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DCBD BOARD OKAYS CONCEPT OF PROGRAM ANNOUNCEMENT TO STIMULATE HUMAN MONOCLONAL ANTIBODY RESEARCH

The Board of Scientific Counselors of NCI's Div. of Cancer Biology & Diagnosis agreed that, despite the explosion of research in progress or anticipated, further stimulation is needed in at least one area of human monoclonal antibodies. The Board gave concept approval for a program announcement to solicit proposals for development of human B cell lines suitable for somatic cell hybridization.

The Board's decision came after a day long discussion of human-

(Continued to page 2)

In Brief

NCI WOULD GET EXTRA $115 MILLION OVER THREE YEARS UNDER BUDGET AMENDMENT BY ALABAMA SENATOR

NCI WOULD get an additional $115 million over three years, above the $966.6 million originally designated in the congressional budget resolution considered by the Senate, under an amendment to that resolution by Howell Heflin (D.-Alabama). The amendment was approved. It would add $22 million in FY 1983, $36 million in 1984 and $37 million in 1985. Senate leaders of both parties supported the amendment. The budget resolution figures are only recommendations, and the appropriations committees still have the last word. The House last week failed to agree on its version of the budget, probably will not include the extra amount for NCI if the House ever does manage to pass a resolution. It would then be an issue for the conference committee to decide. A Heflin staff member said John Durant, director of the Univ. of Alabama Comprehensive Cancer Center, helped sell the senator on the need for more money in the Cancer Program. . . . **INVESTIGATORS PUSHING** to lengthen grant awards face a "double edged sword," NCI Director Vincent DeVita pointed out in a discussion at the recent National Cancer Advisory Board meeting. "If we approve longer awards, that will mean less money that will be available for competing awards," DeVita said. . . . **GUSTAVO CUDKOWICZ**, known for his work in tumor immunology at State Univ. of New York (Buffalo), died May 25 of gastric cancer. He was 54. . . . **PRESIDENT'S CANCER PANEL** meeting June 22 will hear from the following scientists in the continuing discussion of the peer review system: Lawrence Alfred, Charles Drew Medical School; Paul Boyer, UCLA; Lester Breslow, UCLA; Wendy Clough, USC; James Doroshow, City of Hope; Fred Eilber, UCLA; David Golde, UCLA; Denman Hammond, USC; Charles Heidelberger, USC; John Mendelsohn, Univ. of California (San Diego); Malcolm Mitchell, USC; Carol Newton, UCLA; Yosef Pilch, UC (San Diego); and Richard Steckel, UCLA. The meeting will start at 9 a.m., in the A-Floor Auditorium, Jonsson Comprehensive Cancer Center, Louis Factor Health Sciences Building. It will be an open meeting.

HUMAN MONOCLONAL ANTIBODY RESEARCH, WILD MICE GENOMIC LIBRARY APPROVED

(Continued from page 1)

mouse hybridomas, human-human hybridomas, transformed B cell lines, and applications of human monoclonal antibodies by academic and NCI investigators.

Participants in the discussion were Jeffrey Schlom, of NCI's Laboratory of Cellular & Molecular Biology; Anthony Fauci, National Institute of Allergy & Infectious Diseases; Frank Cuttitta, National Naval Medical Center; Warner Greene, Metabolism Branch, NCI; Alan Haughton, Memorial Sloan-Kettering Cancer Institute; Tim Foon, Frederick Cancer Research Facility; Dan Longo, Medicine Branch, NCI; Peter Nowell, Univ. of Pennsylvania School of Medicine; Hilary Koprowski, director of the Wistar Institute of Anatomy & Biology; Michael Potter, Laboratory of Cell Biology, NCI; Stewart Sell, Univ. of California (San Diego); Matthew Scharff, Albert Einstein College of Medicine; Samuel Broder, Clinical Oncology Program, NCI; Nelson Teng, Stanford Univ.; Bruce Mauer, Cancer Biology Branch, NCI; Faye Austin, Cancer Biology Branch; David Sachs,. Immunology Branch, NCI; and Sondra Schlesinger, Washington Univ. School of Medicine.

Also participating were Alan Rabson, DCBD director; Robert McIntire, chief of the Diagnosis Branch in DCBD's Extramural Research Program; and Board members Chairman David Korn, Stanford; Lee Leak, Howard Univ.; Edmund Lin, Harvard Univ.; Renata Cathou, Lexington, Mass.; Lisa Steiner, Massachusetts Institute of Technology; and Barbara Bowman, Univ. of Texas Health Science Center.

"We have finished our studies in mouse imaging," Schlom said. "We're ready now for clinical trials. This debate about human monoclonal antibodies is not something in the future. If we had (appropriate cell lines), we would do it now."

"The issue before us is to see what recommendations we might offer in supporting research in human monoclonal antibodies," Korn said. "There is no doubt about the importance of having the capacity to do these studies in diagnostic and therapeutic research. The question is, is some stimulation desirable? Or is the work progressing nicely enough without it? Is there some specific area that NCI should consider giving some attention to?"

"No one has come in with a proposal to make human myeloma cell lines," DCBD Director Alan Rabson commented.

A suggestion that NCI issue a request for proposals for a contract to support that development did not meet with favorable consideration. "When you don't have the knowledge, an RFP is not the way to go," Scharff said. Others agreed that grant supported research would be more appropriate.

Rabson explained that the Board could recommend a request for applications, which would require setting aside a definite amount of money to fund grants generated by the RFA. A program announcement would result only in applications being submitted through the normal R01-P01 process. McIntire noted that responses to program announcements frequently do not get fundable priority scores but that exceptions could be made permitting funding of grants deemed desirable by NCI staff.

Korn supported use of a program announcement. "My concept is the belief that we're looking for novel ideas rather than just pumping money out. It sounds to me like a program announcement is the first step to take, economically and logically."

The vote to support the program announcement was unanimous.

Board members were skeptical of a request for concept approval of a contract to construct genomic libraries from wild mice for the Laboratory of Cell Biology. The request was presented by Stuart Rudikoff, who explained that the libraries would be used to study evolution of multigene families in a wild mice colony. "We will look at mutational events occuring in related genes during evolution," Rudikoff said. "I'm worried about what's going on in inbreds, and how representative they are. Wild mice may be closer to what's happening in the real world."

Rudikoff estimated the cost of the resources contract would be $150,000 to $175,000 a year if it were done by a for profit contractor, half that if by a university. It would be funded from NCI's intramural budget.

Board members were uncomfortable in approving use of a contract for anything involving a semblance of research. "Why couldn't a university apply for an R01 grant for this, and list you as a collaborator?" Steiner asked.

"They could," Rudikoff answered. "I haven't had anyone ask me to do that. It's my interest, and I'm the principal mover." He said that if the project is done in a university, it would require "one technician and as many graduate students as they would like to involve."

"I sense the opinion of the Board that it is a sound scientific proposal," Korn said. "The logistics are a problem at NCI and that is why it can't be done here. Dr. Steiner reflects the bias of the Board, to be careful in support of directed research. Her opinion is that if it were to come in as a grant proposal, it would do very well."

Rudikoff agreed he would make the libraries available to other investigators through the contract although that would increase the cost.

The DCBD Board presently has only six members out of an authorized 18; appointments to the vacancies are still being processed through NIH and HHS. Until at least a quorum can be convened, votes

on concept approvals are unofficial, but the division will abide by them anyway.

DCCP BOARD GIVES CONCEPT APPROVAL TO THREE NEW RFAs IN EPIDEMIOLOGY

The Board of Scientific Counselors of NCI's Div. of Cancer Cause & Prevention gave concept approval to three new RFAs (request for applications) soliciting grant applications in epidemiology for which $2.8 million will be set aside to provide first year funding.

The Board also approved concepts for new and recompeting contracts with estimated first year funding totaling $3.5 million.

The epidemiology RFAs will be in biochemical epidemiology, with $1.5 million proposed first year funding; etiologic studies of acquired immunodeficiency syndrome, $1 million; and studies to assess the reliability of historic dietary information, $300,000. The immunodeficiency grants would be awarded for five years, the others for three. Staff descriptions of the three research areas:

Biochemical epidemiology—Although a significant proportion of human cancers is thought to be attributable to life style and other environmental factors and therefore potentially preventable, the task of identifying the effects of specific factors and evaluating their relative importance is an enormous one. The process of induction and progression of human cancer is exceedingly complex; multiple exposure to a variety of agents over time is the rule rather than the exception, past exposure is difficult to assess, host factors which may influence susceptibility are poorly understood, and the importance of promoting and/or anticarcinogenic exposures in humans have not been adequately defined.

Epidemiologic studies have resulted in the identification of factors which appear to increase or decrease cancer risk and have suggested the importance of host susceptibility factors. The usual epidemiologic techniques, however, have been limited in their ability to reach firm conclusions by the difficulties in defining past carcinogen exposure levels and susceptibility states, in measuring low levels of risk, in evaluating directly host environmental interactions, and in identifying dietary determinants of cancer. Fortunately, a variety of sensitive and specific laboratory methods is now becoming available which is likely to facilitate such epidemiologic investigations by providing better measures of exposure to initiators, promoters, anticarcinogens and inhibitors of carcinogenesis. Increased collaboration between laboratory scientists and epidemiologists in the application of these emerging techniques would be highly desirable.

Modifying factors related to diet and nutrition have been implicated in cancers of the stomach, large bowel, breast, endometrium and ovary. Hence these types of cancers (among others) might be especially suitable for collaborative studies involving epidemiologists, and experimentalists including biochemists, analytical chemists, immunologists, and nutritionists.

The purpose of this RFA is to stimulate collaboration between epidemiologists and laboratory scientists in developing and/or applying objective measures useful in studying the etiology of human cancer. At a minimum the availability of suitable populations for study, and the collaborative efforts of an epidemiologist and one or more basic scientists will be required.

Examples of types of laboratory measurements which might be appropriate include: 1) Assessment of specific host factors which might influence susceptibility to carcinogenesis (e.g. DNA repair assays, examination of chromosomal defects or susceptibility to cell transformation, assays for immunocompetence or analysis of serum levels of vitamins or micronutrients), 2) detection and quantitation of chemical carcinogens or their metabolites in tissues or body fluids (e.g. analytical chemical measurements, mutagenesis assays or immunologic detection techniques), 3) measurement of interaction of specific agents with cellular target molecules (e.g. adduct formation with proteins and nucleic acids, excretion levels of excised adducts or markers of altered gene expression).

Etiologic studies of acquired immunodeficiency syndrome—Since June 1981 investigators have identified an epidemic of acquired immunodeficiency in the U.S., with some 300 cases thus far of Kaposi's sarcoma and/or opportunistic infections. The affected individuals have been predominantly homosexual men, some 70 percent of the cases have been in New York City or California; and the fatality rate has been about 50 percent in two years. The cases have shown profound quantitative and functional T-lymphocyte abnormalities, evidence of infection with multiple viruses, and exposure to illicit drugs. In addition, thousands of individuals appear to have a prodrome of chronic fever, weight loss, diarrhea, lymphadenopathy, and/or T-lymphocyte immunologic abnormalities. Other immunodeficiency related malignancies, particularly non-Hodgkin's lymphomas, are now appearing in this population. There is no evidence that the epidemic is abating, with one new case per day of Kaposi's sarcoma or opportunistic infections being reported to CDC. Research into this epidemic could yield important new information on the etiology of cancer in man. Study of this emergent health problem provides an opportunity for detecting new risk factors. The purpose of this RFA is to encourage such research by providing support to institutions possessing an interest in the problem, as well as a population of affected patients and/or laboratory facilities and personnel appropriate to the conduct of such research. The intent of this RFA is to encourage innovative, multidisciplinary studies of this problem.

It is proposed that a small number of institutions receive awards to support research into the causes and means of preventing this problem. Awards would be made as cooperative agreements with NCI staff serving as a resource for information on the activities of various members of the working group and acting to facilitate collaboration among involved researchers. With the cooperation of the awardeescollaborative areas will be identified and developed at semiannual meetings with the working group. Studies to be proposed by the applicants should stress innovative approaches including any or all of the following three components:

—Epidemiologic studies designed to identify possible etiologic factors in affected patients or in individuals with prodromal conditions.

—Basic research projects on etiology and pathophysiology. These would include studies in such areas as immunology, microbiology, virology, toxicology, etc. and would include studies of acquired immunodeficiency syndromes, Kaposi's sarcoma, and allied conditions.

—Innovative clinical treatment and prevention research protocols which are linked by hypotheses of etiology. The Board of Scientific Counselors of the Div. of Cancer Treatment has already approved an annual award of $250,000 toward this cooperative project.

Applications from institutions or consortia possessing multidisciplinary resources and expertise in all areas will be encouraged.

Accuracy of questionnaire derived historic dietary information—A recurring problem in the planning and evaluation of cancer epidemiology studies designed to investigate

the initiating or modulating effects of past nutritional exposures is the extent to which questionnaire derived dietary histories can be relied upon to estimate past food consumption or changes in dietary patterns. In the rare event that the investigation is focused on some single, easily recognizable dietary component (e.g. coffee consumption), it might be expected that recall would be reasonably accurate. In the usual situation, however, where the investigation requires that information be obtained on a much broader spectrum of dietary components, or even on the diet as a whole, it can be anticipated that recall will be much less accurate and will be affected by a variety of factors.

It is recognized that no totally accurate methods currently exist for assessing the dietary intake of noninstutionalized individuals. Nevertheless, the cancer epidemiologist needs information which will permit the classification of individuals into low, middle and high consumers of a specific dietary component or food group. Equally important is the need for some objective information as to the degree of reliance that can be placed on questionnaire derived historic dietary data as a function of a number of variables known, or anticipated, to affect its reliability (e.g., elapsed time; age, sex, health status and educational level of respondent; complexity of questioning; dietary variability, etc.).

Although far from an ideal approach to resolving these questions, useful information about the reliability of recall can be gained by comparing information obtained currently about previous diet with actual records of the dietary intake of the same individuals recorded at some discrete time in the past. The primary objective of the proposed RFA is to encourage studies aimed at assessing the reliability of historic dietary information obtained by questioning individuals or their surrogates. Respondents would be expected, in their experimental design, to address the question of how such variables as those previously mentioned impact on the reliability of the information obtained.

The active involvement of persons experienced in the use of historic dietary information in the conduct and analysis of epidemiologic studies will be given significant weight in evaluation of the responses.

Contract concepts for new projects approved by the Board for competition were:

Expert panel review of drugs and cosmetics monographs. First year award, $75,000, two years. A sources sought announcement will determine whether an RFP will be issued. The staff narrative:

The scientific coordinator for environmental cancer acts as an information resource to NCI by maintaining various data bases on individual carcinogens/mutagens present in such multi-media as air, water, food, the workplace, drugs and cosmetics. Since the development of such information resources involves the handling of large volumes of data and encompasses many scientific disciplines within carcinogenesis, toxicology and epidemiology, these activities have been conducted under various contracts.

Two such contracts which address the issues of the "Carcinogenicity of drugs and medical procedures" and the "Potential carcinogencity of cosmetics" have been ongoing since 1980 and are nearing completion. In each case the contractor is preparing monographs on a number of priority chemicals selected with the advice and guidance of a steering committee composed of representatives from government and industry. These monographs contain various chemical, physical, biological and epidemiological data which are presented in a format similar to the International Agency for Research on Cancer (IARC) monographs.

The monographs currently include a summary of the chemical, physical, carcinogenic, toxicological and epidemiological data from the published literature but do not evaluate the data with respect to the evidence for carcinogenicity in animals and/or humans. Therefore, in order to complete these monographs as evaluated and authoritative documents, a rigorous, independent outside review of the adequacy of the animal and human data is required.

Such a review by an unbiased and prestigious expert panel is needed for such an evaluation since these chemical ingredients are widely used by the general public. Furthermore, any decisions made by such an expert panel will have a major impact on the outcome of manufacture, possible regulation and use of these compounds. The need for such a review was agreed upon previously by the DCCP Board of Scientific Counselors.

Due to the sensitive nature of the chemicals that will be reviewed, an expert panel should be convened by a scientific organization that commands the respect of the national and international scientific communities. It is suggested that such organizations include or be comparable in scientific stature to the International Agency for Research on Cancer (IARC), the National Academy of Sciences or the Federation of American Societies for Experimental Biology (FASEB). The imprimatur of such organizations is imperative for publishing such documents that will be disseminated to government, academia and industry.

"The Carcinogenicity of Drugs and Medical Procedures will be a report containing 109 drugs and 15 medical procedure monographs. This report is scheduled to be completed on May 31, 1982. A second series of monographs on the "Potential Carcinogenicity of Cosmetic Ingredients" will contain approximately 75 monographs and is scheduled to be completed on Sept. 29, 1982.

Due to the nature of the time constraints of the above contracts, a cutoff date is necessary to complete the literature search phase of the task. It is expected that an expert panel would review, update and revise the monographs in order to provide the most complete evaluation of the data. Therefore, it is important that this panel be convened as close to the completion date of each contract as possible in order to minimize the magnitude of the literature gap.

Body burden of toxic substances in support of the total exposure assessment methodology study. First year award, $190,000, two years. The staff narrative:

In recent years, it has become possible to measure direct human exposure to about 30 airborne toxic and other carcinogenic substances, including benzene, chloroform, 1,1,2-trichloroethane, and other volatile organic compounds. The method employs a small portable pump and a cartridge containing an adsorbant (Tenax-GC®) which the subject can carry with him while performing his normal daily activities. Integrated air samples of two-hour to 24-hour intervals can be obtained and analyzed by GS-MS to determine exposure at the ppb level. Using identical Tenax cartridges, the subject's breath can also be measured for the same substances following his exposure. The breath measurements reflect the subject's body burden (most particularly his blood levels) and can therefore relate his exposure to his body burden, provided proper heed is paid to biological variability, absorption, metabolism, other routes of exposure and half-lives in the body.

This combined exposure/body burden information has not been obtained previously although data are available separately on ambient levels and breath concentrations). A major study (TEAM) is presently under way that will obtain considerable information on personal exposures through air and drinking water, but, as presently planned, little information on body burden. The proposed addition to the TEAM study will provide several hundred breath samples together with the air and water exposures, thus generating a rich data base on human exposure and body burden.

Biochemical component for a case control study of cervical cancer. First year, $75,000, three years. It is possible this will be awarded to the Center for Disease Control on an interagency agreement; if that can't be worked out, it will be competed.

A case-control study involving 500 newly diagnosed cases of invasive cervical cancer, 500 cases of in situ cervical cancer. and 1000 neighborhood controls will be initiated in the summer of 1982 in five cancer centers, in Philadelphia, Chicago, Miami, Denver and Alabama. Risk factors to be assessed include sexual practices, reproductive-contraceptive-gynecological history, smoking and diet. Low intake of several micronutrients–vitamin A, carotene, folacin, vitamin C, and vitamin E–has been hypothesized to increase the risk of cervical cancer or cancer in general. A number of epidemiological studies have demonstrated inverse associations between the foods that contribute much of the vitamin A in the diet and several epithelial cancers; preliminary analysis of one case control study suggests that cervical cancer risk is doubled in low vitamin A consumers. Limited dietary data make it difficult for these studies to assess whether it is carotene or vitamin A, or fruits and vegetables in general, that is primarily associated with reduced risk. In a small clinical trial of women with cervical dysplasia, all of whom were using oral contraceptives and had low red blood cell folates, oral dysplasia and carcinoma in situ, vitamin C was the nutrient, of the 19 examined, that was most strongly and consistently associated with reduced risk. Laboratory evidence suggests that vitamin E, an antioxidant, may prevent lipid peroxidation and subsequent carcinogenesis.

This case control study will collect sufficiently detailed food frequencies and supplemental vitamin histories to estimate the usual adult intake of these micronutrients and to characterize dietary patterns and nutritional status. A distinct advantage of this study is that for the first time dietary exposures will be evaluated in a large number of patients with invasive cervical cancer, as well as with carcinoma in situ. To complement the estimates of micronutrient intake that the dietary interview will provide, it is proposed to collect blood samples with which to measure serum levels of retinol, carotene, and tocopherol by high pressure chromatography and serum folate and red blood cell folate by radioimmunoassay.

Blood will be drawn from the cases prior to treatment and several months after completion of treatment, with the minimal elapsed time to be based on preliminary studies. At the time of the initial interview in the home the women will be asked if a trained nurse can revisit them to draw blood and to ask a few questions about any recent changes in usual adult diet. The serum collected will also be assayed for antibodies to herpes virus type 2, a suspected risk factor for cervical cancer. The unused serum will be carefully stored in aliquots at -70° C for any micronutrient and/or virus determinations that might be deemed appropriate at some time in the future.

Epidemiology of human T-cell leukemia/lymphoma virus. First year, $400,000, approved for three years if a progress report after a year justifies continuation.

Human T-cell leukemia/lymphoma virus (HTLV) is the first type-C retrovirus consistently isolated from patients with a specific disease. Unrelated to any known animal virus, HTLV is an exogenous human retrovirus demonstrable in malignant T-cells of certain patients with T-lymphoproliferative malignancy. Preliminary epidemiologic data show that HTLV is associated with clusters of a characteristic form of mature T-cell leukemia/lymphoma in certain geographic areas. In particular, HTLV is associated with a newly described disease entity, Japanese adult T-cell leukemia/lymphoma (ATL) in over 90 percent of cases. This malignancy of mature T-cells accounts for 80 percent of adult leukemia/-lymphoma in certain regions of Japan. The clinical and epidemiologic patterns of occurrence of ATL are consistent with a viral etiology, and recently Japanese investigators have also reported virus isolates that we have shown are indistinguishable from HTLV.

The recent discovery that black patients from the Caribbean, with a disease entity indistinguishable from Japanese ATL, are HTLV virus and/or virus antibody positive in all cases, supports the hypothesis that HTLV is linked to a specific disease entity. Studies of normals confirm that HTLV infection is prevalent, but rare in populations where ATL cases occur, and such disease clusters are not seen in the absence of HTLV. Thus, HTLV represents the first candidate Type-C human leukemia virus. Clarification of an etiologic role of HTLV in malignancy should be definable because of its restricted distribution and numerous animal models which offer a strong base of experimental systems to guide future approaches.

This project involves close collaboration with Dr. Robert Gallo, Chief, Laboratory of Tumor Cell Biology, Div. of Cancer Treatment, who discovered HTLV. All molecular biologic and virologic studies, including testing of all tissue and serum samples for HTLV, are to be performed in Dr. Gallo's laboratory. Epidemiologic studies are to be designed and executed, in collaboration with Dr. Gallo, by the staff of the Environmental Epidemiology Branch.

This project involves multiple contracts which are to be competitive, and will be awarded to organizations having departments of pathology, epidemiology and/or infectious disease in HTLV-endemic areas of the U.S. and abroad, regional health agencies to serve as liaison to selected health organizations or universities in virus-endemic areas, or government medical science agencies with nationwide health authority.

This concept deals with allocations of funding for a series of epidemiologic, clinical, and experimental studies aimed at defining: (1) the distribution and determinants of HTLV infection, and (2) the role of HTLV as a cause of cancer. High risk areas are identified by the occurrence of a characteristic type of T-cell malignancy and the presence of HTLV antibodies in the normal population and in cases. Targeted interdisciplinary epidemiologic studies are to be undertaken in these high risk areas through a series of contracts with qualified collaborators. In general, contractors will be selected because (1) they have access to defined populations of patients with malignancy, and corresponding clinically normal populations, and (2) they have the capacity or potential for precisely defining the nature of the malignancy, particularly with regards to T- and B-lymphocyte typing. Other types of investigations to be funded include "follow back" studies of virus positive individuals detected in prospectively collected samples and studies of populations migrating into or out of virus endemic areas.

Since virus endemic areas are frequently located in countries where medical research facilities may be rudimentary at best, a portion of the funds allocated to this project will be used for purchase of equipment for specimen processing and storage, and for immunopathologic typing. Other expenses will include hiring of personnel to assist in specimen and data collection, and for travel and shipping costs. In general, samples for HTLV testing will be sent to Dr. Gallo's laboratory, while T- and B-typing will be performed in the collaborator's laboratory.

In summary, this project is targeted at developing a parallel series of sero-epidemiologic and interdisciplinary studies in selected regions of the world. By coordinating studies of this candidate human tumor virus, it should be possible to delineate the patterns of virus prevalence and T-cell leukemia/-lymphoma, and to clarify etiologic relationships.

Support services to provide water quality data. First year, $110,000, two years.

Geographic correlation studies completed since 1975 sug-

gest an increased risk for cancers of several sites from long term exposures to chlorinated drinking water, especially surface water, as compared to nonchlorinated ground water. Among the suspect sites are urinary bladder, colon, rectum, lung, and brain. Additional evidence is now also emerging from case control mortality studies in which the address on the death certificate is used as a guide to the type of water consumed (ground, surface, chlorinated, nonchlorinated). These more recent studies generally confirm the earlier results, but they are limited because the death certificate is used as the primary information source. Misclassification of exposure, inaccuracies in cause of death classification, and inability to adjust for other risk factors are foremost among these weaknesses.

Several case control studies directed by the Environmental Epidemiology Branch lend themselves to evaluation of the water quality hypothesis, although they were originally designed to estimate risks due to other factors. Among these are studies of (1) colorectal cancer and dietary patterns in Southern retirement areas (Florida), (2) brain tumors and occupational factors (New Jersey, East Texas, Louisiana, Philadelphia region), and (3) lung cancer and environmental and occupational factors (New Jersey, East Texas, Louisiana).

This project will provide for gathering historical information on water sources, treatments, and distribution for all major water utilities serving more than 1000 persons in areas of the country where these case control studies are sited. Using data from an EPA inventory of public water supplies, we estimate a total of 450 such supplies in areas where we do not already have information (areas other than New Jersey and the New Orleans region). After receipt by NCI, the water utility data will be linked to residential/water supply history information on cancer patients (or decedents) and controls, to create a lifetime water quality profile for each study subject. In epidemiologic analyses, we will consider past as well as current water sources in evaluating risk, and will adjust in standard ways for other factors, such as occupational exposures, dietary patterns, and smoking histories.

This approach has proved successful in creating water quality profiles for most of the 9,000 respondents in the National Bladder Cancer study. By linking water utility information with residential histories, we have succeeded in defining specific characteristics of the primary residential water source for approximately 75 percent of the total person-years lived by all study subjects.

The Board approved recompetition of the following contracts:

Biomedical computing software services. This will be a small business set aside, and the present contractor, Information Management Services Inc., will remain eligible. First year, $257,617, three years.

The Clinical & Diagnostic Trials Section of the Biometry Branch provides full statistical support for a number of large clinical trials and develops statistical methodology for the analysis of data gathered from controlled trials and for data analysis related to cancer diagnosis and screening. The section represents an important resource for expert assistance in study design, implementation, and statistical and computer analysis of studies being carried out by many other groups. The necessary data processing and background support cannot be provided by members of the section's staff. Therefore, additional outside support is required.

The current contract, initiated on July 11, 1980, represents a continuation of data processing support services which initially began in May, 1971. The current three year contract requires a one million dollar expenditure by the NCI with approximately $300,000 contributed by the Div. of Cancer Treatment and the remainder from Field Studies & Statistics.

The contractor provides support services in the areas of data coding and editing, data editing both manually and by computer program, data file updating and merging of patient pretreatment and followup data and designing, writing and executing systems of programs to analyze these data. The contractor provides support services for clinical trials which involve patients with lung, testicular and brain cancer as well as ad hoc support for many smaller projects.

Support services for radiation and related studies. Present contractor is Westat, Inc. First year, $1.1 million, five years.

Studies of populations exposed to ionizing radiation are being conducted to investigate further the relationship between cancer risk and exposure to high doses, and to improve estimates of risk associated with lower doses. An immediate practical need is for risk estimates on which to base regulatory and other decisions about the use of nuclear and radiological technology in medicine and industry, and to assess the value of exposure avoidance as a means of cancer prevention. The study of radiation induced cancer is also a promising approach to understanding mechanisms of carcinogenesis in general. In addition, studies are being conducted of patients treated with cytotoxic drugs in addition to radiotherapy, utilizing various clinical trials in collaboration with the Div. of Cancer Treatment.

To conduct a program of radiation and related studies, NCI requires the assistance of an organization highly experienced in providing technical support for all phases of health studies. These phases include designing data collection documents; hiring and training of interviewers and abstractors; collecting, keying, editing, updating, and recoding data; tracing individuals; and creating and manipulating large computer data files. The scientific direction for all projects is determined by the professional staff of the Branch. The contractor provides a team of study managers, abstractors, and interviewers, tracers, computer programmers, coders and keyers, and other support personnel to complete study tasks. A new contract to provide these services will be competed to replace the current contracts with Westat Inc. that terminate in June 1983 and September 1983.

Study designs employed include cohort and case control approaches, coupled with laboratory and biochemical evaluations when appropriate and feasible. All studies are thoroughly reviewed by senior staff of the Branch and Field Studies & Statistics Program, and by expert review groups when appropriate.

Biomedical computing design and implementation. Present contractor is ORI Inc. This will be a small business set aside. First year, $900,000, three years.

We plan to recompete the current contract which expires in September 1983. An RFP will solicit a contractor to provide computer related services in support of the research program of the Environmental Epidemiology Branch. The primary objectives are: (1) research and development in computer science to develop specialized software; (2) the use of existing software and systems; and (3) the development of custom programs and systems. The following are some activities for which computer related assistance and support services have recently been provided or will be needed in the future: (1) study of families and other groups with intrinsic predisposition to cancer; (2) a series of case control studies in counties with high rates of cancer mortality; (3) development and/or utilization of new methodologic approaches and data resources in cancer epidemiology; (4) occupational surveys; (5) nutritional studies; (6) studies of medicinal agents. These are given only to illustrate the variety of activities the contractor will pursue in support of projects in cancer epidemiology.

Collection and evaluation of human tissues and cells from donors with an epidemiological profile. Present contractor is

Georgetown Univ. Medical School. First year, $56,000, four years.

The Laboratory of Human Carcinogenesis develops and employs model systems for the study of carcinogenesis in cultured human cells and tissues. These systems provide opportunities to assess: (a) mechanims of carcinogenesis in humans; (b) host factors influencing individual human susceptibility to carcinogens, e.g., the metabolic balance between activation and deactivation of chemical procarcinogens; (c) methods and designs for the qualitative extrapolation of animal carcinogenesis data to humans, and (d) strategies for the inhibition of neoplastic transformation.

A resource for the collection of (1) normal appearing human lung tissue and cells, including mesothelial cells in pleural effusions, from cancer and noncancer, smoking and nonsmoking donors at the time of surgery, (2) human pulmonary macrophages from normal, noncancer smoking and nonsmoking donors by bronchial lavage, and (3) human peripheral white blood cells is proposed to continue ongoing investigations in the laboratory. The essential components of the resource will include a) approval by the contractor's institutional committee for informed consent and protection of human subjects forms and procedures; b) an epidemiological profile of the donors, c) proven methods for collecting and transporting the specimens in a viable condition, and d) evaluation of functional and pathological aspects of the tissues and cells. The material provided will be used to study metabolic activation of chemical carcinogens and malignant transformation by chemical, microbial and physical carcinogens.

Holding facility for small laboratory animals. Present contractor is Litton Bionetics Inc. First year, $200,000, two years.

The present NCI project was initiated in September 1980 to provide the Nutrition & Metabolism Section, then part of the Laboratory of Carcinogen Metabolism, with adequate animal facilities for the routine performance of chronic and subchronic toxicity studies in which chemical carcinogens and related compounds were administered in the diet to small, rodent laboratory species. The NCI animal facilities then available were inadequate for the routine administration of chemical carcinogens in the diet. The type of services provided include: maintenance of a variety of animals, collection of tissues from dead animals, necropsy, tissue preparation for histology and observation of experimental animals for signs of disease.

In May 1981 NMS became a part of the Laboratory of Comparative Carcinogenesis, which was relocated at FCRF for the primary reason that rodent research facilities exist there that could be made available. The existing SPF facilities at FCRF have now reduced, and over the requested two-year period will eliminate, the requirement by the laboratory for these off campus animal holding facilities. These facilities have allowed flexibility in animal strains used, assurance of adequate animal handling resources and a gradual phaseout of long term studies. This period also permits the orderly phasing in of new long range projects at FCRF, making most effective use of the current allocated space and trained personnel at FCRF.

Facility to hold nonhuman primates for cancer research. Present contractor is Litton Bionetics Inc. First year, $100,000, three years.

A concept describing this contract effort was approved for two years by the DCCP Board of Scientific Counselors at the May 29, 1981 meeting. The RFP was developed and advertised in the fall of 1981. During the final phase of negotiations it was learned that Litton Bionetics Inc. would not be renewing its lease at the Kensington primate facility and will vacate the building by June 30, 1983. Since LBI was the only responder to the RFP and no second choice was available, the contract was awarded for a 16 month period instead of a 24 month performance period (Feb. 16, 1982 through June 15, 1983). Eight studies involving 38 monkeys are projected for continuation beyond that date. These experiments are being conducted under the auspices of the U.S.-U.S.S.R. agreements. The monkeys are assigned to studies conducted by Dr. Boris Lapin and are comprised of 32 old world monkeys, (10 baboons, nine rhesus monkeys, six stump tailed macaques, two pigtailed macaques, five cynomolgous monkeys) and six new world monkeys (five owl monkeys, one whitelipped marmoset). These animals are being held for tumor development and are bled several times per year. In January 1982 one of the stump tailed macaques inoculated with material from a leukemic baboon in 1974 died of a lymphoproliferative disease, and followup studies are in progress. No date of completion has been indicated for these studies.

Dr. Robert Whitney, Chief, Veterinary Resources Branch, Div. of Research Services, NIH, was contacted to determine the possibility of housing the 38 animals at NIH facilities. We have not received a commitment from Dr. Whitney as yet; therefore, we are proceeding with the likelihood that the contract mechanism will be utilized to support the housing of these animals.

Bioassay of chemopreventive compounds by tracheal organ culture systems. Present contract is IIT Research Institute. First year, $168,000, 18 months.

As new retinoids and other compounds are synthesized in small quantities, it is necessary to test them for their potential efficacy in long term animal studies of inhibition of carcinogenesis. Bioassay in the hamster tracheal organ culture system is currently a major screen for such activity. Since the tracheal organ culture assay measures the ability of compounds to control epithelial cell differentation, it may predict the effectiveness of a new compound for prevention of epithelial cancer. Obviously, any in vitro test has dangerous liabilities for prediction of in vivo activity; in spite of these limitations, the tracheal organ culture assay is a most valuable procedure for initial evaluation of the biological activity of a new retinoid. It is extremely sensitive and has been used routinely to evaluate activity of new compounds, the concentration of which may be as low as 10^{-11} to 10^{-12} molar during the assay procedure. Thus, it is possible to measure biological activity with considerably less than a milligram of a new compound. The assay is also relatively brief; results can be evaluated within a month of a test's beginning.

NCI CONSIDERS OPTIONS TO IMPLEMENT NCAB DECISION ON ORGAN SITE PROGRAM

NCI's Organ Site Program staff was in the process this week of considering options available in implementing the decision by the National Cancer Advisory Board to restructure the four national projects by combining the four headquarters into one and bringing review of their grants into the normal NIH/NCI review system.

One of the first decisions that will have to be made will be what to do about new and renewal grant applications which are coming in to the National Bladder Cancer Project, National Large Bowel Cancer Project, National Pancreas Cancer Project, and National Prostate Cancer Project. Since those projects were established, with headquarters at four research institutions, each has reviewed its own grants with chartered working cadre. The NCAB action directs that review now be performed by appropriate NIH-

Div. of Research Grants study sections for individual basic research and epidemiology grants, and by the NCI-Div. of Extramural Activities for program projects and clinical research grants.

One option being considered is to administratively extend the renewal grants for a few months to allow investigators to get into the NIH cycle. The headquarters grants also could be extended until the new single headquarters grant can be competed and awarded.

Andrew Chiarodo, chief of the Organ Sites Branch in the Div. of Resources, Centers & Community Activities, said NCI staff would work on the "nuts and bolts" of implementing the NCAB decision with its Subcommittee on Organ Site Programs and would attempt to develop recommendations for a request for applications for the headquarters grant to submit to the DRCCA Board of Scientific Counselors at its fall meeting.

As might be expected, directors of the four projects were not pleased by the NCAB's decision. Two who would comment on it were Isidore Cohn, who heads the pancreas project, and Gerald Murphy, director of the prostatic project.

"I don't like the idea of combining the four headquarters into one," Cohn said. "I don't really think a single headquarters can handle everything in the same fashion, and I doubt that it will save money or time. I'm not sure what will be accomplished. I feel we have done a good job, and most of the reviews we've had have been favorable."

Cohn said the implication that members of the working cadre all hold grants is incorrect. There have been 29 members of the pancreas working cadre since the group was organized, and only six of them have had grants, accounting for 10 percent of the project's grant dollars.

The statement in ***The Cancer Letter*** (May 21) that the headquarters are funded at a half million dollars each "would be a luxury for us," Cohn said. His headquarters grant amounts to about $275,000 a year.

Murphy said he was "disappointed" in the Board's decision. "I regret that this has to be. I only hope that we will be given some time before this is implemented, so the whole program doesn't get lost."

AMENDMENT TO RFP NCI-CP-FS-21008-77

"Support services for epidemiologic studies to address emergent cancer issues." The date for receipt of proposals has been extended to July 16, 1982.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs to the individual named, the Blair Building room number shown, National Cancer Institute, 8300 Colesville Rd., Silver Spring, Md. 20910. RFP announcements from other agencies reported here will include the complete mailing address at the end of each.

RFP NCI-CP-31004-76

Title: *Production, purification and concentration of tissue culture fluid and cells*

Deadline: *Approximately July 23*

NCI has a requirement for an organization to produce, purify and concentrate tissue culture fluid and cells. The offeror will be required to produce four-five different type-C or type-B retroviruses on a continuing but flexible basis at an overall level up to 20 liters of virus-containing tissue culture fluid per week.

The offeror shall produce these materials without detailed protocols or explicit procedural guidance from NCI. The RNA viruses to be produced and purified may include, but not be limited to, Harvey, Kirsten and feline sarcoma viruses, Friend leukemia virus, Friend-MCF leukemia virus and Moloney leukemia virus with varying times of harvest and methods of processing tissue culture fluids to obtain virus that would favor the subsequent isolation of either structural proteins, high molecular weight viral RNA, or viral glycoprotein.

Production of the RNA viruses should take place in cell systems and with production processes so that final yields of virus, both qualitative and quantitative, are consistent with the latest state of the art.

Contract Specialist: Steve Metcalf
RCB, Blair Bldg. Rm. 119
301-427-8888

NCI CONTRACT AWARDS

Title: Additional effort to "Cancer communication program support services"
Contractor: Porter Novelli & Associates, $473,663.

Title: Operation of a virological diagnostic laboratory, two month extension
Contractor: Microbiological Associates, $63,344.

Title: Cancer Control Program for Clinical Cooperative Groups
Contractor: American College of Radiology, $370,580.

The Cancer Letter _Editor Jerry D. Boyd

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