker studies as approved by a Research Evaluation and Decision Panel.

While initial focus of the Registry is on improving access to formalin-fixed, paraffin-embedded archival breast cancer tissue, applicants can also propose inclusion of archival frozen breast tissue collections where appropriate.

The Registry is not intended to directly support marker assay research, but only to assist investigators funded through other sources with access to tissue and related clinical and outcome data.

Applicant organizations must be located in the U.S., Canada, or Mexico. Support will be through the cooperative agreement (U01). The anticipated average amount of direct cost awards will be $100,000. NCI anticipates making six to ten awards for project periods of up to four years and anticipates that a total of $1,500,000 will be set aside for the initial year's funding.

Awardees must agree to provide tissue for high priority research studies as identified by a committee selected by Registry members, the Research Evaluation and Decision Panel (REDP) and agree to participate as part of a coordinating committee. An assumption of the registry concept is that the establishment of a large cooperative breast cancer tissue resource will make available the specimens necessary for large scale validation studies. It is anticipated that decisions about which research studies will be provided with tissue will be made by a REDP selected by Registry participants according to criteria established by the Registry Coordinating Committee. The Registry REDP, may also act as a "catalyst" bringing together groups with tissues and groups with promising reagents that are ready for validation testing. NCI will help coordinate this process through the program administrator's membership in the REDP. Research studies will not be supported by Registry funding.

Inquiries: Dr. Roger Aamodt, NCI Div. of Cancer Biology, Diagnosis & Centers, Executive Plaza North Rm 513, 6130 Executive Blvd., Rockville, MD 20892-9904, Tel. 301/-496-7147, Fax 301/496-8656.