THE CANCER LETTER

Vol. 10 No. 29
July 20, 1984

Subscription $150 year North America
$175 year elsewhere

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AACI BACKS YEAR 2000 GOAL, SECURES PLEDGE FROM NCI THAT NEW CENTERS WON'T BE ADDED AT EXPENSE OF OLD

Members of the Assn. of American Cancer Institutes embraced the goal of reducing cancer mortality 50 per cent by the year 2000 as proposed by NCI and called for a unified effort by all factions in the cancer community to work toward that goal and to secure the resources that effort will require. AACI also secured once again a commitment from a senior NCI executive for increased support for

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In Brief

ULTMANN NEW AACI PRESIDENT, ROBERT DAY NAMED PRESIDENT ELECT; HULKA NEW DCPC BOARD CHAIRMAN

JOHN ULTMANN, director of the Univ. of Chicago Cancer Research Center, became president of the Assn. of American Cancer Institutes at the organization's recent annual meeting. He succeeds John Durant. Robert Day, director of the Fred Hutchinson Cancer Research Center, was elected vice president and president elect. New directors are Barbara Sanford, director of Jackson Laboratory; John Montgomery, executive vice president of Southern Research Institute and a member of the President's Cancer Panel; and Albert LoBuglio, director of the Univ. of Alabama Comprehensive Cancer Center.... **BARBARA HULKA,** professor of epidemiology at the Univ. of North Carolina, has been named chairman of the Board of Scientific Counselors of NCI's Div. of Cancer Prevention & Control. She succeeds Lester Breslow. She has been a member of the Board since 1981.... **MARY LASKER,** whose untiring effort on behalf of the National Cancer Program was a key factor in selling Congress on the National Cancer Act of 1971, has had the recent 11 acre addition to the NIH campus named after her. President Reagan has signed the bill naming the land, which includes a three story building, the Mary Woodard Lasker Center for Health Research & Education. NIH has set Sept. 19 as Mary Lasker Day, for a ceremony formally establishing the center.... **NCI DID NOT** accept entirely the recommendations of the National Cancer Advisory Board regarding the award of the Organ Systems Coordinating Center to Roswell Park Memorial Institute. The Board recommended funding at the full level approved by the initial review group; instead, the amount was cut by about a third, to a little more than $900,000 including indirect costs. Also, the time of the award was trimmed from five to three years. The phased out headquarters of the bladder, colon and pancreatic cancer projects were given a one month extension, to Aug. 1, to enable them to pack up their files and other material and ship them to Roswell Park. The fourth project, prostatic cancer, was headquartered there under RPMI Director Gerald Murphy and did not need an extension.

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GREENWALD HINTS CANCER CONTROL CORE MONEY MAY BE AVAILABLE TO CENTERS

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cancer centers, including—perhaps—restoration of core support for cancer control.

AACI held its annual meeting last month at Memorial Sloan-Kettering Cancer Center, observing that institution's 100th anniversary. Peter Greenwald, director of NCI's Div. of Cancer Prevention & Control, described briefly the 50 per cent mortality reduction plans, the developing plans to support new centers at minority institutions, and the 1986 bypass budget which includes a request for an increase of $350 million a year to implement and carry out the programs required to meet the goal.

"It's better for us in the scientific community to establish realistic goals rather than have someone else do it for us," Greenwald said. "The goal we have established is reasonable and reachable."

AACI members questioned Greenwald about certain aspects of the bypass budget.

The budget, which would go into effect starting Oct. 1, 1985, calls for funding 40 per cent of approved RO1 grants at full recommended levels, John Durant, Fox Chase Cancer Center, pointed out. "Is that just lip service?" he asked.

"No, we're serious about it," Greenwald said.

Timothy Talbot, Fox Chase, noted that while the language in the bypass budget calls for full funding of RO1s and PO1s, it states only that cancer center core grants would be funded at levels "close to" recommended levels. "If you went to the trouble to make the language different, then your thinking must be different," Talbot said. The bypass request for core grants is $93 million, "which is probably about right for what we do. But if we're going to do anything that will have a real impact on mortality among minorities, we probably will need four times that much."

"You're probably right," Greenwald said. "We are assuming funding at full peer review recommended levels for centers."

NCI's plans to support development of centers at minority institutions at present commits money only for planning grants, Greenwald said. "That will not cost much right now, but it probably will down the road."

"The question of raising the level of care in underserved areas is a real issue," Michael Brennan, Michigan Cancer Foundation, said. "Historically, many centers are located geographically to address that problem. But to go after it means working with cities, counties, and practicing physicians who do not participate in clinical trials. Outreach efforts by centers are possible, but would take substantial resources in outreach cadre to carry it off. Are there any plans for funding that outreach effort?"

"We are looking at how to achieve that impact," Greenwald said. "Our aim is to do studies to determine how to impact cancer mortality. I don't think we will have a large service program."

"If we think of ourselves as research centers alone and avoid public health responsibilities, we'll find ourselves estranged from our sponsors," Brennan insisted.

Richard Steckel, UCLA Jonsson Comprehensive Cancer Center, had argued previously before the President's Cancer Panel for restoration of cancer control core grants for centers (**The Cancer Letter,** April 13). He made his pitch again to Greenwald.

"It's beautiful to see the pieces come together," Steckel said. "I still think that a piece is missing. If you think that centers have a role to play in cancer control and cancer control research, then we need core support for cancer control staff."

"Some support as you mentioned is reasonable," Greenwald said. However, he tied that to NCI's current philosophy that core support must be preceded by a base of funded cancer control grants. "As core support was developed in other areas, you had a reseach base develop first, then core followed. We haven't see that too much yet with cancer control."

John Hisserich, Univ. of Southern California Comprehensive Cancer Center, suggested that Hispanic populations should be included in minority groups needing special attention in reducing cancer mortality. "The incidence may not be as great as it is for Blacks, but Hispanics do have treatment problems," Hisserich said. "In some instances, existing centers have the capability of dealing with that."

Paul Carbone, Wisconsin Clinical Cancer Center, commented that the elderly "are also a disadvantaged group and should figure in the planning."

Greenwald agreed, noting that 50 per cent of cancer occurs in persons over 65 and that NCI is funding some grants for research on cancer and the elderly. The National Institute on Aging also supports some cancer related research.

"According to past experience, the bypass budget is unlikely to be adopted in total," Enrico Mihich, Roswell Park Memorial Institute, said. "Does that mean that if you do not get the bypass figure, the plan will not be implemented? Or will the priorities be the same, on a lesser scale?"

"We will keep the priorities the same," Greenwald answered. "But we're optimistic. I sense a feeling in the Administration and in Congress that they will support a strong cancer control program."

"I'll ask that question another way," Durant

said. "Are you asking for new centers but not for new money?"

"We intend to seek the resources to meet the needs," Greenwald answered. "We do not intend to weaken fine existing programs."

"I would like to have that stated clearly," Durant persisted. "What you are saying is that there won't be any new centers without new money."

"I can't say that absolutely," Greenwald replied. "There might be a short interval" between funding of new centers and securing additional money to support them. "But it is not our intent to fund new centers at the expense of old ones."

Talbot made an appeal for a united approach in supporting the year 2000 goal and the bypass budget requests.

"Here we have something we can defend item by item," Talbot said. "But only if we stick together."

"That is very important, that this become everyone's effort," Durant added.

SCHMIDT SAYS CANCER ACT PAID OFF "WELL BEYOND OUR HOPES AND DREAMS"

No single individual has had a greater impact on the National Cancer Program than Benno Schmidt. A New York investment banker, Schmidt chaired the Yarborough panel, a group of citizens and scientists organized by Sen. Ralph Yarborough in 1970 to develop recommendations for reorganizing the federal government's cancer research effort. Those recommendations resulted in the National Cancer Act of 1971, the vastly increased funding of cancer research through NCI, and the resulting "avalanche of scientific discoveries well beyond the hopes and dreams of those who proposed this program," Schmidt said in addressing the Assn. of American Cancer Institutes.

After the Act was signed into law, Schmidt was appointed the first chairman of the President's Cancer Panel and helped guide the Cancer Program in that capacity for eight years. When necessary, he carried the fight to the White House and Congress, demanding that the mandate of the National Cancer Act be upheld, and was successful most of the time.

Schmidt continues to be intimately involved in the Cancer Program as chairman of the Board of Trustees of Memorial Sloan-Kettering Cancer Center.

Schmidt told NCI members that "it was you and your colleagues, the scientists and doctors at our cancer institutions who provided the major impetus for the Cancer Act." He noted that federal support for cancer research rose from $180 million in 1970 to $1 billion in 1980.

"At the same time, the budget of the National Institutes of Health went from $1 billion in 1970 to $4.56 billion in 1985 (the President's request for NIH for the year starting Oct. 1, 1984), thus belying the fear so widely expressed in 1970-71 that any increase in the cancer budget would be at the expense of other institutes within NIH. Many of you will recall our determination that increases in cancer research should not be at the expense of other biomedical research, and I often assured our adversaries that it would not be true. I recall telling the then director of NIH, who was not on our side to put it mildly, to remember the old truth that the next best thing to getting a raise yourself is for the fellow next door to get one. Happily, that has proved true and the NIH budget as a whole has, over the past 15 years, increased four and one half times while the cancer budget over the same period was increasing sixfold. And there is no doubt that the cancer budget was the engine that was pulling the entire biomedical research budget.

"Happily, and I am sure wisely, we extended our arms to embrace those in the scientific community who had opposed our efforts for an enlarged, enhanced and accelerated cancer research program. The research that needed to be done could not be done without the help of scientists in the laboratories of the great universities throughout this land. They came on the Cancer Panel, they came on the Cancer Board, they served on the peer review committees, they received support from the Cancer Program, they participated in the science which made up the program and made an immeasurable contribution to the total progress so that today it is very difficult to find a scientist anywhere who feels that the actions taken in 1970-71 were other than in the best interests of this nation, its people and its scientific community.

"... We hear very little today about this money being wasted, about our throwing money at a problem that we could not know how to attack, or even about the money being misspent. About the only complaint we hear these days is from the scientists who are unable to obtain funding, or who are unable to obtain all the funding they need for the science which they propose. These complaints are often well founded, because even at the enormously increased levels that I have outlined, federal support is far from adequate to fund the biomedical research level of which this country is capable.

"Having lived with the Cancer Program intimately at the federal level for 10 years and less intimately at the federal level but very intimately at the institutional level for the past four years, I can say without the slightest hesitation that I know of no federal dollars that have been spent with the wisdom, care, and merit that has characterized the expenditure of the biomedical research dollars administered by the National Institutes of Health.

On the whole, I believe that the peer review system of NIH has served the nation well in maintaining standards of excellence unmatched in any other area of federal spending.

". . . The result has been an avalanche of scientific discoveries well beyond the hopes and dreams of those who proposed this program. Our basic understanding of events past the cellular level has increased to the point that almost no edition of the daily papers appears without reference to some discovery or development which 15 years ago would have seemed behind the realm of the imagination... I cannot resist reflecting on how much of this research came out of the much maligned virus cancer program. It is dangerous for even the most brilliant scientist to be too positive about what will or will not be productive in basic research.

"So great is the excitement of the new developments which have come out of the basic biomedical research of the past 15 years that over $1 billion of risk capital has been poured into the equity of new companies to develop these technologies for pharmaceutical, agricultural, and indusrial uses. In addition, over $1 billion a year is being spent in these and other commercial establishments for basic science of a type which, 10 years ago, was being done only in university and academic laboratories. For the first time in our history, the basic biomedical science being done in a large number of commercial enterprises in this country is of a caliber comparable to that done in the best academic institutions. All of this is an unexpected dividend from the impetus provided by the Cancer Act.

". . . As a result of the confluence of all of these forces, we are getting more and better biomedical research today than ever in the past. So rapidly are new developments occurring that I am optimistic for the first time in my life that I will live to see an order of magnitude in our ability to deal with cancer."

Schmidt said that one of the most important provisions of the Cancer Act was that which encouraged development of comprehensive cancer centers. It was Congress' intent, he said, "to provide the American people with institutions where persons with cancer or cancer symptoms could go and expect to receive the best in cancer care. Congress was trying to reduce the margin between the cancer care which people received at the average hospital from the average physician and the care which embodied the best technology in the hands of the most highly skilled doctors... It was hoped that the cancer centers would improve that situation both by the better treatment that would occur in their own institutions and by the knowledge they would impart to others."

DCE BOARD GIVES CONCEPT APPROVAL TO EIGHT CONTRACT RECOMPETITIONS

Eight additional contracts have been approved for recompetition by the Board of Scientific Counselors of NCI's Div. of Cancer Etiology, including the master agreement for task orders in tracing individuals for environmental epidemiologic studies on cancer.

The Board deferred action on a staff proposal for a new contract to fund a case control study of cancer and drinking water contaminants.

Tracing individuals for environmental epidemiologic studies on cancer. This will be recompetition of five year master agreements for task orders which will be competed among those selected under the master agreements, at an estimated total cost of $450,000 a year. Present contractors are Pinkerton's Inc., Johns Holding Co., Equifax Inc., Westat Inc. and Hooper Holmes Inc.

The master agreements of those firms already in the tracing pool will be extended from two years to five years, and additional acceptable firms will receive five year master agreements. The scope of work involves only phase 1 of the tracing process, i.e., tracing difficult to find individuals who are being followed up mostly in cohort studies, and who could not be located through phase 1 sources such as the Social Security Administration, National Death Index, state mortality files, etc., conducted by other support contractors. Between 65 and 80 per cent of each cohort are located through phase 1 tracing efforts; the remainder undergo tracing by master agreement holders.

Tracing sources used under this project are credit bureaus, motor vehicle bureaus, vital statistics offices, public directories and lists, and other sources such as employers, neighbors, utility companies, schools and colleges, social service records, court records, union records, property records, churches, libraries, funeral homes, obituaries, clubs, and community associations.

George Burton is the project officer.

"This contract is necessary to assure the quality of followup studies," Board member William Haenzel said. "The expense is the price we have to pay for the lack of organization of medical records."

Production, characterization and distribution of avian myeloblastosis virus reverse transcriptase. Estimated total cost, $3.2 million for five years. Present contractor is Life Sciences Inc. DCE expects that only the $581,000 estimated for the first year cost actually will come from the NCI budget, since the cost recovery system, in which investigators reimburse the contractor for material received, will pay for the cost of the contract.

An important aspect of studies in biological carcinogenesis involves the production of cDNA copies of oncornaviral genomes, or parts of such genomes, for use as probes to identify viral sequences in normal or malignant tissues, to compare viral and cellular sequences for homology, to determine the relatedness of viruses, to permit

expression of viral sequences in a bacterial system, and for other studies of the molecular biology of viruses. For a number of years, this contract and its predecessors have been the major worldwide supplier of avian myeloblastosis virus and AMV reverse transcriptase to the scientific community for cancer research.

Should the need for these products diminish, we will decrease the funding for the effort accordingly. However, for the immediate future, we anticipate that 500-550 laboratories will continue to utilize the enzyme and virus.

John Cole is the project officer.

Inter and intraspeciies identification of cell cultures. The estimated total cost for three years is $1 million; however, DCE expects that some portion of that will be recovered through the payback system. Present contractor is Children's Hospital of Michigan.

The Biological Carcinogenesis Branch supports a broad spectrum of research on the relationship of viruses to the processes by which tumor formation is initiated or promoted. An obvious experimental approach is the study of cultured tumor cells of animal and human origin. Many experimental techniques in virology, immunology, cell biology, and biochemistry require the precise duplication of cells or mixtures of cells, with the result that cell identification services are of great importance. The extensive use and informal cross supply of cell cultures among investigators has resulted in a major problem of frequent erroneous or mislabeled cell lines. Correctly identified cell lines are of critical importance since research utilizing misidentified cell lines is a waste of time and research funds. This project is a resource effort for the inter and intraspecies identification of cells in culture. Over the past 11 years, more than 2,600 cultures have been examined or tested, and over the past year approximately 250 cultures have been submitted from 50 laboratories for examination and testing. The need for proper cell culture identification remains high, since over 20 per cent of the cell lines submitted for cell identification have been discordant with the presumed identity. Approximately this same level of cell species discrepancy has persisted throughout the duration of the effort. This work benefits NCI and the virological research community by providing qualified investigators with access to identified cell lines; applying uniform standards of quality control; cost savings by minimizing the duplication of effort at numerous laboratories; and comparability of results from different laboratories since the same species or type of cell lines are used.

This contract took in approximately $7,000 in cost reimbursement receipts if FY 1982 and $51,000 in 1983. Thus it appears that interest in this service is increasing in the scientific community.

This project provides a cell culture identification service that utilizes three systems: isoenzyme analysis, immunofluorescent staining, and cell chromosome analysis. Since it is not physically possible or economically feasible for all laboratories using tissue or cell cultures to have expert in house capability to identify cell lines in use, and since 20-25 per cent of the lines submitted for identification are not what the submitting laboratories presumed them to be, there is a need to continue this service.

John Cole is the project officer.

The Board approved the recompetition with the provision that DCE make an effort to more widely publicize the availability of this resource.

Marmoset colony for cancer research. Total estimated cost, $820,000 for three years. Present contractor is Oak Ridge Associated Universities.

This contract was initiated in FY 1982 to maintain an already existing, NCI owned breeding colony of cotton topped marmosets, so that appropriate numbers of these nonhuman primates would be available for experimental use by investigators in cancer research. This NCI contract currently provides fiscal support for 102 cotton topped marmosets and two white lipped marmosets. In the past, marmosets have been successfully used as a primate animal model for studies of certain RNA and DNA tumor viruses. With the isolation and recognition of human T-cell leukemia/lymphoma virus as a human cancer virus, studies are being initiated to determine the effect of HTLV on marmoset cells in vitro and on the transplantation of these infected cells into marmosets. The recent isolation of type C viruses (HTLV like viruses) and type D viruses from Rhesus monkeys has aroused interest in the use of marmosets in host range and primate animal experimentation studies. There have also been recent reports on the natural occurrence of colon carcinoma in adult marmosets belonging to the Oak Ridge Associated Universities and in two other marmoset colonies, the New England Primate Research Center and the Univ. of Bristol, England. Marmosets may thus provide a valuable primate animal model of human colon cancer. Because marmosets are also highly susceptible to the development of colitis, there is considerable interest in this animal model in the studies of colitis and establishing the possible connection between colitis and development of colon cancer. It appears, therefore, that the marmoset is a potential animal model for a number of preneoplastic and malignant diseases.

Objectives of the new contract are to maintain a breeding colony of no less than 60 cotton topped marmosets; to assure that the number of offspring produced per year will be a minimum of 28 cotton topped marmosets; to provide space for a conventional holding colony for juveniles scheduled to replace old breeders or awaiting experimentation; to provide an isolated holding colony to house approximately 50 experimental animals; to provide a separate biohazard containment nursery for inoculation and housing of neonatal animals; to administer potentially oncogenic materials to marmosets; to provide clinical support services to monitor the health of the colony and provide services in accordance with experimental protocols; to collect, store and provide appropriate biological specimens, such as serum and tissues, to interested investigators; to make available both biopsy and

necropsy specimens of marmosets to investigators for other studies relating to cancer. The experimental animals and services will be made available to extramural and intramural investigators under the resources payback system.

Padman Sarma is the project officer.

DCE Director Richard Adamson said that if one third or more of the cost is not being recovered through the payback system after a year, the contract would be phased out. Board member Edward Bresnick offered a motion to approve the concept with the provisions that availability of the resource be widely advertised and that if the payback does not reach 30 per cent within 18 months, the project be terminated. The motion was approved.

Breeding facility for woodchucks. Estimated total cost, $825,000 for three years. Cornell Univ. is the present contractor.

In 1978, Summers et al. discovered a virus morphologically similar to hepatitis B virus in the sera of eastern woodchucks. The woodchuck hepatitis virus (WHV) appeared to offer a unique opportunity for the understanding of the role of these unusual viruses in chronic hepatitis and its sequalae. Approximately 30 per cent of woodchucks captured from the wild in Maryland, Pennsylvania and New Jersey were chronically infected with WHV. Virtually all chronically infected animals maintained in captivity exhibited chronic liver disease and died with hepatocellular carcinoma (HCC). Animals not chronically infected with WHV did not develop HCC. Interestingly, woodchucks captured in Vermont, Iowa or New York show little or no evidence of WHV infection and do not develop HCC.

The woodchuck is the only animal model available for studying HBV-like infection, acute and chronic liver disease, including HCC. In 1980, NCI and the National Institute of Allergy & Infectious Diseases ventured into a collaborative effort to develop the woodchuck model, for persistent infection and associated disease. To develop the model, it was considered necessary to develop a breeding colony of woodchucks so that unexposed animals would be available for experimentation in a controlled environment. Little was known about the chances for successful production of woodchucks under laboratory conditions and a five year effort was undertaken in which NCI provided funds for the breeding effort and NIAID provided expertise for the animal experimentation (intramural and contract scientists) and experimental facilities. Results of these efforts to date indicate:

1. Woodchucks will breed in captivity and produce about 1.8 pups per litter. There is one litter produced per year and about 50 per cent of females bred in captivity conceive. Approximately 60 per cent of pups survive. Methods to improve conception rates and increase pup survival are currently under investigation.

2. Many experiments conducted by NIAID scientists were performed with woodchuck pups born to pregnant females captured from the wild. While satisfactory for many experiments, there will be a continuing need for colony born animals as controlled studies for mechanisms of carcinogenesis or cocarcinogenesis are undertaken.

3. Sensitive and specific assays for markers of WHV infection have been developed. Assays for serologic markers of liver disease (e.g. enzymes) and HCC are currently under development.

4. A series of monoclonal antibodies has been developed to define the major epitopes of WHsAg. Passive immunization studies are planned.

5. Pools of infectious WHV have been established and titered to endpoint in susceptible woodchucks. WHV DNA from these pools have been cloned by recombinant DNA methods and are being sequenced. This DNA will be used to probe the state of WHV DNA in appropriate tissues.

6. A WHV vaccine, similar to that for HBV, was prepared and was effective in preventing WHV infection in animals challenged experimentally with WHV. Chemically synthesized peptides predicted from nucleotide sequences of the WHV DNA (S gene) are being evaluated as immunogens.

7. Acute and persistent infections have been induced in colony born animals. Experimentally induced carriers are being carefully monitored for liver disease and HCC development. Appropriate control animals are also being monitored.

8. Chronically infected woodchucks are susceptible to human delta agent infections and will provide a valuable model for this defective human virus and its relationship to hepatitis B-like virus infection.

9. Serum samples, tissues, and woodchucks have been provided, insofar as possible, to other investigators with similar research interests.

The colony is currently maintained at Cornell Univ. in Ithaca, N.Y. It produces 80-90 pups a year, 30 of which were derived from colony bred females in 1983. The experimental use of the pups is performed by Robert Purcell of NIAID and John Gerin of Georgetown Univ. Hans Popper, Mount Sinai Medical Center, is an active collaborator with these laboratories. Experimental facilities for the woodchuck work are at Cornell and Meloy Laboratories.

John Cole is the project officer for NCI and Franklin Tyeryar for NIAID.

"I have mixed feelings about this," Board member Myron Essex said. "I agree this is a wonderful model. I feel something should come together so these very valuable animals can be made available so other interested investigators could do comparative studies. My question is, who should make the decision who gets the animals? They should come in with competitive proposals, and someone should review them."

Adamson said DCE is doing a survey to determine how many intramural and extramural investigators would use the resource.

Essex' motion to approve the concept with the provision that a review system be established to consider proposals for use of the animals was approved.

Resource for xenotransplantation and evaluation of human tissues and cells in athymic nude mice. Estimated total cost, $1.14 million over four years. Present contractor is Litton Bionetics.

The Laboratory of Human Carcinogenesis develops and employs model systems for the study of carcinogenesis in cultured human cells and tissues. The program design involves collection (surgery or immediate autopsy); in vitro maintenance and treatment; and xenotransplantation of normal, preneoplastic and neoplastic carcinogen treated and untreated human tissues in athymic nude mice. This contract, established in 1974, provides the xenotransplantation segment of the study. During its 10 years, the project has achieved one of the most disease free nude mouse colonies known. Under the rigid conditions of a closed, self sustaining facility, requiring sterility of all materials and supplies entering and antibacterial showers for personnel; the nude mice live a normal life span of 24-36 months; human target tissues are successfully transplanted and maintained in nude mice for more than 16 months; methods have been established for in situ exposure of human tissue to carcinogens; immunological, enzymatic, and karyological methods are used for marker identification of human tissues in nude mouse recipients; preneoplastic lesions in human tissue xenotransplants have been obtained; and the development of tumors in nude mice from oncogene transfected human bronchial epithelial cells has been accomplished.

In continuing this resource, the contractor, employing an essentially pyrogen free facility, will provide an enclosed colony of 600-900 athymic nude mice to be bred and maintained on a continuing basis; methods for long term survival of xenotransplants of human tissues in nude mice; and long term animal holding experiments, housing athymic nude mice for periods of up to two years. Xenotransplanted human tissues will be frequently monitored in vivo for viability and the integrity of tissue specific characteristics, and in some experiments, the xenotransplants will be treated with carcinogens in vivo. All growing tissues will be transplanted to new mice, characterized microscopically and histologically, and provided to the LHC for in vitro studies at NIH.

Glennwood Trivers is the project officer.

In vitro radiosensitivity and DNA repair in persons at high risk of cancer. Estimated first year cost of the three year award is $433,000 (See below for Board's changes). Present contractor is Atomic Energy of Canada Ltd. The project also involves an interagency agreement with the Brookhaven National Laboratory, at an estimated cost of $264,000 for the first year. The contract will be recompeted, interagency agreement renewed.

The purpose of this project is to examine the in vitro response to gamma radiation, ultraviolet light or sunlamp radiation, and chemical carcinogens of cells from persons with radiogenic, sunlight or chemotherapy induced tumors, or with multiple primary malignancies or familial tumors suggestive of genetic causation. Abnormalities detected in cells from individuals in these categories are studied further to determine the underlying cellular defects. Additionally, cells from blood relatives, both with and without cancer, are also studied to determine if the defects in in vitro response to DNA damaging agents can be directly correlated with increased cancer risk, or segregate within families in a mendelian fashion.

Two approaches will be used for screening specimens for unusual responses to carcinogens. The currently used method measures the ability of single cells exposed to various treatments to survive to form colonies. Increased or decreased cell killing, though commonly accepted as a suitable endpoint in these types of studies, may not reflect changes at the level of DNA, and thus may be unrelated to host susceptibility to cancer. Since mutagenic events are undoubtedly important in the development of at least some malignancies, a more specific assay may be the measurement of a cell's mutagenicity following carcinogen exposure. A commonly used mutagenic endpoint is the frequency of mutations from 6-thioguanine sensitivity to 6-thioguanine resistance. This or a similar assay, in conjunction with colony survival, would provide a more sensitive screen for cellular defects that may be related to enhanced cancer susceptibility.

Dilys Parry is the project officer.

"This is producing interesting results, but the budget has gone beserk," Board member Louise Strong said.

"I would suggest continuing this for one year at the existing level, with continuation depending on results of a site visit," Board member Marcel Baluda said. That was the action the Board approved, cutting the estimated budget back to about $390,000 for the contract and $250,000 for the interagency agreement.

Support services for occupational studies. Total estimated cost, $1 million a year, three years. Present contractor is Westat Inc.

Occupational groups may receive heavy and prolonged exposure to potentially hazardous substances and may, therefore, serve as indicators of hazards to the general population. Studies of the cancer experience of working populations have provided much information about chemical carcinogenesis in man. The objective of the Occupational Studies Program of the Environmental Epidemiology Branch is to generate and test hypotheses concerning environmental determinants of cancer associated with the workplace. To meet national needs the Branch must have the capability of responding promptly to new developments or requests in the area of occupationally related cancer.

Study designs to be employed include cohort, case control and proportionate mortality or morbidity approaches depending upon study objectives and the availability of resources. All studies are thoroughly reviewed by senior staff of the branch as well as by interested parties such as other government agencies, labor unions, companies and industrial organizations, professional societies, collaborating scientists, and expert review groups, where appropriate. Feasibility studies and pilot projects also will be conducted, where appropriate.

To conduct a program of occupational studies, NCI requires the assistance of an organization highly experienced in providing technical support for all phases of occupational health studies including the

design of data collection documents; hiring and training of interviewers and abstractors; collecting, keying, editing, updating and recording data; tracing individuals; evaluating and estimating exposures in the workplace; collecting and transporting biologic tissues to be used for biologic measures of occupational exposures; and creating and manipulating data files. This contract also provides support for tracing activities to other investigators in the Epidemiology & Biostatistics Program by operating a receipt control system. The scientific aspects of all projects are determined by the professional staff of the branch. The responsibility of the contractor is to provide a team of study managers, abstractors and interviewers, computer programmers, coders and keyers, industrial hygienists, and other support personnel to complete study tasks. A new contract to provide these servcices will be competed to replace the current contract with Westat Inc. which terminates in September, 1985.

Work will continue on projects not yet completed. Feasibility and pilot studies of new projects will be initiated where appropriate. Studies of pesticide applications from California and aerial applicators from throughout the U.S. are under way. These studies and a nested case control study are designed to followup the finding of an excess of lung cancer among Florida applicators. Grain millers and handlers are being studied to evaluate the cancer risks associated with exposure to grain fumigants including ethylene dibromide, carbon tetrachloride, phostoxin, and malathion. Shipyard workers, sanitary ware manufacturers, and foundry workers are being studied to assess the cancer experience of persons exposed to silica and/or talc. The carcinogenicity of the widely used solvents tetrachloroethylene and trichloroethylene is being evaluated in studies of dry cleaners and jewelry workers. The mortality of furniture workers exposed to wood dusts, paints, varnishes, metal fumes, and urea formaldehyde glues is nearing completion. The mortality of workers exposed to chromium and nickel is being assessed in studies of stainless steel welders. Under consideration are nested case control studies of leukemia and brain cancer among anatomists and embalmers to clarify risks for these cancers noted in recently completed mortality studies. The feasibility of a study of workers having contact with titanium dioxide is under consideration. Titanium dioxide is widely used as a pigment in the paint, paper and plastic industries and has recently been shown to cause lung cancer in rats exposed by inhalation.

Aaron Blair is the project officer.

Board member William Haenszel commented that the recent site visit to the branch resulted in three recommendations: Either the staff be increased or fewer projects undertaken; an emphasis on case control, dose response industrial hygiene studies; and closer collaboration with the National Institute of Occupational Safety & Health.

"These recommendations would modify the concept under which the branch has been operating," Haenszel said. "That has not been addressed directly in this written concept. If the concept (of the branch's program) is modified, is this resource contract the appropriate one? I think the staff should be put on notice they should be responsive to changes."

Haenszel asked if "whether any great difficulty would be created if approval is for less than five years," as requested by staff.

"That gets to the heart of the matter," Board Chairman Barry Pierce said.

Blair said that in response to the three recommendations from the Board's review of the branch, "One, that we get more people or undertake fewer studies, we've done both. Two, case control studies is the thrust of the new work that is going on. Three, we are planning more studies in collaboration with NIOSH."

Adamson added that a three year extension would put the support contract "in sync with the next review of the branch." Bresnick's motion to approve the concept for three years was approved.

The Board deferred a new contract supported project costing an estimated $425,000 a year for three years for a case control study of cancer and drinking water contaminants. Members felt that the study as planned was not likely to get any meaningful results on disease sites, and that there are probably too many confounding contaminants in many sources of drinking water. The motion to approve the concept carried on the first vote, but with more abstentions than members voting. A second motion by C.C. Cheng to defer until a new proposal could be developed with the Environmental Protection Agency was approved unanimously.

CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY: RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

The Cancer Letter _Editor Jerry D. Boyd

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