THE CANCER LETTER

Vol. 14 No. 12

March 18, 1988

Subscription: $175 year North America, $190 year elsewhere

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Reauthorization Battle Warms Up; Administration, But Not Wyngaarden, May OK Cancer Act Renewal

The battle over reauthorization of biomedical research, including renewal of the National Cancer Act, was beginning to shape up this week when at least one reauthorization bill probably will be introduced. One promising development arose

(Continued to page 2)

In Brief

John Young To Leave NCI For ELM; Yates Looking For Chief Of Outpatient Services At RPMI

JOHN YOUNG, 23 year veteran of NCI's epidemiology and biostatistics programs, will join ELM Services Inc. next month when he retires from the Public Health Services Commissioned Corps. Young, who spent almost all of his professional career at NCI, will be vice president for epidemiology and research at ELM, starting April 18. He is chief of the Demographic Analyusis Section in the Operations Research Branch of the Div. of Cancer Prevention & Control . . . . **ROSWELL PARK** Memorial Institute is seeking a chief of outpatient services. Qualifications include clinical or community cancer research credentials which would qualify the candidate as an associate or full professor in a medical school department. Send CVs to Jerome Yates, associate director for clinical affairs, at RPMI, 666 Elm St., Buffalo, NY 14263. . . . **ANNETTE SULLIVAN** is the new managing editor of "Oncology Nursing Forum," the official journal of the Oncology Nursing Society. Sullivan has been managing editor of the "Connecticut Law Tribune." **Susan Baird**, who has served as editor of the Forum since 1979, continues her association with the publication, with respon-sibility for article acquisition and editorial content. Baird, who is a former chief of the NCI Cancer Nursing Service, recently joined the Univ. of Pennsylvania School of Nursing as project director of a home care grant funded by the NIH National Center for Nursing Research. Ruth McCorkle is PI for the grant. . . . **UNIV. OF SOUTHERN** California's Kenneth Norris Cancer Hospital & Research Institute has received a $4.5 million grant from the Kenneth and Eileen Norris Foundation toward construction of a $24 million addition to the facility. The addition will add 70,000 square feet which will house expanded outpatient facilities, a relocated clinical laboratory, offices for physicians, two floors of research laboratories, and accomodations for outpatient surgery patients and their families.

Whte House Goes Along With Cancer Act Renewal, Wyngaarden Does Not

(Continued from page 1)
last week when a draft of amendments proposed by the White House was leaked. It had only one change in the Cancer Act, an innocuous one at that, except for recommendations on authorized appropriations.

The Reagan Administration has opposed renewal of the National Cancer Act in the past, and was expected to do so again. The President vetoed it along with the rest of the biomedical research reauthorization two years ago. Congress overwhelmingly overrode the veto.

In the draft of the Administration's amendments obtained by **The Cancer Letter,** language was added in the section on the makeup of the National Cancer Advisory Board which specifically states that the ex-officio members are nonvoting. That was omitted two years ago, and since then the ex-officio members have had the legal right to vote, although they seldom did.

The draft recommends that definite authorization figures be included for the 1989 fiscal year for NCI, the National Heart, Lung & Blood Institute, National Research Service Awards and medical library assistance. For the final two years of the proposed three year reauthorization, the draft asks that instead of specific figures, the language state that "such sums as may be necessary" may be appropriated.

If the draft bill turns out to be what the Administration wants, the special authorities granted NCI in the National Cancer Act of 1971 and subsequent amendments would remain intact--authority to develop and submit directly to the President a "bypass" budget; the President's Cancer Panel with powers to report directly to the White House information on problems encountered in the Cancer Program; presidential appointment of the NCI director and the National Cancer Advisory Board; special authority to conduct peer review; construction grant authority; cancer center authority; clinical and laboratory research training; expert/consultant authority; cancer control authority; appointment of special advisory committees; authority to enter into contracts; emphasis on information dissemination; and foreign research authority.

Some of those authorities are available through NIH under other provisions of the law, but they were included in the National Cancer Act expressly to permit NCI to use them without going through the bureaucracy.

NCI and the National Cancer Advisory Board have recommended those special authorities be continued and have asked for a few additional provisions, most of which are needed to clarify authorities obscured in the last renewal:

*Restore and clarify NCI's peer review appointment authority. Originally, the National Cancer Act specifically stated that the NCI director could appoint members of NCI review committees. All NCI contracts, and grants for cancer centers, cancer control, research manpower, clinical trials and program projects are all reviewed by committees managed by NCI's Div. of Extramural Activities. The legislation two years ago left the door open for appointments to those committees by the NIH director, or at least permit him to review appointments. NCI would prefer to avoid delays in that process, even if the NIH director does not object to NCI's appointments.

*Restore and clarify use of boards of scientific counselors as reviewers of intramural research. NCI established the use of BSC's for intramural review, setting the pattern for the rest of NIH. Lack of specific authority for the BSCs to do that job has not been a problem, but NCI would like for that to be spelled out, since the law does require NIH institutes to conduct intramural peer review without saying who should do it.

*Restore ability of NCI to receive its appropriation directly from the President. In the last renewal, the pertinent provision was changed to read, "may" receive the appropriation directly from the President instead of "shall," as it was in the original National Cancer Act. That was all the opening needed by the Office of Management & Budget to implement its infamous "apportionment" system that plagued NCI for the past two years. OMB, under great pressure, has stopped that practice, but NCI would like to have the protection written into law.

*Specific authority for cancer centers to engage in cancer control research. They can do that under the general authority in the Public Health Service Act, as long as no one objects. NCI would like to have the specific authority, in case someone does.

*Appoint an ex-officio member to the NCAB from the Dept. of Energy. The Depts. of Defense and Labor, along with the FDA,

National Institute of Environmental Health Sciences, Veterans Administration, and National Institute for Occupational Safety & Health all have ex-officio seats. Energy is involved in cancer research, through the Fermi and Oak Ridge labs and elsewhere.

*Establish appropriate authorizing funding levels. In the 1970s, Cancer Program advocates fought hard to keep authorizing levels in the Cancer Act. They reasoned that high authorizing levels would give the appropriations committees goals at which to aim and would tend to lift the amounts voted. In recent years, authorizing levels were too close to actual levels to be effective stimuli.

Those recommendations are relatively non-controversial, except perhaps among those who oppose any special authorities for NCI (see below). The Cancer Letter herewith offers four additional proposals certain to draw fire from several quarters, and equally certain, if enacted, to enhance the National Cancer Program:

1. Transfer the authority to approve investigational new drug (IND) applications from FDA to NCI. That was one of the recommendations brought to the Yarborough Panel of Consultants by the late Solomon Garb, a member of the Panel. Garb had seen how INDs could get hung up at FDA, and felt the way to overcome that problem was to get the process away from the regulators and into the hands of those charged with developing new anticancer drugs. Although he won many of his points, Garb lost on that issue, and the provision did not survive in the legislation of 1971.

Hardly a year has passed since in which NCI and FDA have not battled over INDs. NCI staff members feel that Steven Rosenberg's LAK/IL-2 regimen was unnecessarily delayed for a year or more by FDA requirements that the agents be tested separately before combining them. Experienced investigators, sometimes world famous who are the top authorities in their fields, have suffered the indignity of having their INDs turned down or delayed for reasons they feel were unimportant, irrelevant, or capricious.

For their part, FDA staff members feel they have to follow law and regulations as they see them. They have worked hard to reduce the time for approval of new drug applications (NDAs, clearing a drug for marketing), and have made great strides in that regard. The proposal here is to leave the NDA regulatory process at FDA, with NCI assuming control over INDs.

2. Put some teeth into the bypass budget. The bill written by Sen. Edward Kennedy in 1971 would have taken NCI completely out of NIH and out of the department, establishing it as the "National Cancer Authority" and reporting only to the President. That horrified many people, including most NCI staff members, who wanted to remain in NIH. Congressman Paul Rogers came up with the compromise, which provided NCI with the various special authorities. To satisfy the Yarborough Panel's determination to overcome the roadblocks between NCI and the White House, the compromise created the President's Cancer Panel, with direct access to the White House, and the bypass budget.

The bypass budget is supposed to be what NCI and its advisors determine is the optimal amount of money needed to conduct cancer research. For the most part, that is what it has been. It is transmitted to the White House through NIH and HHS, both of which may comment on it but not alter it.

It was clearly the intent of Congress that NCI's bypass budget would be its only budget. However, in practice, the Office of Management & Budget has ignored it. The budget it submits for NCI, along with the rest of NIH, is a figure that has been developed independently of the bypass budget by NCI from a total given by the NIH director and the assistant secretary for health.

Needless to say, the figure that goes to Congress through those channels is far less than the bypass budget's "optimal" figure. For the 1989 fiscal year, the bypass request was $2 billion; the Administration's, $400 million less.

Ideally, OMB would take the bypass budget and submit it intact along with budgets of the rest of NIH and the department. Why not make that a requirement in renewal of the National Cancer Act?

At the very least, a provision could be added requiring NCI to distribute copies of the bypass budget to members of Congress. At the appropriations hearings, committee members usually ask what the bypass total was, but they don't see the supporting comments, unless someone has sent them a copy.

3. Permit NCI to produce publications without clearing them with the Government Printing Office. The Cancer Act requires NCI to disseminate information to health

professionals and the public. NCI's Office of Cancer Communications and the International Cancer Information Center have done a remarkably good job of that. But they frequently are hamstrung by the bureaucratic requirement of going through GPO. The professionals at OCC and ICIC don't need GPO's advice and consent.

4. Spell it out clearly that NCI may exercise all of its special authorities without clearing it with NIH, the assistant secretary for health, or the Dept. of Health & Human Services. The NCI director, the President's Cancer Panel, and the National Cancer Advisory Board are all presidential appointees. Let them be responsible only to the President. No one in the chain of command from NCI to the White House knows more about what needs to be done in cancer research than the NCI director. He serves at the pleasure of the President, and if he gets out of line, the President can sack him with a phone call.

If in the bureaucratic scheme of things an end run such as that is intolerable, then perhaps Kennedy and the Yarborough Panel had the right answer all along: take NCI out of NIH.

Lest NCI staff members have nightmares again over that prospect, consider this: removing NCI from NIH administrative control does not necessarily mean physical separation. NCI pays rent and other fees to NIH now; that arrangement could be continued, appropriate sharing of various NIH resources could remain in place, the inter-institute collaborations could stay in place.

An administrative separation would be most noted by two persons--NCI Director Vincent DeVita and NIH Director James Wyngaarden.

Surprisingly, Wyngaarden may be the most ardent advocate of a move to separate NCI from his domain. That would not be his first choice, but he'll take it if it is the only way to get DeVita off his back.

Wyngaarden told **The Cancer Letter** last week that in a discussion with DeVita on reauthorization, he had said he had no objections to DeVita speaking out in favor of retaining the National Cancer Act. "I also said that while I would not actively oppose it, I would not support it if asked about it."

Wyngaarden based his opposition to two provisions in the Act which considers "unwise"--the bypass budget and the President's Cancer Panel.

The bypass budget "has never achieved anything," Wyngaarden said. "There is no reason for it." As for the President's Cancer Panel, that is something "ready made to produce unending conflict. It has not achieved anything, at least not since I've been here (1981)."

The Cancer Act gives the NCI director and the Cancer Panel "the right to go around the NIH director and the assistant secretary," Wyngaarden said. He acknowledged that the language of the Act specifically charges the Panel with bringing to the attention of the President "any delays or blockage" of cancer research.

"Vince has interpreted that as placing the responsibility on him to tell the Panel about what he sees as delays or blockage. It's a source of conflict anytime he gets a negative answer from the NIH director," Wyngaarden said. "It is unnecessary and disruptive. The Cancer Institute is in good shape now, without that. It is time to fold NCI back into NIH."

Wyngaarden noted that authorization for other institutes requires only five or six lines each. "There is no reason why NCI should have any of that detailed authorization."

When it was pointed out to him that Congress fully intended the NCI director to go around NIH and the department when he felt it was necessary, Wyngaarden said "that may have been necessary, before I came here. It isn't now."

Wyngaarden said that if Congress didn't bring NCI back "into the NIH fold," and treat it the same as the other institutes, "I would rather see them take it off by itself."

Completely out of NIH, as the Kennedy bill would have done?

"Yes. It would be less disruptive for all of us."

Members of the Assn. of Community Cancer Centers were scheduled to conduct their annual blitz of Capitol Hill this week as part of their annual meeting in Washington. Renewal of the National Cancer Act and adequate funding for NCI, especially for community cancer programs, are things they usually talk to their representatives and congressional staff about.

The National Coalition for Cancer Research has scheduled a "Capitol Hill Day" for April 21 to discuss reauthorization with members of Congress and their staff. Coalition members will meet in the morning, have luncheon with members of Congress and staff and then meet

with their respective congressmen and senators in the afternoon. Those interested in participating may contact Margeurite Donoghue, Legislative Director, Capitol Associates Inc., 426 C St. NE, Washington DC 20002, phone 202/522-1880.

Young To Head Centers & Community Program, Meyers To Medicine Branch

NCI has found the person to head the Centers & Community Oncology Program, one of its own.

Robert Young, chief of the Medicine Branch in the Div. of Cancer Treatment's Clinical Oncology Program, was named last week as associate director of the Div. of Cancer Prevention & Control and director of Centers & Community Oncology.

Young will take up his new job April 4. It is a Senior Executive Service position, requiring appointment by the HHS secretary. Until that comes through, Young will technically be acting associate director.

"Bob is one of the 10 top medical oncologists in the country," NCI Director Vincent DeVita said. "People in the centers and CCOPs will get along well with him." Young, 48, has been at NCI for 21 years.

In addition to cancer centers, and the Community Clinical Oncology Program, Young's domain will include research facilities, organ systems and rehabilitation.

Replacing Young as chief of the Medicine Branch will be Charles (Snuffy) Meyers, now chief of the Clinical Pharmacology Branch. Meyers, 45, is a 17 year veteran of NCI.

Meyers' first and most pressing task will be defending the Branch against recruiting efforts of Marc Lippman, one of NCI's most prominent clinical investigators who is leaving to become director of the Lombardi Cancer Center at Georgetown Univ. Lippman has vowed to take many of his brightest colleagues with him; DCT Director Bruce Chabner and Clinical Oncology Program Director Samuel Broder are equally determined to keep them.

Meyers is one of NCI's most popular staff members and could be of major assistance in the competition with Lippman.

While DeVita and Chabner were upbeat about losing Lippman ("Some turnover is a good thing," DeVita said), Broder said, "When I think about the whole issue, I get depressed. It's getting harder and harder to retain people at NIH. There is no solution, in the near term at least, that I can see. There is a very substantial salary differential."

Higher salaries in industry, academia and private practice frequently become available at a time in a person's career that coincides with the need to consider the education of his/her children, Broder noted. "The disease we're suffering from here at NIH is mal tuition," he quipped.

NIH scientists frequently move on to industry at as much as three times their government salaries. Lippman said he can offer twice what some of his colleagues are making. With reciprocal free tuition arrangements sometimes available for children of faculty members, universities can hold their own in competing with industry for persons with college age offspring. "We're out of that loop," Broder said.

The other side is that the NIH intramural program "is such a great place to work. It is unique, in that it is a government institution that can do what it is supposed to do. We can transfer technology from the lab to the patient faster than anywhere. We can participate in finding cures for major diseases."

The prospect of losing the rest of his branch chiefs is causing Broder to be "as disturbed as I've ever been. I don't see how we're going to keep people like John Minna, Eli Glatstein and Steve Rosenberg."

Gallo To Stay, For Now, DeVita Says; Core Grants Facing Big Cut

One person NCI will not be losing, at least in the immediate future, is another of its all stars, Robert Gallo.

Director Vincent DeVita told the House Labor-HHS-Education Appropriations Subcommittee last week that "we can probably count on Dr. Gallo leaving eventually, but not in the immediate future." He was responding to a comment by Congressman Silvio Conte (R-MA), "I was very disturbed that you almost lost Dr. Gallo."

Also disturbing to subcommittee members was DeVita's information that the 1989 budget for cancer centers, in the President's recommendations, would require that center core grants be reduced 31 percent from recommended levels. "Either that, or we will have to drop some centers," DeVita said.

Congressman Joseph Early (D-MA) and Steny Hoyer (D-MD) argued that the President's request was too low. Noting that the bypass

budget asked for $2 billion (the President asked $1.6 billion), Hoyer asked what NCI's "through channels" request was. The answer: $1.8 billion.

Subcommittee Chairman William Natcher (D-KY) was not optimistic about getting much of an increase for NCI over the President's budget. "We have to look carefully at the division of funds. The 1989 fiscal year will be a right difficult one."

DCE Board Approves Recompetitions

The Div. of Cancer Etiology Board of Scientific Counselors gave concept approval to the following recompetition of contracts at its recent meeting. The Board also approved noncompetitive renewal of contracts with West Indies Univ. and Caribbean Epidemiology Center for HTLV-1 studies.

Resource for xenotransplantation of human tissues and cells into athymic nude mice. Recompetition of a contract held by Hazleton Laboratories America Inc. Four year award, total estimated cost $1.6 million, estimated first year cost $370,350.

The Laboratory of Human Carcinogenesis develops and employs model systems for the study of carcinogenesis in cultured human cells and tissues. The program design involves (1) collection (from surgery and autopsy sources); (2) in vitro adaption, maintenance and treatment; and (3) xenotransplantation of normal, preneoplastic, neoplastic, carcinogen exposed, human tissues in athymic nude mice. This contract provides the vital third phase xenotransplantation segment of the studies. Under the rigid conditions of a closed, self sustaining facility, requiring sterility of all materials and supplies entering and antibacterial showers for personnel, the mice generally have a lifespan of at least 24 months. Human tissues are successfully transplanted and maintained in cobalt irradiated nude mice for more than 20 months. Methods have been established for in situ exposure of human tissue to carcinogens; immunlogical, enzymatic, and karyological methods are used for marker identification of human tissues in nude mouse recipients. The development of tumors in nude mice from oncogene transfected human bronchial epithelial cells has been accomplished.

The primary objective of this project is to contribute to the understanding of chemical carcinogenesis in humans. LHC proposes the recompetition of this contract as a necessary and integral part of ongoing studies to further develop and refine in vitro and in vivo model systems for studying carcinogenesis directly in human target tissues.

These systems provide opportunities to assess mechanisms of carcinogenesis in humans; host factors influencing individual human susceptibility to carcenogens, e.g., the metabolic balance between activation and deactivation of chemical procarcinogens; methods and designs for the qualitative extrapolation of animal carcinogenesis data to humans; and strategies for the inhibition of neoplastic transformation. Ultimately, LHC seeks to establish and apply model systems that provide for the study of the mechanisms of carcinogenesis in human epithelial cells and tissues.

This contract will serve as the continuation of a resource for the in vivo assay of the transplantability of normal, premalignant and malignant human tissues; the effects of pretreatment in vitro with carcinogens and anticarcinogens on the growth patterns and cellular integrity of various human tissues as xenografts; and the relationship between carcinogen-DNA adduct formation, activation of proto-oncogenes, and malignant transformation of human tissue in vitro as xenografts.

Specifically: employing a pyrogen free facility, the contractor will provide an enclosed colony of 900 animals to be bred, irradiated and maintained on a continuing basis; methods for the long term survival of xenotransplants of human tissues in nude mice; and for long term animal holding experiments, housing athymic nude mice for periods of up to two years. Xenotransplanted human tissues will be frequently monitored in vitro for viability and the integrity of tissue specific characteristics, and in some experiments, the xenotransplants will be treated with carcinogens in vivo. Tumors will be transplanted to new mice, characterized microscopically and histologically and provided to LHC for in vitro studies at NIH.

LHC Chief Curtis Harris said the average census of the mice maintained for the program by Hazleton is 1,000. "I don't think you're asking for too much money," Board Chairman Hilary Koprowski said.

Resource for collection and evaluation of human tissues and cells from donors with epidemiological profiles. Recompetition of a contract held by the Univ. of Maryland. Four year award, total project cost estimate, $2.2 million, estimated first year award, $522,122.

Model systems for the study of carcinogenesis using cultured human cells are providing new opportunities to assess mechanisms of carcinogenesis in human cells; host factors that influence individual susceptibility to carcinogenic agents; logical approaches for the qualitative extrapolation of carcinogenesis data from experimental animals to humans; and methods to inhibit the multistage processes of neoplastic transformation and progression. An important aspect of this approach is to conduct parallel studies in epithelial tissues and cells from experimental animals so that interspecies comparisons can be made.

A resource is required for the collection of normal appearing and neoplastic human bronchial, intestinal, pancreatic and hepatic tissues and cells at the time of surgery (cancer and noncancer donors) and at immediate autopsy (noncancer donors). A resource is required to conduct case control biochemical epidemiological studies of lung cancer risk. Normal tissues and cells taken at the time of immediate autopsy from donors without cancer will be used in LHC to study malignant transformation caused by chemical, microbial and physical carcinogens and cocarcinogens.

Essential components of the resource will include (a) approval of the institutional committee for the protection of human subjects; (b) an epidemiological profile of the donors obtained by trained interviewers administering an NCI designed, Office of Management & Budget approved questionnaire; (c) collecting and transporting the immediate autopsy specimens in a viable condition to NIH; (d) evaluating (characterizing) the type, functional and pathological status of the tissue by histochemical and immunological methods and by light and electron microscopy. Tumor marker analysis should include AB/PAS (+ or - glycogen) for mucus and adenomatous differentiation; immunostaining for keratin and epithelial origin of tumors and differentiation; cytoskeletal proteins (i.e., actin, tubulin, calmodulin), growth factors (EGF, EGF

receptors, and alpha TGF), hormones (alpha HCG, beta HCG), and oncogene products (ras, raf, myc and fos protein); and neuron specific enolase for neuro-epithelial differentiation.

The contractor will also provide the laboratory with matched normal and malignant tissues from surgical donors who have cancer. These normal and malignant tissues will be used for studies of DNA polymorphisms, i.e., restriction enzyme fratment length polymorphisms using DNA probes on selected human chromosomes.

The contractor will recruit, interview and provide biological specimens (blood, urine and tissue) from lung cancer cases and appropriate control subjects for studies of biochemical epidemiological studies of lung cancer risk.

Harris, responding to Board member Janet Butel's question on how the estimated cost was arrived at, said that it was based on the need for six full time persons (FTEs) taking 1,200 samples a year.

The samples are used primarily by Harris' lab and the lab's collaborators. Board member Peter Magee asked if they would be made available to other investigators with good proposals.

"Yes, if it fits in with our epidemiology work," Harris said. "It is not a resource that is available to anyone, but we've developed some very good collaborations."

"I am strongly in favor of this program," Board member Allan Conney said. "The track record of Dr. Harris and his colleagues is very, very good."

An interdisciplinary prospective study of infection with human papillomavirus. The prime contract is held by Westat Inc., which was awarded last year for a total of $1 million. This new competition will be for a clinical component of the study. It will be a three year award, estimated total cost, $650,000, estimated first year award, $385,000.

The prime contract was awarded in September, 1987, after the Board of Scientific Counselors approved the concept of a prospective study of genital infection with human papillomavirus (HPV). The objective of the study is to estimate the risk of developing cervical intraepithelial neoplasia (CIN) following infection with HPV. The background and methods for this project have not changed since concept approval, but additional funds are now requested to supplement the $1 million awarded originally.

Following competitive selection and contract award last year, the coordinating center contacted possible clinical settings. All 13 prepaid health plans in the United States with a sufficient number of yearly Pap smears were encouraged to submit competitive proposals for the clinical setting subcontract. As responses were received and followup conversations held, it became clear that the project could not be completed for the budgeted amount of money. We have delayed choosing a clinical site until budgeting issues are resolved. The following unexpected expenses explain the large difference between the current cost estimates and those made in May, 1986, when this study was conceived:

1. We underestimated the costs for the baseline screening and enrollment effort. Based on earlier discussions with prepaid health plans, we had budgeted $5 for each sample and presumed that informed consent procedures could be streamlined. The cervical-vaginal lavage involves only a 10 ml sterile saline rinse. It is without any known risk, and takes less than 15 seconds to perform. In two clinical centers, at least, it is now part of routine clinical care during the Pap smear visit. Unfortunately, in the clinical centers appropriate for this investigation, the lavage cannot be incorporated into standard practice. Complete informed consent procedures will also be required from all 25,000 women. The health plan must be reimbursed for the clinician time and other costs incurred by the disruption of current routine procedures. Project clerks will be hired to stock examination rooms with prefilled syringes and complete all paperwork accompanying the samples. Project nurses will be needed to oversee the intake effort. Finally, a co-investigator at the clinical site will be required to gain clinician acceptance and promote project activities as part of clinic scheduling (Additional funding requested, $500,000).

2. Labor costs in the clinical setting were higher than anticipated, since the prepaid health plans have required the employment of their own clinical personnel for patient interviewing and other activities involving contact with health plan members (additional funding requested, $150,000).

Overall, increased costs associated with clinical activities raise the total budget to $1.65 million instead of the $1 million currently obligated. An additional year is requested, to permit the originally planned period of followup despite the present delay in choosing a clinical site.

The need for this investigation, we believe, is greater than ever. To our knowledge, no study of its kind is under way, although HPV researchers routinely proclaim the need for a large, careful prospective study. We are concerned that the HPV-CIN association will soon be widely judged by the medical community to be a causal relationship in advance of epidemiologic evidence. Laboratory studies strongly suggest an oncogenic potential for HPV but, to determine the risk to women infected with the virus, followup studies are needed. With supplemental funding, we can begin patient enrollment within six months as the prime contract is already in place.

RFAs Available

RFA 88-CA-08
Title: Mechanisms of tobacco and alcohol related carcinogenesis of the oral cavity
Application receipt date: May 23
Letter of intent receipt date: April 8

NCI's Div. of Cancer Prevention & Control, through the Organ Systems Program, announces the availability of a request for applications on the above subject.

Epidemiologic studies have demonstrated that there are at least two tobacco related causes of oral cavity cancer: snuff dipping and the combination of chronic alcohol consumption and cigarette smoking. The latter is a major risk factor for squamous cell cancer of the oral cavity. In view of this epidemiologic lead, studies are needed on mechanisms by which alcohol enhances oral cavity cancer induced by tobacco smoke.

To test mechanisms proposed, there is a need for development of suitable animal model systems that mimic alcohol enhancement of tobacco induced squamous cell cancer of the oral cavity, as observed in man. Organ culture or cell culture systems could also prove useful for investigating mechanisms of oral cavity carcinogenesis.

The use of smokeless tobacco, especially snuff dipping, has increased remarkably in the U.S. in recent years particularly among young males. Surveys for 1985 indicate that 16 percent of U.S. males between 12 and 25 years of age used smokeless tobacco. Several scientific groups have concluded that snuff dipping is a cause of oral cancer in humans. Thus, research on the mechanisms of oral cancer induction by local application of snuff or its constituents is likewise necessary and timely.

The objective of this RFA is to invite investigators to use appropriate experimental animal models, organ culture systems, or cell culture systems to

elucidate mechanisms by which tobacco use may increase the risk for squamous cell cancer of the oral cavity. Studies should focus on mechanisms of induction of oral cancer by snuff dipping or the combination of chronic alcohol consumption and tobacco smoking. Appropriate studies could include development of model systems for such studies, as well as research on the mechanisms of oral cancer induction by smokeless tobacco, tobacco smoke or their carcinogenic constitutents. Other novel approaches with appropriate rationales are also encouraged.

Support for this program will be through the traditional NIH investigator initiated research grant (RO1). It is anticipated that approximately five awards, for project periods of up to three years, may be made as a result of this RFA. Applicants are encouraged to submit a letter of intent and to consult with NCI program staff before submitting an application.

Copies of the RFA, and further information, may be obtained from Dr. Elizabeth Anderson, Organ Systems Program, DCPC, NCI-NIH, Blair Bldg Rm 717, Bethesda, MD 20892, phone 301/427-8818.

Title: The NCI outstanding investigator grant
Application receipt date: June 15

NCI will continue to accept applications for the outstanding investigator grant (OIG), the purpose of which is to provide long term support to experienced investigators with outstanding records of research productivity. The OIG is intended to encourage investigators to continue or embark on projects of unusual potential in cancer research. Emphasis will be placed on evidence of recent substantive contributions (i.e., seminal ideas and innovative approaches to resistant problems) and the potential for continued work of high caliber.

Special features of the OIG include: (1) seven year project periods; (2) the delegation of authority to grantee institutions to carry over more than 20 percent of the direct cost authorization of OIGs from one budget period to the next, with the approval of NCI; (3) alleviation of the need to manage more than one grant instrument through consolidation of the OIG principal investigator's current cancer related and peer reviewed support.

Applications may be submitted only by domestic institutions on behalf of investigators who have recently demonstrated outstanding research productivity for at least five years. There are no age restrictions. Only U.S. citizens, nationals or permanent residents may be presented as candidates for this grant.

Applications will be accepted by NCI only when they are cancer related as defined by the Div. of Research Grants grant referral guidelines. Investigators whose current research support is derived predominantly from sources other than NCI may not be eligible and are encouraged to discuss their research objectives with appropriate NCI officials before applying.

The OIG PI is required to commit 75 percent of his/her time and effort to the OIG project and the institution sponsoring the OIG application is required to commit itself to providing 25 percent of the investigator's support.

The date of receipt of all OIG applications will be June 15 of each year. They will be processed for review at the earliest possible meeting of the NCAB.

For complete copies of this program announcement and further information, contact Mrs. Barbara Bynum, Director, Div. of Extramural Activities, NCI, Bldg 31 Rm 10A03, Bethesda, MD 20892, phone 301/496-5147.

RFA 88-CA-09
Title: Developmental research in special populations
Application receipt date: June 17

The Div. of Cancer Prevention & Control of NCI invites applications for developmental studies which assess cancer control needs, determine barriers to cancer control, and/or validate intervention methods and assessment instruments in special populations--i.e., Alaska natives, American Indians, Asian Americans, Blacks, blue collar groups, the elderly, Hispanics, low income groups, and native Hawaiians. These studies are limited to applicants from within the United States.

The term "special populations" refers to those population segments which may experience or are known to experience high cancer rates and are underserved in terms of cancer prevention and control programs, e.g., smoking or screening programs.

Cancer control is defined as the reduction of cancer incidence, morbidity and mortality through an orderly sequence from research on interventions and their impact in defined populations to the broad, systematic application of the research results.

Cancer control research studies are classified in the five phases which represent the orderly sequence progression noted in the above definition: 1, hypthesis development; 2, intervention methods development and testing; 3, controlled intervention trials to establish cause and effect relationships; 4 research in defined human populations; and 5, demonstration and implementation studies.

The research of interest in this RFA falls into either phase 1 or phase 2 studies. Hypothesis development (phase 1) studies should focus on the assessment of cancer prevention and control needs in communities or organizaations with large special populations; or studies which identify barriers to cancer prevention and control in special populations. Methods development and testing studies (phase 2) should focus on validating the use of existing intervention methods (e.g., dietary modification, health services, tobacco cessation) as applied in the special populations; the development and pilot testing of unique methods which are sensitive to the needs of the special populations described above; or the development and validation of assessment instruments to measure the cancer control related needs of special populations or for use in evaluating the effectiveness of intervention methods in special populations.

Studies to determine the efficacy of chemotherapy, surgery, radiotherapy and other primary treatment interventions are not considered developmental intervention research under this RFA. Other animal studies are not allowed.

Applicants may be established researchers, new investigators, and qualified staff of public health departments and collaborating agencies.

Approximately $1 million has been set aside for direct costs for all projects for the first year. Funding under this RFA is limited to a maximum of three years.

Copies of the complete RFA and additional information may be obtained from Gregory Christenson, PhD, Director of Evaluation, or Patricia Von Bargen, MPA, Special Populations Studies Branch, DCPC, NCI-NIH, Blair Bldg Rm 1A01, Bethesda, MD 20892, phone 301/427-8597.

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Published forty-eight times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter.