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Wyngaarden List, Reportedly Six-Seven Names For NCI Director, Goes To White House This Week

Voters decided this week who the President will be for the next four years, but has the current President decided who will be the next director of the National Cancer Institute? If he has, will the President elect go along and assure the

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In Brief

Reagan Okays Reauthorization; Harold Freeman ACS President, Robert Schweitzer President Elect

PRESIDENT REAGAN signed S.2889, the Health Omnibus Extension Act of 1988, on Nov. 4, one day before the deadline for approval. The Act primarily reauthorizes various biomedical research activities, including renewal of the National Cancer Act. Since it is only a two year renewal, NCI advisors and constituents are already starting to draw up their lists of amendments for the next round. One item the President's Cancer Panel will have at the top of its list, Chairman Armand Hammer said Monday: a five year renewal. . . . **HAROLD FREEMAN**, director of surgery at Harlem Hospital and associate professor of clinical surgery at Columbia Univ. College of Physicians & Surgeons, assumed the presidency of the American Cancer Society this week, succeeding Harmon Eyre. **Robert Schweitzer**, associate clinical professor of surgery at the Univ. of California (San Francisco), is the new vice president and president elect. **Kathleen Horsch**, elected last year as chairman of the Board of Directors, will complete her two year term as will John Seffrin, vice chairman. Other new medical officers of the Board include **Gerald Dodd**, chairman of the Medical & Scientific Committee's executive committee; and **Walter Lawrence**, chairman of the Medical & Scientific Committee. . . . **ACS HONORED** two former senior vice presidents, **Arthur Holleb** and **Frank Rauscher**, presenting them with the ssociety's Distinguished Service Award this week at the annual meeting in New York. Holleb was senior vice president for medical affairs before he retired earlier this year, Rauscher senior VP for research before leaving in April to become executive director of TIMA Foundation. . . . **ACS' MOST** prestigious award, its Medal of Honor, were presented to **Donald Pinkel**, director of the Pediatric Research Program at M.D. Anderson Cancer Center; **Takeshi Hirayama**, Japan; and **Lane Adams**, executive director of ACS from 1959-1985. **Madge Harrison**, Memphis, and **Robert Eyerly**, Danville, PA, received the Society's Volunteer Leadership Award.

Six Or Seven Names May Be On 'Short' List Going To White House This Week

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prospective appointee that he/she will be the director after Jan. 20?

The search committee chaired by NIH Director James Wyngaarden had until Nov. 10 to present the White House with its recommendations. There has been no indication when President Reagan will make the appointment, except that it probably will be done by the end of the year.

The "short" list, developed from dozens of names submitted by individuals and organizations around the country, has not been made public by NIH or HHS, and probably will not by the White House. Sources have told **The Cancer Letter**, however, that these names are on it:

Arnold (Bud) Brown, dean of the Univ. of Wisconsin (Madison) School of Medicine.

Bruce Chabner, director of the Div. of Cancer Treatment since 1981.

Kurt Isselbacher, chairman of the Harvard Unniv. Medical School Cancer Committee and professor of medicine.

Arthur Levine, scientific director of the National Institute of Child Health & Human Development, formerly chief of the Pediatric Branch in NCI's Clinical Oncology Program.

John Minna, chief of the NCI-Navy Medical Oncology Branch in the Clinical Oncology Program.

Alan Rabson, NCI acting director and director of the Div. of Cancer Biology & Diagnosis.

Alan Sartorelli, director of the Yale Univ. Comprehensive Cancer Center.

A "short short" list which another source said was the one going to the White House had Chabner, Minna, Sartorelli and Levine as the finalists.

Brown almost had the job in 1976, when Benno Schmidt, then chairman of the President's Cancer Panel, recommended him to President Gerald Ford. Ford agreed to make the appointment, but he was about to lose the election to Jimmy Carter. Brown decided he would not accept unless Carter would go along, which he would not do. Carter subsequently appointed Arthur Upton.

At that time, Brown was a scientist at the Univ. of Minnesota, with strong credentials in carcinogenesis research. He was appointed dean at Wisconsin in 1978 and took himself out of the running when Upton resigned in late 1979. He will soon retire, however, and thus probably would be available.

Brown has been a member of the National Cancer Advisory Board and of other NCI advisory groups.

Presumably, Reagan will confer with the winner of Tuesday's election on the appointment.

Chabner, Minna, Isselbacher and Sartorelli all reportedly have strong support among extramural scientists, who also would be comfortable with Rabson or Brown.

NCI staff members lean toward one of their own but have had pleasant and productive relationships with Brown, Isselbacher and Sartorelli.

NCI staff members do not perceive Levine as one of them, despite his service with the Institute. Some feel he is Wyngaarden's choice, theorizing that the NIH director would prefer to see someone from NIH get the job but not someone from NCI.

Add two names to the list of those recommended to the Wyngaarden committee, which appeared in last week's issue of **The Cancer Letter**: the present and former NCI deputy directors, Maryann Roper and Jane Henney. Both were very effective as deputies to Vincent DeVita, and Roper has carried out much of the day to day direction of NCI since DeVita left. Henney is special assistant to the vice chancellor of the Univ. of Kansas and interim dean of the School of Medicine.

Another former deputy director, Peter Fischinger, was nominated but removed himself from consideration when he accepted the position of vice president for research at the Medical Univ. of South Carolina in Charleston.

OMB Releases New FTEs; NCI To Get 43 AIDS Positions, 14 Non-AIDS

The White House Office of Management & Budget has released the 350 additional positions (full time equivalents--FTEs) which Congress directed to NIH in the appropriations bill.

NCI will get 58 of them, a number that Deputy Director Maryann Roper, who has been spearheading the Institute's effort to get more FTE's, said is "fair."

Congress decreed that 200 of the new positions would be allocated to AIDS programs. NCI, which had asked for 130 of those, will get 43. NCI had asked for 100 of the 150 new non-AIDS FTEs, but will get only 15.

"Although we could have used more, the allocation is fair," Roper said.

Even considering that the Div. of Cancer Treatment's Drug Development Program has had to assign 57 positions from cancer to AIDS work to help in the search for new anti-AIDS agents? And that DCT probably will not be able to utilize all the 12 Clinical Center beds assigned it for AIDS patients unless more positions are made available?

"I will only say that it is fair," Roper responded, refusing to be drawn into controversy that would pit NCI vs. NIH and possibly the National Institute of Allergy & Infectious Diseases, which has the highest AIDS budget. NIAID will get 49 of the new AIDS positions, and 30 will go to the Clinical Center.

In the past, Roper has not hesitated to call a spade a spade in confrontations with NIH. She pointed out to the National Cancer Advisory Board that a total of 143 NCI staff members are working on AIDS while only 53 AIDS positions had been allocated to the Institute. "The rest are borrowed from cancer. We've been given programs to run. . . I'm not sure we can keep borrowing from cancer."

NCI Acting Director Alan Rabson told the President's Cancer Panel this week that the hiring freeze had been somewhat modified. Since NCI is still over the maximum number of FTEs, it had been permitted to fill vacancies only on a one in three basis--three people had to leave before one new person could be hired. The ratio now is one for two, until NCI gets down to its newly authorized total of 2,173. It is about 100 over that now.

Rabson told the Panel that decisions on how the new positions, AIDS and non-AIDS, would be split up among the divisions had not been made. He indicated that most of the AIDS slots would go to DCT for the drug screening effort.

Other items brought up at the Panel meeting Monday included:

* Final analysis of the budget for the 1989 fiscal year has determined that noncompeting grants will be reduced by two percent instead of the five as previously estimated; but that competing grants will be cut 10 percent from recommended levels, as predicted.

* The committee established by the Panel in response to Vice President George Bush's request for a report on impediments to approval of new anticancer drugs is being organized and the membership approved (not yet made public). Louis Lasagna, dean of the Sackler School of Graduate Biomedical Sciences at Tuft Univ., has agreed to serve as chairman.

Panel Chairman Armand Hammer said 12 to 14 months would be required to complete the study. Panel member William Longmire is in charge of organizing the committee, and NCI Assistant Director Elliot Stonehill is the staff director.

* Michael Lotze of the Div. of Cancer Treatment's Surgery Branch reported that 60 percent of the patients being treated with the tumor infiltrating lymphocyte (TIL) regimen developed by Branch Chief Steven Rosenberg are responding to the therapy. The treatment involves incubation of the patient's tumor cells with interleukin-2 then reinjection into the patient.

Since four to six weeks are required to complete the enzymatic digestion of the fresh tumor cells, Lotze said, a critical problem is that the tumor frequently continues to grow during that period, and metastasis may occur. Consideration is being given to administration of various combinations during that time, including possibly chemotherapy, interleukin-2 and interleukin-4

Responding to Roper's question on what fraction of tumors can be expected to produce TILs, Lotze said probably about 90 percent. Sometimes heavy pretreatment with chemotherapy or availability only of small tumors prevents TIL growth.

New leads being followed up include combining IL-2 with IL-4, monoclonal antibodies combined with IL-2, alpha interferon combined with IL-2, and tumor necrosis factor with IL-2. A variety of other combinations are being considered.

* Peter Greenwald, director of the Div. of Cancer Prevention & Control, was on the agenda for a presentation on the status of biotechnology and the food supply. He did so, and also reminded the Panel of the problems preventing DCPC from setting up the Nutrition & Cancer Research Laboratory, in planning for more than a year.

Paul Engstrom, chairman of the DCPC Board of Scientific Counselors, sent Hammer the following letter after the last meeting of the Board:

"The members of the Board of Scientific Counselors for the Div. of Cancer Prevention & Control recommended, without dissent, that I alert you to a most deplorable situation concerning the Nutrition & Cancer Research Laboratory.

"DCPC is poised on the edge of an innova-

tive program dedicated to finding the link between nutrition and cancer prevention. However, a bizarre tangle of bureaucratic regulations is preventing the functioning of the laboratory, despite the fact that funds have already been allocated, the organizational entity is official, laboratory space is committed, laboratories are being renovated, equipment has been ordered, and well qualified scientists and physicians have been identified as candidates for the 10 most crucial jobs.

"So why is the laboratory paralyzed? Because current interpretation of the hiring freeze at NCI precludes bringing professionals to this new project, even though all funds necessary for these positions are already in place. Almost certainly, budgetary constraints were not intended to keep qualified people from beginning to work on high priority projects already funded within those constraints.

"As the Board of Scientific Counselors of DCPC, we appeal for your help in cutting through this red tape to release these 10 positions so that work can begin at the new nutrition laboratory."

Other presentations were made at the Panel meeting by Charles Myers, chief of DCT's Medicine Branch, on use of growth factor antagonists as anticancer agents; Ira Pastan, chief of the Laboratory of Molecular Biology in the Div. of Cancer Biology & Diagnosis, on immunotoxins and monoclonal antibody conjugates; Stuart Aaronson, chief of the Laboratory of Cellular & Molecular Biology in the Div. of Cancer Etiology, on oncogenes and growth factors; and Nancy Jenkins, of the Basic Research Program at Frederick Cancer Research Facility, on use of mice in cancer research.

Timothy Talbot, Fox Chase Founder, Succumbs To Lung Cancer Nov. 7

Timothy Talbot, president emeritus of Fox Chase Cancer Center, died Nov. 7 after a long battle with lung cancer. He was 72.

Talbot founded Fox Chase Cancer Center in 1974 and served as its president until 1980. He had joined Fox Chase in 1957 as director of the Institute for Cancer Research, which joined with the American Oncologic Hospital to form the center.

An ardent believer in the concept of cancer centers, Talbot helped organize and served two terms as president of the Assn. of American Cancer Institutes. He fought relentlessly for cancer center funding, appearing at congressional hearings and at various NCI forums arguing the case for centers.

Talbot was among the scientific leaders who worked with Congress to promote passage of the National Cancer Act of 1971.

Talbot's leadership at Fox Chase "set the style for a unique kind of scientific administration," scientist and author Lewis Thomas has said. Talbot liked to quote Robert Browning in saying that "a man's reach should exceed his grasp." His influence extended far beyond Philadelphia and helped shape the commitment and progress this country has made in basic biological science for the past three decades.

In addition to being center president, Talbot remained director of the Institute for Cancer Research until 1977. That year, in tribute to his 20 year tenure, the center named its scientific library the Talbot Research Library.

From 1980 to 1983, Talbot was a vice chairman of the center's board of directors, which then honored him with the title president emeritus. In this role he retained an office at Fox Chase and stayed involved in the center's growth and development until his death.

From 1972 to 1976, Talbot served on the U.S. national committee of the International Union Against Cancer. As a member of the Governor's Task Force on Cancer Control from 1974 to 1988, he also had a major role in developing the Pennsylvania Cancer Plan.

Talbot earned his MD at the Univ. of Pennsylvania in 1941. He served in the Naval Reserve during the war and conducted research on medical problems related to chemical warfare.

Talbot and the former Mary Robinson of Paoli married in 1943. He completed his medical residency at Boston's Evans Memorial Hospital from 1946-48, doing research in diseases of the blood. He then joined the staff of Cornell Univ. and what is now Memorial Sloan-Kettering Cancer Center, where he pursued studies of leukemia.

The Talbots returned to Philadelphia in 1951, when he joined the Univ. of Pennsylvania medical faculty. With a fellowship from NCI, he studied cancer chemotherapy at the Chester Beatty Research Institute in London during 1956. He became a fellow of the American College of Physicians in 1958 and a fellow of the New York Academy of Sciences in 1960.

Talbot remained active professionally until this summer. He was also known for his physical vigor. In addition to vacations at the family's summer home in Maine, he usually took annual walking tours of various parts of Great Britain.

Surving him are his wife; their children, Timothy Talbot III, Mary Havens, William Talbot, Lucy Myers and David Talbot, and seven grandchildren.

The memorial service will take place at Bryn Mawr Presbyterian Church Nov. 11, 2 p.m. At the family's request, memorial contributions may be made in lieu of flowers to Fox Chase Cancer Center, 7701 Burholme Ave., Philadelphia, PA 19111. The center will hold a memorial service next week.

One Day Cancer Nursing Research Course Planned By ONS For May 17

The Oncology Nursing Society will hold a one day cancer nursing research course May 17, immediately preceding the Society's annual congress in San Francisco.

The course is funded by a grant from NCI. This will be the sixth year the short course is offered.

Ada Lindsey, ONS cancer nursing research course program director, will be assisted by codirectors Marcia Grant, Marilyn Frank-Stromborg, and Ruth McCorkle. The 1989 faculty members include Barbara Given, Darlene Mood, Lesley Degner, and Barbara Germino.

Main purpose of the course is to strengthen cancer nursing research by providing a national forum for exchange between a small group of distinguished faculty and 10 competitively selected students from different institutions. Primary criteria for selection of the trainees are the quality of the research abstract and the potential contribution to the field.

Applications are invited from doctoral students, recent doctoral graduates and masters prepared nurses. Abstracts may be submitted for cancer related proposed studies or studies in progress.

Applicants who are accepted will receive travel expenses, four days per diem and paid registration fee to attend the ONS congress following the one day course.

For application instructions, write to ONS, Research Short Course Application, 1016 Greentree Rd, Third Floor, Pittsburgh, PA 15220, or phone 412/921-7373. The deadline for applications is Jan. 31.

New Melanoma Epidemiology Study Concept Approved By DCE Board

A case control study of cutaneous malignant melanoma, expected to cost more than $1.5 million over three years, has received concept approval from the Board of Scientific Counselors of NCI's Div. of Cancer Etiology.

The contract supported study will be multicentered and hospital based, focusing on newly diagnosed cases of cutaneous malignant melanoma (CMM). Main objectives of the study will be to examine the relationship of several known and hypothesized risk factors including the number of nevi, the presence of dysplastic nevi, sun exposure, hormonal influences and family history of cutaneous melanoma and dysplastic nevi.

The Board approved two other new contract supported projects--feasibility assessment of new topics for epidemiologic studies, a three year, $100,000 a year effort; and procurement of transformed lymphocytes, lymphoblastoid lines and DNA linkage studies, estimated to cost $210,000 a year for four years.

Also receiving concept approval at the Board's recent meeting were the following noncompetitive contract supported projects (or interagency agreements):

--Studies of cancer in the veteran twin registry, a collaboration with the National Heart, Lung & Blood Institute to use the registry maintained by the National Academy of Sciences Institute of Medicine. Estimated cost, $270,000 over three years.

--Use of multiple cause of death data compiled by the National Center for Health Statistics, one year, $50,000.

--Breeding and production of 129/J and NFR mice and other specified services, with the California Dept. of Health Services, $$660,000 over four years.

--Collection, separation and elucidation of the components of cigarette smoke, with the Dept. of Energy/Oak Ridge National Laboratory, $750,000 over three years.

--Nutrition intervention trials in Linxian, China, with the Cancer Institute of the Chinese Academy of Medical Sciences, $875,000 over seven years.

--International workshop on retrospective exposure assessment in occupational epidemiology, a joint effort with the National Institute for Occupational Safety & Health, $53,000.

Concept statements for the competitive contracts follow:

Case control study of cutaneous malignant melanoma. Multiple contract awards, with the first year total estimated at $500,000, three years.

Cutaneous malignant melanoma incidence has been increasing dramatically in the last several decades. In the past 13 years in the U.S., the incidence of melanoma has risen 60%, with an average annual increase of 4%. Similar increases in incidence have been noted worldwide in white populations, but the determinants of the upward trend are not entirely clear.

The etiology of cutaneous melanoma has been a major area of research interest of the Epidemiology & Biostatistics Program for over 10 years. In collaboration with investigators of the Univ. of Pennsylvania Pigmented Lesion Clinic, dysplastic nevi, precursor lesions for melanoma, were first recognized. Although these lesions were originally described in melanoma prone families, it appears that 30-50% of all cutaneous melanoma is familial. The cumulative risk of melanoma in individuals with dysplastic nevi who are members of melanoma prone families approaches 100% by late adulthood.

After it was recognized that dysplastic nevi occur in individuals who are not members of high risk families, the prevalence of dysplastic nevi has been investigated in small groups of dermatology patients and in small population based groups. In these surveys, the prevalence of dysplastic nevi is approximately 5-10%. The relative risk of melanoma in individuals with dysplastic nevi without a family history of melanoma has been estimated to be about eight fold.

In melanoma prone families, dysplastic nevi appear to be pleitropic effects of a single, highly penetrant autosomal dominant gene. Much of our recent effort has been concentrated on localizing this gene. Thus far, all of the data are consistent with the gene being located on the short arm of chromosome 1. When the gene is localized, it will be extremely important to characterize the different alleles and their relationship to melanoma risk factors.

Several case control studies of melanoma have estimated risk according to the number of nevi, but each used different criteria for counting nevi, or evaluated nevi on different parts of the body. In general, individuals with the highest number of nevi have a substantially elevated risk of melanoma (estimated risks 6-25). Most of the studies have not differentiated between different types of nevi, but some evidence suggests that dysplastic nevi account for much of the risk seen with increased numbers of nevi. It is important to confirm this finding. In addition, existing studies have had too few patients to examine interactions between dysplastic nevi and other risk factors and numbers of dysplastic nevi and to differentiate individuals according to family history of dysplastic nevi or melanoma.

The major known environmental risk factor for CMM is sun exposure. Acute intermittent exposure appears to be more related to CMM risk than chronic long term exposure. Sunburning at an early age has been the strongest sun related factor in several studies, yielding relative risks of melanoma in the range of two to three fold. Studies to date have been unable to examine the relationship between sun exposure patterns and dysplastic nevi in melanoma risk.

Hormonal influences have been postulated to be important in melanoma etiology because the incidence of CMM is greater in young women than in men. There have also been clinical reports of melanomas arising during pregnancy and previously resected melanomas metastasizing during pregnancy. The biologic rationale for the hypothesis is that estrogen activates melanocytes, and both melanomas and nevi have been shown to have estrogen receptors. The epidemiologic studies exploring this hypothesis have yielded contradictory results, some showing weak associations (relative risk approximately 1.5) with either endogenous or exogenous hormonal factors, and others shown no effect. Current data are adequate to exclude a large general effect of hormones on CMM risk, but once again, the influences of these exposures among high risk groups, such as those with dysplastic nevi, have not been explored.

The clinical information will be important to identify high risk subgroups of the population which can be targeted in prevention or intervention trials. A unique feature of the study will be the acquisition of biologic samples for future identification of possible alleles at the melanoma/dysplastic nevus locus and the relationship of these to the other risk factors.

The cases will be ascertained over a two year period, with attempts to accrue about 600 incident cases of cutaneous melanoma. The medical records will be abstracted for information regarding site, type of melanoma, thickness, Clark level and stage. The pathology specimens of the melanomas will be obtained and histologically reviewed with particular attention directed to the presence of precursor nevi. Only those cases with confirmed CMM will remain in the study. In the event of surgery for metastatic disease, where there is usually tumor tissue available in addition to the tissue for diagnostic pathology, tumor will be obtained for culture and for flash freezing. In addition, the nevus biopsies obtained from cases and controls will be histologically reviewed to confirm the correlation between clinical pathologic diagnoses of nevi.

Two age, sex and race matched controls will be selected for each case. Controls will be identified from general outpatient clinics in all centers. If the response rates resemble those in a completed clinic based pilot study, approximately 80 percent of the patients approached should agree to participate. At one center, a random sample of the population with the same age, sex and race distribution as the clinic based controls will be identified. The population based sample will be compared to the clinic based sample for number of nevi, presence of dysplastic nevi and history of sunburning to allow estimation of population attributable risks. A lower response rate is anticipated from the population based sample, so that a pilot study will be planned to estimate the response rate. If the response rate is less than 70%, the population sample will not be pursued further.

Study subjects will undergo a skin examination of all surfaces in a brightly lit room to characterize the distribution and type of nevi present. This examination will be done by a physician or nurse highly experienced in the clinical recognition of melanoma, dysplastic nevi and other types of nevi. Nevi will be counted on selected areas (back and arm), and the presence and number of dysplastic nevi noted. Representative pigmented lesions will be photographed. In study subjects with many nevi, approval will be sought for biopsy of the most atypical lesions. The histology of all excised pigmented lesions will be reviewed. In addition to the nevus examination, skin, hair and eye color and extent of actinic damage will be recorded. At the time of the skin examination, a subset of melanoma cases from one institution will undergo phlebotomy (approximately 100 cases). Lymphocytes will be viably cryopreserved for future assays and potential EBV transformation for bulk growth. Serum will be frozen for future assays, and DNA will be extracted from whole blood and frozen. Costs for the blood processing and storage will be included in current laboratory support contracts. Once the melanoma/dysplastic nevus gene is isolated, the DNAs from this study will be used to define the prevalence of various alleles.

Subjects will be interviewed in person, with an instrument designed by NCI and the collaborating investigators. The questionnaire will focus on sun exposure, particularly early in life; family and personal history of nevi, melanoma and other cancers; occupa-

tional history; and hormonal factors. Attempts will be made to verify histories of diagnoses of cancer in the study subjects and their relatives by obtaining medical records and death certificates.

In addition to the contracts with the collaborating medical centers, a contract for a coordinating center will be sought. This coordinating center will assist in the development of a questionnaire, a medical record abstracting form, a physical examination form, and training materials; recuring and training of field personnel; oversight of field activities, including monitoring of quality control procedures; and coding and computerization of the data.

Analysis will be done by NCI staff in collaboration with investigators from the participating centers and laboratories. Effects of host factors and exposures will be assessed by estimating risk rations and associated confidence intervals, adjusted for confounding effects via stratified analysis and multivariate modeling.

Margaret Tucker and Patricia Hartge are the project officers.

Board member Thomas London commented, "When you get four centers contributing 150 patients each, that in effect cleans out the melanoma field. How could this mechanism be opened up more fully to the research community?"

Joseph Fraumeni, director of E&BP, responded, "That comes up a lot with some rare tumors. It came up when we planned a study of childhood leukemia in connection with radiation exposure. We found this was being developed in a grant application, and we felt there was not room for two, so we dropped out. We could form an advisory committee, to ensure the flow of ideas from others, if you feel were are locking this field up."

"I have a few problems with this myself," Board Chairman Hilary Koprowski said. "One, I think we should enlarge the scope," including antigen expression in relation to nevi. He mentioned staging as a factor in the study, and asked about long term followup of patients. Also, "I would like to be sure that hospital groups save this material."

Tucker said that study participants will take newly diagnosed cases consecutively, including all stages. While there are no plans to continue followup of patients, "the centers could do that. I don't think they will be lost to followup."

Board member Noel Weiss said, "Some of these activities do not seem necessary. This is a Cadillac study."

Koprowski suggested that the Board "might be more comfortable if I appoint a committee to discuss with Dr. Tucker the various aspects of this, and develop the concept to include concerns of Board members."

Responding to Board member Anna Barker's question whether the committee would focus on longer range issues, Koprowski said it would take into consideration all concerns expressed by members.

The Board approved the concept on that basis. Koprowski appointed London, Weiss, Pelayo Correa and Moyses Szklo to the committee.

Feasbility assessments for new topics. Three year contract, $100,000 a year.

Many studies of cancer epidemiology require major commitments of financial and personnel resources. Because the commitment can be great, assessments of feasibility are increasingly being conducted to determine the likelihood that an effort will meet the study objectives. In occupational studies, the determination of feasibility requires the indepth evaluation of exposures (including confounding exposures), location of study sites and populations, and identification of the outcomes of interest. Two ongoing examples are the determination of the feasibility of investigating an apparent excess of leukemia and brain cancer among embalmers and the feasibility of locating suitable populations to conduct a cohort mortality study of workers exposed to methylene chloride.

Before any epidemiologic research is initiated, accurate and timely determination of feasibility is critical. New topics which are candidates for study are constantly emerging, requiring prompt response to collect the information needed for an assessment of feasiblity. While the importance of pursuing these new topics is unquestionable, investigators at NCI and NIOSH have to balance these activities with their ongoing projects. The purpose of this proposed project is to establish a contract mechanism to facilitate investigation of new topics. This contract would provide information on the extent of occupational exposure to a chemical of interest and the characteristics of potential study populations to NCI and NIOSH investigators so they can evaluate the feasibility of conducting epidemiologic studies. Topics which aare evaluated and determined to be feasible would be candidates for collaborative research through the interagency agreement.

A competitive task order contract will be awarded to an organization experienced in the monitoring and evaluation of workplace exposures. The contractor will be carefully directed by NCI and NIOSH, and representatives from the agencies may accompany the contractor throughout the plant visits and field studies. Topics for evaluation under this contract will be selected jointly by NCI and NIOSH through an interagency working group which will meet regularly to review topics of potential mutual interest to both agencies. The information to be obtained by the contractor will be specified by NCI and NIOSH, and will depend upon the topic being considered for study. It may include the location and identification of facilities where a chemical is produced or used or facilities where an industrial process is conducted; the extent of worker exposure to the agent of interest; the size, length of time since first exposure and other characteristics of potential study populations; the availability of personnel and industrial hygiene and production records for describing the historical exposures and operating history of candidate study sites, and the presence of potential confounding exposures. This information will be obtained from sources including the scientific and engineering literature, government agencies, individuals and associations representing industry, workers and academia, and site visits and exposure monitoring surveys at individual facilities and worksites. The information will be compiled and summarized to provide the documentation needed for for NCI and NIOSH to determine the feasibility of conducting an epidemiologic study.

Feasibility assessments typically cost approximately $50,000 for each new topic. The major costs of a feasibility assessment are associated with background data collection on the topic; field expenses (including travel to candidate study sites, environmental sample collection and analysis, and collection of personnel and other workplace records); and data evaluation and report writing. The total project plan amount ($300,000) would provide for investigation of six topics over the three year period of the contract.

Aaron Blair, Sheila Zahm and Patricia Stewart are the NCI project officers.

Procurement of transformed lymphocytes, lymphoblastoid lines, and DNA for genetic linkage studies. Four year contract, $210,000 a year.

The Family Studies Section of the Environmental Epidemiology Branch and the Clinical Epidemiology Branch need support for ongoing genetic studies of cutaneous malignant melanoma, multiple neoplasia type 1, lung, renal and bladder cancers and Waldenstrom's macroglobulinemia. These studies require DNA prepared

either from whole blood or from lymphoblastoid cells which have been transformed. As the volume of this work has been steadily increasing, collaborators can no longer be prevailed upon to perform the tasks of lymphocyte transformation and DNA extraction.

Genetic linkage studies, where efforts are made to find the chromosomal location of major genes contributing to disease in man, require the observation of coinheritance of the disease phenotype with a polymorphic genetic marker.

Restriction fragment length polymorphisms (RFLPs) are DNA markers which are eminently useful for this purpose. Hundreds of RFLPs have been characterized and localized to human chromosomes, bands and regions. Disease loci which have been mapped using this technique include Huntington disease, neurofibromatosis types 1 and 2, cystic fibrosis and familial polyposis coli.

Several mechanisms are currently in use to test the DNAs obtained on individuals evaluated by EEB and CEB staff. A contract with Integrated Genetics of Framingham, MA, provides 50 RLP typings covering all the human chromosomes on 150 individuals yearly. There are both intramural and extramural (MIT, Univ. of Pittsburgh) collaborations for those disorders where a specific chromosome or region has been targeted.

This approach has thus far enabled program staff to exclude several candidate regions of the genome suggested as locations of the hereditary melanoma gene, to continue evaluation of chromosome 1 (the most likely location of the melanoma gene), to aid in mapping of NF1, to confirm the location of the gene for MEN1, and to continue studies aimed at mapping the genes for diabetes insipidus, familial eosinophilia, nevoid basal cell carcinoma syndrome and the familial syndrome consisting of soft tissue sarcoma, breast cancer and other neoplasms.

Another project which utilizes DNA from study subjects is the search for genetic markers in individuals susceptible to lung cancer. It has been shown that persons with the extensive metabolizer phenotype for debrisoquine metabolism have an increased risk for lung cancer. This is particularly true of EM individuals who both smoke and have occupational exposure to asbestos and polycyclic hydrocarbons.

The gene which controls debrisoquine metabolism is a member of the p450 gene family and has been localized to chromosome 22. Staff members, in collaboration with the Laboratory of Human Carcinogenesis, have been attempting to correlate the allelic differences at the DNA level in the debrisoquine gene with phenotypic expression.

The contractor will provide all laboratory and personnel support to process up to 600 fresh whole blood and 60 frozen lymphocyte samples/year. DNA will be extracted directly from the majority of the fresh blood samples. A minority of these samples will be used for lymphocyte transformation, bulk growth of cells to 1 gram quantities and then extraction of DNA (with an aliquot of lymphoblastoid cells saved for future use). Similarly, frozen lymphocyte samples will be used for transformation, expansion and DNA extraction.

Sherri Bale, Gail Shaw and Dilys Parry are the project officers.

DCE Director Richard Adamson said that this work eventually may be performed at the Frederick Cancer Research Facility.

NCI Contract Awards

Title: Record linkage study of patients exposed to diagnostic radioactive iodine
Contractor: Israel Center for Registration of Cancer and Allied Diseases, $180,950; the Institute of Oncology, Cancer Registry of Slovenia, Ljubljana, Yugoslavia, $71,400

Title: Tracing through publicly available directories to determine the vital status and current address of persons treated for peptic ulcer
Contractor: Equifax, $12,600

Title: Tracing through other sources and resources to determine the vital status and current address of patients treated for thyroid disorders in Boston hospitals
Contractor: Equifax, $74,423

Title: Evaluation cohort survey for community intervention trials for smoking cessation
Contractor: Westat Inc., $341,637

Title: Evaluation of chemopreventive agents by in vivo screening
Contractor: IIT Research Institute, $358,482 and $387,745; SRI International, $228,814; and Univ. of Nebraska, $368,818

Title: Preclinical toxicology of chemopreventive agents
Contractor: International Research & Development Corp., $685,232 and $318,649

Title: Evaluation of chemopreventive agents by in vitro screening
Contractor: SRI International, $108,450; IIT Research Inst., $226,909; NSI Tech. Service, $157,143 and $295,866.

Title: Efficacy studies of chemopreventive agents in animal models
Contractor: American Health Foundation, $499,998; IIT Research Inst., $358,001 and $546,945

Title: Technical and logistical support services for the Div. of Cancer Etiology
Contractor: Crosspaths Management Systems Inc., $1,939,838

Title: Shallow water marine organism collection
Contractor: Harbor Branch Oceanographic Institute, $801,701

Title: Chemical synthesis of anti-AIDS compounds
Contractor: Southern Research Institute, $900,955; and New Mexico State Univ., $538,878

NIH Expands Some Grant Authorities

As the result of a demonstration project involving 10 Florida universities designed to find ways to reduce administrative burdens, NIH has implemented a program to expand authorities of grantee organizations. The new rules apply to R10 cooperative clinical research grants; R18 research demonstration and dissemination projects; and R43 and R44 small business innovation grants. They include extensions without additional funds, preaward costs, carryover of unobligated balances and cost related prior approvals.

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