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PRESSURE ON REAGAN TO APPOINT SCIENTISTS TO NCAB INCREASES WITH DEMAND FROM POWERFUL CONGRESSMAN

Pressure on President Reagan to appoint qualified basic scientists to at least some of the six impending vacancies on the National Cancer Advisory Board mounted last week when powerful Congressman John Dingell (D.-Mich.) released a letter he had written to Reagan demanding he fill the vacancies "with individuals whose research qualifications are impeccable." The terms of the six members leaving

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In Brief

SCHEPARTZ TO LEAVE NCI FOR ACADEMIA; WOOLLEY NAMED TO HEAD CLINICAL RESEARCH AT LOMBARDI

SAUL SCHEPARTZ, deputy director of NCI's Div. of Cancer Treatment, will become associate vice president for academic/industrial relationships of the Univ. of Medicine & Dentistry of New Jersey June 4. Schepartz played a major role in the Institute's Drug Development Program. He joined NCI in 1958 to work in the Cancer Chemotherapy National Service Center and became chief of CCNSC in 1964. NCI was reorganized about a year later and Schepartz was named associate director for drug research and development in the Chemotherapy Program under Gordon Zubrod. When DCT was established in the early 1970s, the drug development effort evolved into the Developmental Therapeutics Program, with Schepartz as its head. He was named DCT deputy director by then DCT Director Vincent DeVita in 1976, and served for one and a half years as acting DCT director when DeVita became NCI director. DCT administrative officer Michael Goldrich will chair the search committee which will look for a new deputy for DCT Director Bruce Chabner. Schepartz' impending departure forced Chabner to replace him as chairman of two other search committees seeking to fill key vacancies. Eli Glatstein now heads the committee looking for a new director for the Radiation Research Program, and Robert Wittes chairs the committee lining up candidates for director of the Biological Response Modifiers Program.... **GREGORY CURT** is Chabner's new special assistant for clinical affairs.... **PAUL WOOLLEY,** professor of medicine and pharmacology at Georgetown Univ. Medical Center, has been named associate director of clinical research and chief of the Div. of Medical Oncology at Georgetown Lombardi Cancer Research Center. He replaces Phillip Schein, who left last year for a position with SmithKline.... **CYCLOTRON UPDATE:** Financially troubled Cyclotron Corp. did tell NCI that it was going to file Chapter 7 bankruptcy, as Chabner told the DCT Board of Scientific Counselors last month (The Cancer Letter, Feb. 24). However, the company did not proceed with that action, and at last word, was still in business. Possibility remains the company will be sold.

DINGELL TELLS REAGAN HE UNDERVALUED SCIENCE IN 1982 NCAB APPOINTMENTS

(Continued from page 1)

the Board expire March 9. Dingell is chairman of the Committee on Energy & Commerce and also heads that committee's Subcommittee on Oversight and Investigations.

Energy & Commerce is the parent of the House Subcommittee on Health & Environment, which writes health authorization legislation. Dingell's Subcommittee on Oversight & Investigations is respected (and sometimes feared) for its probes of federal agencies.

In his letter to the President, Dingell pointed out that NCI policy is guided by recommendations of the National Cancer Advisory Board. "The priorities and quality of the research agenda can be strongly and positively influenced by the expertise of the scientific appointees to the Board. Conversely, the absence of the full range of scientific authority can result in failure to advance knowledge in key areas and, therefore, amount to a misuse of resources with potentially avoidable and devastating effects on the health of the American public.

"The National Cancer Institute was created to promote the very best research which the nation's leading scientists are capable of directing in pursuit of prevention, early diagnosis and successful treatment of cancer," Dingell's letter continued. "Given our current lack of understanding of the causes of cancer, basic biomedical research is of the utmost importance and urgency.

"I have long been a staunch supporter of the programs of the National Institutes of Health and proud of the scientific integrity of the Institutes. The high scientific standards have been maintained through the efforts of the advisory boards, the staff, the peer review process, and the biomedical research community."

Dingell quoted the section of the National Cancer Act spelling out qualifications of NCAB members, then continued:

"With the retirement of six members this year, the majority of whom are scientists, I feel compelled to draw your attention to the requirement that scientific and medical appointments be (quoting again from the Act) 'leading' authorities who are 'outstanding' in their fields and 'who by virtue of their training, experience and background are especially qualified to appraise the programs of the Institute.' While it may be appropriate to have some representation of practicing physicians, the requirements of the statute will be met only when the 12 scientific and medical slots are filled by research scientists who are known to have made significant contributions to the knowledge about the causes, diagnosis and treatment of cancer. Most often this will mean appropriate candidates have had experience as principal investigators on NCI grants, have published their findings in leading research journals, and are well known and highly respected in prestigious academic and research communities.

"As the Board's responsibilities include advising the director of NCI on the distribution of resources across the many possible avenues of scientific inquiry, broad representation of the various scientific perspectives is critical. Presently, the Board is either underrepresented or has no representation at all in at least the following areas: virology, immunology, carcinogenesis, pediatric oncology, and medical oncology.

"Your appointments in 1982 did not adequately address the basic research emphasis which is essential to significant gains in cancer research," Dingell told the President. "The unfortunate propensity of your Administration to undervalue substantive scientific expertise cannot be tolerated. As we have learned with the recent controversy surrounding EPA, the failure to make appointments with strong scientific credentials can have detrimental and broad ranging effects.

"I will be most attentive to your 1984 appointments to the National Cancer Advisory Board and expect you will take this opportunity to fill the gaps in scientific expertise with individuals whose research qualifications are impeccable. Only full compliance with the statutory provisions cited above will be acceptable. I believe you and your senior staff would be well advised to pay closer attention to the nominations of the National Institutes of Health than you did in 1982 or to be certain that alternative appointees are of equal or superior calibre."

The six retiring members of the NCAB are Roswell Boutwell, professor of oncology at McArdle Laboratory; Maureen Henderson, professor of medicine and epidemiology at the Univ. of Washington; Janet Rowley, professor of medicine at the Univ. of Chicago; Irving Selikoff, director of the Environmental Sciences Laboratory at Mount Sinai School of Medicine; Sheldon Samuels, director of health, safety and environment of the AFL-CIO Industrial Union Dept.; and Morris Schrier, legal consultant for Music Corp. of America. The latter two are lay members, although Samuels could be considered as one of the five (as required by the National Cancer Act) "knowledgeable in environmental carcinogenesis, including carcinogenesis involving occupational and dietary factors."

Dingell ignored that requirement of the Act in his emphasis to the President on the areas of research not adequately represented, although it was in the section of the Act he cited in the letter.

Selikoff and Samuels were appointed by President Carter as a direct result of that requirement written into the Act by former Congressman Andrew Maguire in 1978 amendments. With other members who have since gone off the Board, Selikoff and Samuels filled out the five.

Boutwell also could be considered as an expert in environmental carcinogenesis research, and he is the only one of the six likely to be reappointed, since he is already a Reagan appointee, having been named to fill out an unexpired term. Unless some of the new appointees have expertise in environmental, occupational and/or dietary carcinogenesis, the requirement of the Act will not be met.

The "Washington Post" this week published parts of Dingell's letter in an article by science writer Christine Russell. The Post also mentioned Rowley's campaign, through letters to "Science" magazine, to upgrade NCAB appointments.

The White House has been responding to letters on NCAB appointments with a form letter which says in part, "We are currently in the selection process and are reviewing a number of excellent candidates. We believe that when the President makes his announcement the scientific community will be pleased with the caliber and expertise of the new members."

Another important advisory vacancy occurred last month with the expiration of Armand Hammer's term on the President's Cancer Panel. There is little doubt that Reagan will reappoint Hammer, if that is Hammer's desire, and Hammer has seemed to relish the job.

At press time this week, White House sources told The Cancer Letter that neither the NCAB nor Panel appointments had been made.

DCE BOARD APPROVES CONCEPTS OF FOUR NEW GRANT PROJECTS, FOUR CONTRACTS

The Board of Scientific Counselors of NCI's Div. of Cancer Etiology gave concept approval last week to four new grant supported research projects with a total estimated cost of $6 million and $2 million to be set aside for first year awards.

The Board also approved the concept of four competitive contract supported procurements worth an estimated total of over $5 million and eight noncompetitive contracts and interagency agreements with an estimated total of $8.7 million.

Three of the new RFAs (request for applications) are aimed at stimulating RO1 applications--for research on biologic markers of past or present dietary exposure which can be utilized for epidemiologic studies; carcinogenic potential of involuntary inhalation of tobacco smoke; and obesity and cancer risk in women. The fourth RFA will be for a cooperative agreement for studies on bovine leukemia virus. A contract concept for maintenance of a herd of cows for the bovine leukemia virus study was also approved.

RFA concepts approved were:

Biologic markers of past or present dietary exposure which can be utilized for epidemiolgic studies--Proposed first year funding, $500,000, two years.

The current emphasis on nutritional factors as modulators of carcinogenesis in human populations has created a need for these biologic markers. Experimental studies have indicated that the intake of specific dietary components is an important determinant of cancer risk. Attempts to apply these findings to humans are hindered by the difficulty of classifying individuals into exposure categories.

Attempts at assessment of nutritional status are usually based on questionnaires or interviews. Problems exist in determining which data reflect actual intake (e.g., selective recall, limited knowledge of food composition and complexity of diet), the extent to which utilization is a measure of bioavailability (e.g., absorption efficiency and the possibility that specific dietary components may be ingested in a form which renders absorption difficult or impossible) and individual variability in metabolic handling of substances after absorption.

It would clearly be advantageous to have available biochemical measures (preferably minimally invasive) which would provide unambiguous markers of the level and distribution of dietary constituents in individuals. Such methodology would facilitate the design, conduct and interpretation of epidemiologic studies focused on the relationship between diet, nutrition and cancer risk.

Because of the latency period involved in the carcinogenic process, it can be anticipated that current cancer risk will have been modulated by dietary patterns which existed at some time in the past. These past events are not always well defined by data on current dietary patterns for several reasons, among these, the fact that dietary patterns may vary significantly over time and because of our limited knowledge of the changing composition of foods. Biochemical markers of past dietary experiences are, therefore, of special interest in cancer epidemiology and some evidence from experimental studies suggests a potential for the development of markers which reflect integrated past exposure. Examples would include the existence of persistent DNA adducts following exposure to specific materials, the accumulation of substances in the body which are excreted extremely slowly, and alterations in tissue composition which reflect past intake (e.g., body fat, hair or nails).

Clearly, the more persistent the marker the greater its utility for this purpose. Because the methods to be developed will ultimately be utilized in epidemiological studies, it is important that consideration be given at the outset to feasibility in this context. Such factors as ease of conduct and expense as well as collection, storage and transport problems should be considered along with the

accuracy and validity of the method. The range of materials, for which markers of exposure are of interest, is extremely diverse. Included would be any foods, food groups, or nutrients which have been proposed to alter the risk of malignancy and for which human exposure is likely to have occurred. Documentation of interindividual variation, both in absorption and metabolic utilization and in persistence of markers, is of interest.

Board member Renato Dulbecco asked if "some dramatic example" of food consumption related to cancer and going back 10 or 15 years, "as with smoking," may be possible to identify through markers.

"No, we can't go back 30 years, even with strong carcinogens," DCE Director Richard Adamson said.

"Man is so variable in diet," Board member Louise Lombard said. "Why not include animal studies, where you can control and change the diet?"

"We will entertain animal studies for validation," program director A.R. Patel answered.

"The problem in epidemiology is that it is so difficult to get diet and nutrition information from a questionnaire alone," commented Joseph Fraumeni, director of the Epidemiology & Biostatistics Program. "But it may be possible to make dietary measurements through body fluids."

"But cancer is frequently caused by something that happened years ago," Dulbecco insisted.

"That is a problem," said Board member Allan Conney. "The main thrust here is to determine present dietary intake. The hope also is that we can assess what people were eating earlier. We hope to stimulate the biomedical community to start thinking about this."

"We still need to know what happened 30 years ago," Board member Nicholas Petrakis said. "We need something like a tree ring, maybe some pathological material in jars somewhere."

"We can utilize measures to look at past exposure," said John Cooper, acting chief of the Extramural Programs Branch. He mentioned DNA changes as one example. "We would like to push back time as long as possible. There may be markers there and we would like to look for them."

"This is an enormous project," Board member Gilbert Omenn said. "Some attention should be paid to dose responses. I doubt if there are many things you can measure that are tied to specific foods."

Carcinogenic potential of involuntary inhalation of tobacco smoke--Proposed first year funding, $500,000, two years.

There is a major public health controversy about the long term effects of involuntary smoking on the nonsmoker. The reactions to brief exposure to tobacco smoke in the environment range for the nonsmoker from slight irritation of the eye to serious allergic reaction; the reaction usually disappears following a period free from exposure to tobacco smoke. Also reported is a dysfunction of small airways in nonsmokers chronically exposed to tobacco smoke; and a significantly lower forced midexpiratory flow rate has been found in nonsmoking persons whose spouses currently smoked at least 10 cigarettes a day. Many chemical constituents of mainstream smoke are also found in sidestream smoke, with some constituents occurring in markedly higher concentrations, but actual absorption of smoke constituents by nonsmokers in a smoke filled environment has not been characterized. A few studies have, however, examined the absorption of carbon monoxide by measuring carboxyhemoglobin levels in exposed nonsmokers. The pattern of involuntary inhalation of smoke is probably different from that of voluntary inhalation by the smoker, which would influence the amount of deposition or absorption of smoke constituents in nonsmokers compared to smokers. A question, therefore, arises whether a person exposed to the cigarette smoke of others over a long period inhales sufficient amounts of carcinogens to elicit a carcinogenic response.

In recent years, a number of epidemiologic studies have been carried out to examine the influence of long term involuntary exposure to cigarette smoke in nonsmoking women. A prospective study of 91,540 nonsmoking wives, aged 40 and above, conducted by Hirayama showed a significant increase in lung cancer risk in nonsmoking wives of smoking husbands compared with nonsmoking wives of nonsmoking husbands. Exposure to the products of their husbands' smoking increased the mortality from lung cancer in nonsmokers up to two fold, with evidence of a dose response relationship. In a recent update, Hirayama also reported a significantly enhanced risk of cancer of the paranasal sinuses in nonsmoking wives in his cohort.

Trichopoulos et al, in a case control study of nonsmoking Greek women, supported Hirayama's findings. However, an analysis of prospective data from the American Cancer Society failed to show a significant dose response relationship between amount of cigarette smoking by the husbands and the mortality of their nonsmoking wives from lung cancer. This discrepancy may be partly due to differences in methodology of the two prospective studies. Chan, in a study in Hong Kong, also found no difference in risk of lung cancer due to involuntary inhalation of smoke.

Correa et al recently reported that heavy smoking by wives may increase the lung cancer risk of light smoking husbands, but smoking by husbands did not significantly affect the risk in women who smoked. Moreover, it was noted that the smoking behavior of the mother, but not that of the father, influenced the lung cancer risk of offspring who smoked. From an analysis of histological data, it has been suggested that the differences in composition of mainstream and sidestream smoke may produce different proportions of histological types of tumors.

Studies of interest include, in order of priority, (1) pilot studies designed to quantify involuntary exposure to tobacco smoke. This may involve laboratory measurements of selected constituents of tobacco smoke in a variety of settings and development of an appropriate questionnaire designed to elicit accurate histories of exposure to tobacco smoke. (2) Modification of existing

epidemiologic studies such as ongoing prospective or case control studies, prepaid medical services data bases, and intervention trials to obtain or refine information relating to involuntary smoke exposure. (3) Development of case control studies of lung cancer in areas of the world where involuntary exposure to smoke is not nearly universal.

Board member Pelayo Correa commented that the money earmarked to support these studies "is not enough to cover the different possibilities."

"How much do we know about different types of tobacco in different parts of the world?" Board member Charlotte Friend asked. "Are some more carcinogenic than others?"

"In France, smokers of black French tobacco are usually men in rural areas," Board member Dietrich Hoffmann said. "That tobacco is very unique. It is rich in nitrites, which are precursors of nitrosamines. It has been demonstrated in animals that nitrosamines are powerful carcinogens. The sidestream smoke is also dangerous, although it is quickly diluted."

"The study should probably be limited to certain specific areas in order for data to be meaningful," Board member C.C. Cheng said.

"The problem of passive smoking is complicated by the small number of observational settings," Board member William Haenszel said. "You should exercise considerable care in deciding which proposals to fund. They will need additional funding in subsequent years. This amount is probably enough to get started."

Board member Edward Bresnick offered a motion approving the RFA concept for studies one and two (above) but dropping the case control studies outside the U.S., citing possible confounding variables. Correa and Petrakis objected. "Why exclude the rest of the world? We might find out something."

Omenn said he is "quite skeptical" about the RFA. "It involves quantitative observations where a few more or less could tip the scales one way or another. I have plenty of reservations about the methodology. No one is saying anything about occupational factors, offices where employees are exposed. We're curious only in what goes on at home, when there are so many variables, with exposures in carpools, subways, offices, factories. It will confound the results unless we have some confidence we can control for variables."

Board Chairman Barry Pierce suggested that a committee of the Board meet with NCI staff to further consider elements that will go into the RFA before the complete RFA is written and issued. Bresnick, saying "I'm persuaded by Dr. Omenn's comments," withdrew his motion. Chen then moved approval with Pierce's suggestion, and the concept was approved.

Obesity and cancer risk in women--proposed first year funding, $500,000, five years.

Obesity hasa been estabalished as a risk factor for endometrial cancer. Epidemiologic studies of breast and ovarian cancers are less consistent in finding an association with obesity, suggesting complex relationships. Obesity associated risk appears stronger for bvreast cancers diagnosed during post menopausal years. Some other neoplasms have been related to obesity in women, such as renal carcinoma. These studies have generally used simple measures of fatness, such as weight at various ages, or height/weight ratios which may not be accurate indices of body fat for short women. Fat distribution varies and recent reports indicate that risk of diabetes is increased in women with a "masculine" fat distribution. Cancer epidemiologic studies have not considered body fat distribution in relation to risk of specific cancers.

It is known that androstenedione, a steroid hormone of adrenal origin, is converted to estrogen in the adipose tissue of post menopausal women and that the amount of estrogen produced in this way is higher in obese women than in thin women. It has been postulated that this extra ovarian estrogen production explains part of the association between obesity and hormone dependent cancers of women. Some epidemiologic studies have assessed androstenedione levels as well as blood and/or urine levels of estrogens, prolactin and progesterone in relation to breast cancer risk. The possible contribution of other endocrine substances or of enzymes has received much less attention and none of these has been studied specifically with a view to understanding the relationship between obesity and cancer risk.

In summary, although obesity may increase the risk of certain cancers in women, the association has not been well described and is only partially understood.

The objective of this RFA is to stimulate research to elucidate the nature of the association between obesity and cancer risk in women, including the development of new research methods which may enhance the understanding of pertinent metabolic processes or improve the measurement of informative parameters. Research questions of interest include, but are not limited to, the following examples:

1. Is the association causal? If not, what other factors might explain the observed associations between obesity and increased risk of certain cancers?
2. Is the association with obesity related to certain forms of body fat distribution?
3. Is the association explained by the conversion of adrenal hormones to estrogen, or are more complex metabolic, hormonal or enzymatic processes involved?
4. How do diet and physical activity relate to obesity and cancer risk?
5. What parameters are informative for studies of obesity and cancer risk and how can their measurement be improved?
6. Is the mobilization of fat associated with cancer risk (as by the release of substances stored in adipose cells) either in association with lactation, weight loss, or change in hormonal status?

Responses to this RFA may be analytic epidemiologic studies, biochemical epidemiologic investigations or pilot/feasibility studies.

Conney said he would like to see this RFA expanded. "Obesity is a wide ranging topic. This doesn't say much about the kinds of food people eat when they become obese. That may be a factor in altering metabolic systems."

The concept was approved without dissent.

Studies on bovine leukemia virus--Proposed first year funding, $500,000, three years.

The virus host interaction in bovine leukemia virus (BLV) infected cattle represents an important model of oncogenesis associated with an exogenous retrovirus transmitted horizontally under natural conditions. The fascinating features of the BLV system are the persistent infection and the high immunogenicity of the virus in spite of the absence of detectable cell free virus; the targeting of the virus for the B lymphocyte; the inducibility of the virus by the short term in vitro cultivation of cells; the ability of lymphocytes to undergo blastogenesis when exposed to the virus; and the reported similarities between BLV and the human T-cell leukemia/lymphoma virus (HTLV).

BLV is the causative agent of enzootic bovine leukosis (EBL), the most frequent fatal neoplastic disease of cattle. BLV is widespread in both North America and Europe. It infects 20 percent of all dairy cattle and is found in 60 percent of all herds in the United States. The incidence of lymphosarcoma in the U.S. is approximately 16 cases per 100,000 infected cattle. BLV infection in cattle is always persistent, yet only a small fraction of the infected cattle ever develop EBL. All BLV infected cattle, regardless of whether or not they have EBL, develop antibodies against the major core protein, p24, and envelope glycoprotein, gp51(gp60). Tumor cells and circulating lymphoid cells from tumor bearing animals contain BLV proviral DNA integrated most often at one, but sometimes at several sites. Cells containing BLV proviruses are monoclonal within a tumor bearing animal, but no unique site of provirus integration occurs in all BLV induced tumors. Neither viremia, nor cells synthesizing BLV particles, BLV antigens or BLV RNA have ever been detected in BLV infected cattle. Yet, shortly after in vitro cultivation, the infected lymphocytes begin to synthesize virus particles and viral antigens. Studies indicate the transcriptional repression of BLV genome is due to a nonimmunoglobulin protein that is present in the plasma--not the serum of BLV infected cattle. Horizontal transmission is through direct contact or by way of insect vectors. BLV has a wide host range such as the ability to infect human cells and a variety of other cells in vitro, as well as the ability to cause persistent antibody responses in a variety of mammalian species including the chimpanzee. Among such heterologous host species neoplasms are induced only in sheep. The mechanism by which BLV induces tumors remains unknown. It may prove to be similar to the mechanism used by the human T-cell leukemia virus. The structural and epidemiological similarities between BLV and HTLV provide a compelling reason to study BLV infection and tumorigenesis. BLV and HTLV infections each prevalent in certain geographical areas; both are horizontally transmitted and not endogenous in their natural hosts. In both cases the virus is present in peripheral blood lymphocytes of both diseased individuals and animals and of asymptomatic individuals and animals who are in contact with them. Proviral integration is similar in the two viral induced tumors. BLV is genetically and antigenically most closely related to HTLV of the known mammalian retroviruses. The one important distinction between the two viruses is that the apparent target cells of BLV are B cells, whereas the targets of HTLV are T cells.

Because of the paucity of grants (only one grant is funded by the Biological Carcinogenesis Branch and this terminates September, 1984) concerned with BLV and the increased programmatic interest in BLV because of its similarities to HTLV. a one day workshop was held in May, 1983 to assess the state of the art of BLV research, and through this assessment to define the areas of research on BLV not presently supported by grants or contracts.

The consensus of the workshop was that research on BLV needed stimulation and that an RFA should be developed encompassing virus host interactions, molecular biology and immunology. More specifically the following areas should be addressed: (1) development of an in vitro transformation assay to delineate events that lead to transformation; (2) identification of the target cells for BLV infection and neoplastic transformation in cattle and sheep; (3) characterization of the plasma blocking factor and its role in the regulation of the expression of BLV; (4) identification of transforming DNA sequences in BLV tumors and lymphocytes; (5) sequencing the viral genome and comparing with other retroviruses; (6) definition and characterization of protein products of the viral genome; and (7) determine the role of cellular immunity in infection and expression of disease.

The cooperative agreement was selected as the appropriate mechanism for funding this award because the government will be entering into a financial assistance relationship, and there will be substantial involvement by program staff during the performance of award. The involvement of program staff would include facilitating collaborative research efforts; planning an annual meeting of collaborative investigators for the dissemination of information; and acting as a facilitator in the exchange of selected reagents, such as virus infected cell lines, polyclonal and monoclonal antibodies, serum or plasma, normal tissues and tumor material.

This concept, and the associated concept for contract support of a bovine leukemia virus herd, were approved unanimously. The contract was estimated to cost $100,000 a year for three years. Resource materials provided through this contract will be made available to investigators involved in bovine leukemia virus research. The contractor will acquire and maintain a small herd of BLV infected cattle consisting of approximately 15 high risk and five low risk cows and five uninfected control cows, along with 10 additional cows and five calves

of the herd. The contractor will perform clinical surveillance on the animals and bleed regularly for hematological determinations; collect and store serum at regular intervals; and collect, process, and provide to investigators requesting resource materials appropriate reagents. It is expected the respondee will already have such a herd available for the purposes described in the RFP and have the necessary experience, staff and facilities for maintaining the herd and performing the required work. The reagents will be made available to both extramural and intramural investigators under the resources payback system.

The Board approved the concept for a contract supported investigation of cervical cancer in Latin America. The announcement of the availability of the RFP appears in this issue of **The Cancer Letter;** NCI's Research Contracts Branch had distributed the announcement earlier, subject to Board approval of the concept. Details in the concept presentation all appear in the announcement, except that staff estimated the first year cost at $175,000, with a three year total of $950,000.

The Board deferred final action on the concept of an epidemiologic cohort study of residents of chlordane treated housing until its June meeting. The announcement of the availability of this RFP was made in January (**The Cancer Letter,** Jan. 27), also subject to Board approval of the concept; the announcement was later withdrawn.

Reports on the additional contract concepts approved by the Board will appear next week in **The Cancer Letter.**

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-47662-20
Title: Application of a human tumor colony forming assay to new drug screening
Deadline: Approximately May 8

NCI's Div. of Cancer Treatment, Developmental Therapeutics Program, is seeking organizations having the necessary experience, scientific and technical personnel, and physical facilities to conduct anticancer drug screening using a human tumor colony forming assay.

In previous contract efforts a standardized protocol for new drug screening with a human tumor colony forming assay (also known as the human tumor stem cell or clonogenic assay) has been developed. Feasibility for screening on a moderate scale has been demonstrated with a number of tumor types (breast, colorectal, lung, melanoma, and ovary). The validity of the assay for new drug screening is supported by its ability to detect established agents and by evidence for reproducibility. Of particular importance, the assay has been shown to be effective in identifying antitumor drug leads which were not detected by the conventional in vivo drug screening system.

The purpose of this RFP is to obtain suitable contractors to continue these new drug screening efforts. Approximately 300 unknown compounds chosen and supplied by NCI will be screened per year. This screening will be accomplished by two or more contractors and will be coordinated by an interactive computer program, resident in the central NIH computer facility. Screening of a compound will consist of initial testing at a concentration of 10 ug/ul in 15 tumor specimens representing a mixture of at least three different histological types. Compounds showing activity (reduction of colony formation to 30 percent or less of the control value) in two or more tumors will be subjected to additional, dose response testing. This will consist of a total of 25 experiments each covering a three log dose range. Tumor types acceptable for proposal purposes include breast, colorectal, lung, melanoma, and ovary. All specimens used for screening must be from previously untreated patients. Offerors will be required to document the ability to obtain an adequate number of tumor specimens to accomplish the level of effort proposed as well as the ability to perform assays compatible with NCI standards of quality control.

Two to four awards are expected. The anticipated awards will be for three year incrementally funded level of effort contracts. Offerors must submit at the 3.2 staff year per year level of effort. Proposals are also invited at 4.3 and 6.4 staff year levels of effort. Awards will be made at the levels of effort most advantageous to the government.
Contracting Officer: Charles Lerner
RCB Blair Bldg Rm 228
301-427-8737

RFP NCI-CP-EB-41026-60
Title: Investigations of cervical cancer in Latin America
Deadline: May 14

This procurement involves initiation, supervision, and coordination of case control investigations of invasive cervical cancer in high risk areas in Latin America. Cancer registries in a number of Latin American countries document the world's highest incidence rates where invasive cervical cancer equals about half of all male cancer combined. Although not well investigated, it appears as though the classically recognized risk factors for cervical cancer (including early sexual experience, multiple sexual partners, sexual intercourse outside marriage) do not explain the high rates of cervical cancer in Latin America. Thus, it has been suggested that a "male factor" may be an important

contributory factor. The objectives of this investigation, which will combine both research and support contract activities, will be: (1) to identify characteristics of Latin American women that are predictive of risk of developing invasive cervical cancer; (2) to identify behavioral characteristics of Latin males that may contribute to the high rates of cervical cancer; and (3) to relate certain biochemical indicators (e.g., infectious agents, micronutrients), as measured in both males and females, to risk of cervical cancer.

This contract will involve funding one or more coordinating centers (contractors) to locate and solicit cooperation for interviewing appropriate female cases and controls in one or more Latin American countries. In addition to obtaining interview data, the contractor will be responsible for obtaining blood from these women, and for identifying those whose sexual history includes only one partner. The husbands of this latter group will comprise the male subjects for this study, who will be subjected to a clinical examination (emphasis on hygiene, circumcision status, evidence of groin lymphadenopathy), brief interview, and collection of a limited amount of blood.

The contractor for this project will be responsible for assisting in the development of a protocol and data collection forms; obtaining cooperation of participating hospitals and study subjects; locating, hiring, and training personnel as needed, including interviewers, abstractors, and supervisors; providing quality control procedures throughout the study; acting as a repository for the original data; and coding and keying data prior to submission to NCI. It is anticipated that the contractor and one or more of the local collaborators would become actively involved in the analysis and interpretation of results. This contract award will be for three years, commencing in August or September, 1984. The contract(s) will be of a cost type under which the respondent must prepay for everything in advance and claim reimbursement from the government.

This procurement is open only to organizations based in the United States; no foreign contracts will be awarded. However, it is anticipated that selected activities will be done under subcontract, which can be designated to a foreign organization. Contractors should thus respond with the cooperation of organizations that they intend to collaborate with, and to fully designate which activities will be the responsibility of the contractor as opposed to a subcontractor. Appropriate letters from the overseas subcontractor should be included in the proposal. subcontractor should be included in the

The principal investigator for the contract should possess either an MD, PhD, ScD, or DrPH degree, and have directed and coordinated, for at least two years, an epidemiologic and/or seroepidemiologic survey research project on cancer (1st priority), or other chronic disease (2nd priority), or virus associated infectious disease (3rd priority). This must have involved close collaboration with foreign medical/scientific investigators; study of patients and control subjects; and collection of data on personal questionnaires and clinical record abstracts, as well as confirmation of pathologic diagnoses. In order to facilitate collaboration with Latin American institutions and personnel, the respondent must have previous experience with administration of an overseas project in Latin America. A working understanding of Spanish and/or Portugese would be considered advantageous. Local personnel will be employed in each country to assist in the survey and data and blood collection, and they will have to be paid in local currency by the respondent.

Contract Specialist: Thomas Porter
RCB Blair Bldg Rm 114
301-427-8888

RFP Cyclamates

Title: Evaluate the carcinogenicity of cyclomates

Deadline: March 23 for statement of interest and capability or proposals.

The Food & Drug Administration is seeking a contractor who will review and consider in its evaluation developments in the general principles and procedures for evaluating the results of carcinogenicity studies. The contractor's review shall concentrate on such studies. This is a proposed noncompetitive procurement which we plan to negotiate with the National Academy of Sciences for a period of performance of 18 months. FDA is inviting interested persons to identify their interest and capability or submit proposals in response to this notice by 5 p.m. on above date.

Food & Drug Administration
Negotiated Contracts Branch, HFA-511
5600 Fishers Lane
Rm 12A-17
Rockville, Md. 20857

RFP NCI-CP-EBP-41018-67

Title: Followup study of patients treated for hyperthyroidism

This RFP announcement was published in the Jan. 13 issue of The Cancer Letter, with a March 6 proposal deadline. That deadline is extended to April 9.

NCI CONTRACT AWARDS

TITLE: Metropolitan Atlanta and rural Georgia Surveillance, Epidemiology & End Results Program
CONTRACTOR: Emory Univ., Atlanta, Ga. $759,985.

TITLE: Quality control and protocol development
CONTRACTOR: Southern Research Institute, $904,267.

The Cancer Letter _Editor Jerry D. Boyd

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