THE CANCER LETTER

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House Committee Provides $2.1 Billion To NCI, Deletes Breast Cancer Earmark, Forward Funding

The House Appropriations Committee last week approved a bill that contained no earmarks for breast cancer and gave NCI $2.1 billion, an increase of $102.9 million from FY 1993.

The Committee's appropriation is also $40.9 million above the President's budget proposal. The full House was expected to vote on the bill Wednesday. The Committee also eliminated the President's suggested

(Continued to page 2)

In Brief

William Roper To Head Health Research Center; Announcement Of New NIH Director Is Imminent

WILLIAM ROPER, who had announced he would leave as director of the Centers for Disease Control & Prevention, will head the newly established National Center for Health Care Research in Atlanta, an organization supported by Prudential Health Care Systems. Prudential said it will commit $20 million to the center over the next few years for research to evaluate and improve medical care delivery. . . . **NEW NIH DIRECTOR** was expected to be announced by the Clinton Administration this week. **Bernadine Healy** was to leave office on June 30. Two candidates that appear to have the lead are **Judith Rodin**, psychologist and Yale provost, and **Harold Varmus**, virologist of Univ. of California, San Francisco. . . . **KRISTINE GEBBIE**, Secretary of the Washington State Dept. of Health, was appointed White House AIDS policy coordinator last week. Gebbie, a nurse, participated in the American Nurses Assn. federal appointments project, which recruited nurses for federal posts and advanced their names to transition officials. . . . **NCI'S DIV.** of Cancer Etiology soon will lose two of its laboratories. **Takis Papas** will take most of his Laboratory of Molecular Oncology to Hollings Cancer Research Center at Medical Univ. of South Carolina, where he was recruited by center Director Peter Fischinger, former NCI deputy director. **PETER HOWLEY** will take his Laboratory of Tumor Virus Biology to Harvard Univ. . . . **DCE BOARD** members whose terms expired after last month's meeting are **Marcel Baluda, James Felton, Lawrence Fisher,** and **Stephen Hecht**. . . . **FOUR MEMBERS** of the Div. of Cancer Biology, Diagnosis, & Centers Board of Scientific Counselors have completed their terms: **Margaret Kripke, Carolyn Whitfield, Babu Ventkataraghavan,** and **Noel Warner**. New members are **Esther Chang,** pathologist and molecular geneticist, Uniformed Univ. of Health Sciences, and **Alan Solomon,** head of human immunology and the cancer program, Univ. of Tennessee Medical Center. Two more appointments are expected.

Capitol Notes

House Committee Raises NIH, NCI Budgets Above President's Request

(Continued from page 1)
provision for $100.8 million in forward funding for research in breast cancer.

The committee bill gave NIH $10.9 billion, an increase of $610 million over FY 1993 and an increase of $268.7 over the President's budget proposal.

The report called on the new NIH Director to develop a multiyear budget "based on balance and stability without sacrificing the ability to respond to new programs."

The excerpted text of the committee report follows:

The bill includes $2,082,267,000 for NCI, which is an increase of $40,943,000 over the comparable amount requested for FY 1994 and $102,926,000 over the comparable 1993 appropriation.

The Committee has not approved $100,798,000 of forward funding requested in the President's budget for FYs 1995-97 research costs.

Breast cancer--The Committee fully supports the President's commitment to increase NIH funding for breast cancer research. The Committee bill reflects continued support for a multiyear effort to significantly expand research on this critical health problem which kills 46,000 women each year.

NCI is expected to expand all facets of breast cancer research, including basic studies at the genetic level; epidemiology studies focused on environmental carcinogenesis; prevention research and vaccine development; detection research; treatment studies and rehabilitation efforts.

Prostate cancer--The Committee is encouraged by the efforts of NCI to expand prostate cancer research but remains concerned about the growing incidence of prostate cancer--now estimated to be 165,000 new cases in 1993 and 35,000 deaths--and its disproportionate impact on minorities. The Committee strongly urges the Institute to continue to make prostate cancer research one of its top priorities.

Other gender specific cancers--The Committee continues its support for an aggressive effort to prevent, treat and cure other gender specific cancers including ovarian and cervical cancer. This includes continued research on the problems associated with use of the drug DES.

Other concerns--The Committee recognizes the value of and the need for a balanced cancer research program. Basic research is the foundation for prevention and the development of improved treatments for cancer once it occurs. The Committee believes that basic cancer research must be given equal emphasis with disease specific research in allocating scarce research resources.

The Committee heard testimony about the continuing burden of leukemia, lymphoma and related cancers and supports continued development of research in this area. The Committee urges NCI to consider the full range of research mechanisms as it manages this research.

The Committee is supportive of the bionutrition activity of NCI and urges the Institute to utilize a portion of its increase m breast cancer funding to expand the work it is doing regarding the role of nutrition in breast cancer.

Proton beam research has been supported by NCI because of its potential in the treatment of inoperative cancers and certain vascular diseases. The Committee believes that this research should be continued based on the results to date.

The bill includes sufficient resources to finance the next stage of this research initiative.

Committee Funding Policies--The Committee bill deletes $132 million of forward funding requested in the President's budget for FY 1995 through 1997 costs of certain research projects.

The Committee has a longstanding policy of not providing funds on a forward funded basis because of the distortion which this causes in determining the real level of support for research in a given fiscal year. The Committee has reallocated these funds together with $269 million of additional funding to meet FY 1994 research needs at NIH.

These additional amounts will provide for inflationary adjustments for each of the Institutes and Centers and for real growth of at least one percent for each Institute and Center to address its highest priorities.

THE CANCER LETTER

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The Committee is fully supportive of the high priority given to research on breast cancer and AIDS in the President's budget and has identified other diseases in this report as of urgent concern. Neither the bill nor this report, however, identifies a specific funding level for a particular disease. The Committee believes strongly that the specific allocation of funds among diseases and among research programs should be determined by the scientists and science managers at NIH based on the scientific opportunities available.

These judgements are based on a fair system of peer review administered by NIH in consultation with its established system of advisory councils.

Financial Planning and Management--While the bill provides substantial resources for NIH, budgetary constraints have made it impossible for both the executive and legislative branches to fund biomedical research at levels which are compatible with both the critical health problems of our population and the quality of the scientific opportunities available.

This problem has been exacerbated by the lack of consensus between the executive branch and the Congress on a realistic multiyear financial and budget plan for NIH.

There has also been great concern about reallocations within NIH to expand research in certain high priority areas without sufficient attention to the negative impact which such shifts cause within other diseases or research programs.

The lack of a budget plan and the shifting of large amounts of funding within the base has resulted in uncertainty in the scientific community about the federal commitment to a broad range of biomedical research investigation and to basic science in particular.

The most critical manifestation of this problem has been substantial fluctuations in the number of new grants which can be funded in any given year. In 1991, NIH published an interim financial plan in response to Congressional concerns in this area. Unfortunately, this plan was largely abandoned in the President's fiscal year 1994 budget request.

The Committee hopes that the additional resources added in the bill will partially restore the plan and result in a significant increase in the number of new grants. More importantly, the Committee expects the new Director of NIH, who is expected to be on board at NIH within a few months, to give high priority to development of a multiyear budget plan which is based on balance and stability without sacrificing the ability to respond to new problems.

As a central part of the FY 1996 budget planning cycle, the Committee expects the new Director of NIH to review carefully the role, size and cost of the intramural program. This research is currently allocated about 11 percent of the NIH budget.

The Committee is concerned that the composition of this research is not based on a well thought out division of labor between the extramural and intramural programs, but rather on a case-by-case review of research proposals submitted by NIH scientists independent of necessary discussion of whether this research could be adequately addressed through other external mechanisms.

In addition to these issues, the Director's review must take into account the limits on space and facilities available on the campus. These facilities are already outdated and need to be replaced at very substantial costs. It is not practical to assume that alternative facilities, such as a new campus, can be built in the foreseeable future.

NIH must put together a system for allocating resources to and among its intramural programs based on a thoughtful analysis of these issues.

The Committee believes that budget planning should also review aggressively the growth of research management and support costs including staffing to determine whether the resources devoted to overhead at NIH are excessive.

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The National Breast Cancer Coalition is hoping that the Department of Defense Appropriations Subcommittee would continue funding the DOD's $210 million breast cancer research program.

"We believe that to maximize the investment of these funds, the program must continue at this level for more than two years," NBCC president Fran Visco wrote in a recent letter to John Murtha (D-PA), chairman of the DOD subcommittee.

The Administration's budget proposal transfers the DOD breast cancer research program funds to NIH, where, under the President's plan, the funds would be spent over three years.

The Labor, HHS and Education bill approved by House Appropriations Committee eliminated the multi-year funding provision of the program.

"The scientific community must believe that this is not a one time only infusion of funds, but one that will be sustained over the next few years," wrote Visco, who was recently appointed to the President's Cancer Panel and who last year spearheaded the NBCC's successful drive that resulted in the DOD appropriation.

"The influx of new investigators will need to know that the funds for training and recruitment are ongoing and that this is not just a two-year fad,"

Visco wrote. "It is unlikely that many institutions will make a commitment to providing a research environment that will support... predoctoral research slots for breast cancer unless they are confident of a long term sources of funding."

The DOD appropriations subcommittee is yet to mark up its version of the budget.

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Sen. Tom Harkin (D-IA) pledged that he would make it possible for the NIH Office of Alternative Medicine to hire five staff members who would seek out effective treatments available from unconventional practitioners.

At the June 24 hearing last week Harkin described the new staff members' function as "investigation and validation" of unconventional treatments. However, several sources said they were not certain what the Senator meant by those terms. Another hearing is expected next fall.

At the same hearing, Harkin said he planned to ask NCI to account for its planned trials of "antineoplaston," an agent available at the Houston area clinic of the controversial physician Stanislaw Burzinsky.

NCI has received a $750,000 transfer from OAM to conduct two phase 2 trials of the agent. The trial has been in planning stages for over a year and is yet to begin.

"I'm going to get [NCI Director Samuel] Broder up here," Harkin pledged, while questioning another witness. "It's not the first time I've had him up here in the hot seat. Where did the money go? I can't find out."

NCI officials told **The Cancer Letter** the Institute is about to file an IND required for the trial, and, according to Institute sources, Burzinsky is expected to file his portion of the materials, the "master file," directly to FDA.

Preparation for the trial involved negotiations with Burzinsky over patient selection, dosage and administration schedules. According to NCI sources these issues have been resolved.

The Institute and Burzinsky also have resolved their differences over the purity of the material the physician has supplied for the trials, Institute sources said. The trials, in adult brain cancer patients, are expected to be conducted at Memorial Sloan-Kettering Cancer Center and Mayo Clinic.

At last week's hearing Harkin encouraged OAM director Joseph Jacobs to press Broder on the status of the "antineoplaston" trial:

"I hope that you will ask Dr. Broder what they've done with this money," Harkin said to Jacobs. "Push him. Move the process faster. There's been a tremendous amount of delay. You give money to NCI, and it's like putting money into a black hole.... My responsibility is to the taxpayers and to see that this thing gets moving.

"If there's any foot-dragging, then you can be sure you'll hear from me," Harkin said.

NCI To Study Relationship Of Vasectomy To Prostate Cancer

NCI will undertake an epidemiology study of prostate cancer risk among men who have undergone vasectomies, following concept approval of the proposed contract by the Div. of Cancer Etiology Board of Scientific Counselors.

The three year, $1.4 million study (the total approved by the board) will be carried out by the Biostatistics Branch of DCE's Epidemiology & Biostatistics Program. A contract will be awarded competitively.

The concept was triggered by reports from two studies that found an excess of 60% risk among vasectomized men, and an NCI study which found that the increase in risk was greater among men with vasectomies before age 35. An NIH consensus conference earlier this year was unable to reach a conclusion about the relationship of prostate cancer and vasectomy.

The American Cancer Society compiled reports on recent studies of vasectomy and prostate cancer and distributed the compilation to its Medical Affairs Committee last month. Most of the reports recognize an increased risk and call for a definitive study of the issue.

DCE board members Barbara Hulka and Peter Fischinger expressed concern about biases resulting from methods of detection and the fact that detectable prostate cancer frequently is preceded by long latent periods. "To minimize bias, you have to look at stage and method of diagnosis," Fischinger said.

Joseph McLaughlin, project officer for the contract along with Ann Hsing and William Blot, said measures to evaluate biases will be built into the contract.

The board also approved recompetition of six multiyear contracts with an estimated cost of more than $26 million. The largest of these is renewal of a five year contract for support services for the Viral Epidemiology Branch, estimated at a total of $10 million. Research Triangle Institute is the present contractor.

Other recompetitions approved are a $7.4 million,

five year contract for biochemical epidemiology support services, for which Microbiological Associates is the incumbent contractor; a $4 million, five year contract now held by Hazleton Laboratories America for studies on induction of tumors in nonhuman primates; support services for Robert Gallo's Laboratory of Tumor Cell Biology, for research on retroviral pathogenesis, treatment, and prevention, totaling an estimated $2.3 million over four years; nearly $2 million for a four year renewal of a contract for a laboratory rodent and rabbit facility for the Laboratory of Cellular Carcinogenesis and Tumor Promotion, a contract now held by Biocon Inc.; and a $750,000, three year contract presently held by the Dept. of Energy's Lawrence Livermore National Laboratory, for biodosimetry of populations exposed to ionizing radiation.

The recompetitions were all approved unanimously, and in the case of the Gallo support contract, without discussion.

The board sent the proposal for noncompetitive renewal of the Laboratory of Experimental Carcinogenesis' contract with the Chinese Academy of Medical Science back to the drawing board. The $240,000, three year award would continue DCE's collaboration with the Chinese for cellular and molecular studies of human hepatocarcinogenesis studies. Board member Ru Huang and others objected to the design of the studies and questioned some of the premises related to dietary factors.

Following are the concept statements:

Emergent cancer studies: Prostate cancer risk following vasectomy. New RFP, $1.4 million over three years.

Support services are sought under the Emergent Studies Master Agreement mechanism to evaluate prostate cancer risk following vasectomy in a retrospective cohort of 10,590 pairs of men with and without vasectomies. The cohort was assembled during 1977-82 to evaluate the health effects, particularly autoimmune diseases, following vasectomies performed for contraceptive purposes in a healthy male population. The vasectomized cohort included men living in four U.S. cities (Rochester and Minneapolis, MN, and Los Angeles and Eureka, CA) receiving vasectomies during 1946-76. The average age at vasectomy was 36 years, and the average year of the procedure was 1970. Neighborhood controls without vasectomies were selected by matching on age and race and assembled as a comparison group.

All cohort members will be traced, contacted, and interviewed by telephone with a brief questionnaire. It is estimated that 12% of the study subjects will have died by 1994. Attempts will be made to contact next of kin of deceased subjects for a surrogate interview. Death certificates will be obtained and reviewed for all deceased subjects. During the telephone interview, cohort members or their next of kin will be asked whether they have had a diagnosis of cancer, and particularly prostate cancer.

To assess the level of medical surveillance in vasectomized and nonvasectomized men between 1982 and 1994, information on utilization of medical care, urologic screening (digital rectal examination and prostatic specific antigen test) and hospitalizations will be obtained, even though there was no difference in the level of medical surveillance in these two cohorts during 1977-82. For cases, questions on how prostate cancer was diagnosed will be asked to provide additional information on medical surveillance. Personal consent will be sought in order to obtain pathological or medical records and biopsy slides to validate reported cancer diagnoses and to ascertain information on clinical stage and histologic grade of prostate cancer cases.

Attempts will be made to review biopsy slides of the prostate cancer cases and to compare pathological characteristics of cases identified from vasectomy and nonvasectomy cohorts. The distribution of these clinical variables in vasectomized and nonvasectomized prostate cancer cases will provide additional information on the level of medical surveillance in the two groups. In addition, information on pertinent risk factors, such as family history of cancer, prostatitis, and benign prostatic hyperplasia, will be elicited.

Besides the relationship between vasectomy and prostate cancer, associations of multiple risk factors, including smoking and drinking, body mass index, occupation, and medical histories (epididymitis, orchitis, and prostate diseases) with subsequent prostate cancer risk can be investigated, since the risk factor information was collected during 1977-82. In addition, risk of other cancers associated with these factors can be assessed in this retrospective follow-up study.

With a median age of 62 in 1994 and an estimated median follow-up of more than 20 years, we would expect about 300 incident cases of prostate cancer (about 65 prostate cancer deaths), based on SEER age-specific prostate cancer incidence rates. Assuming a 10% loss of follow-up, using a one-sided alpha of 0.05, the study has 90% power to detect a 40% excess in prostate cancer risk associated with vasectomy.

Support services for viral epidemiology. Recompetition of a contract held by Research Triangle Institute, $10 million over five years. Project officers: James Goedert and William Blattner, Viral Epidemiology Branch, DCE.

The current request is for renewal of the major support services contract that has been the cornerstone for VEB epidemiologic studies of AIDS and related viruses. The expertise of branch staff is focused on the formulation, design, quality control, analysis and interpretation of studies, while the actual data collection and associated activities are contracted to an experienced survey research firm.

NCI requires the assistance of an organization highly experienced in providing technical support for various phases of epidemiologic studies including the design of data collection instruments; hiring and training of interviewers and abstractors; collecting, keying, editing, updating, and recording data; tracing individuals; collecting and transporting biologic tissues and fluids to be used for virologic and immunologic analyses; and creating and manipulating data files. The scientific methods for all projects are the responsibility of 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, nurses, and other support personnel to complete assigned study tasks.

In some studies, the contractor is responsible for virtually all field activities. A second manner in which the contractor assists is by providing only selected types of support activities that cannot be accomplished by the locally-based collaborators.

A number of prospective cohort studies will be supported or expanded, while other activities will be terminated or the source of funding shifted.

Support services for biochemical epidemiology. Recompetition of a contract held by Microbiological Associates Inc. Total $7.4 million over five years. Project officers: James Sontag (EBP) and Peter Shields (LHC).

The Epidemiology and Biostatistics Program and the Laboratory of Human Carcinogenesis have a long-standing interest in interdisciplinary studies, termed biochemical or molecular epidemiology. Since the program and laboratory plan to continue these studies, it is necessary to maintain a prime contractor for procuring laboratory support services. In the new award, the scope of laboratory support services will be expanded to include analyses of environmental samples (e.g. pesticides in soil) collected as part of epidemiologic studies. A major function of the prime contractor will be to evaluate the scientific credentials and experience of potential support services laboratories, award subcontracts, and monitor performance to ensure the production of high quality data and adherence to contractual obligations.

An RFP will be issued describing the biochemical epidemiological support services required. These services fall into two main areas: 1) maintenance of a biospecimen repository and related logistical support, and 2) procurement of laboratory services. Functions related to the repository include the short term storage of field-collected biospecimens; bioprocessing of specimens; on-line data entry on the identity, characteristics, and status of biospecimens in the repository; and logistical support related to the collection and shipment of biological specimens.

The competitive procurement of laboratory support services involves: 1) developing RFPs specifying the NCI principal investigator's requirements, 2) identifying laboratories interested in providing support services and issuing them as RFPs, 3) determining the most qualified laboratories, and 4) awarding subcontracts for support services.

Studies on induction of tumors in nonhuman primates. Recompetition of a contract held by Hazleton Laboratories America Inc. Total $4 million over five years. Project officer: Unnur Thorgeirsson, DCE Office of the Director.

This long term chemical carcinogenesis study in nonhuman primates has been continuous since its inception in 1961. It has been carried out under contract at Hazleton Washington since 1961. The colony consists of three species: Macaca fascicularis (cynomolgus), Macaca mulatta (rhesus) and Cercopithecus aethiops (African green). For the past seven years, only the cynomolgus monkeys have been bred due to their smaller size and very low (1.5%) spontaneous tumor rate. The colony consists of 31 breeders and 301 experimental animals, including 203 cynomolgus, 81 rhesus, and 17 African green monkeys. Since 1961, 31 compounds have been tested for their carcinogenic potential in the monkey colony. Due to the longevity of Old World monkeys, exposure to chemicals for many years can be comparable to that experienced in humans. The project has generated a wealth of data which have been computerized and are easily accessible. A valuable collection of paraffin blocks and microscopic slides is available for histological and genetic studies.

Presently, the main emphasis of the project is on the heterocyclic amines, IQ, MeIQx, and PhIP. During the next contracting period, the objectives will be as follows: 1) continued assessment of the carcinogenic potential of IQ, MeIQx and PhIP following chronic oral administration, 2) continuation of histopathological studies of IQ mediated cardiotoxicity, 3) collection of blood, urine, feces, and tissues for metabolic and DNA adduct studies following short term dosing, 4) initiation of long term studies on the prevention of IQ induced hepatocellular carcinoma and cardiac toxicity by protease inhibitors. Short term studies will be performed to determine which of these agents will most efficiently reduce or prevent DNA adduct formation, 5) initiation of studies to evaluate if a diet high in saturated fat promotes malignancy in monkeys chronically dosed with PhIP. Since PhIP has been shown to induce mammary and colon carcinomas in rodents, special efforts will be made to check for breast tumors and carry out endoscopic examination of the colon for detection of micro and macroscopic lesions, 6) undertaking of genetic studies (oncogenes and suppressor genes) of IQ induced hepatocellular carcinoma in collaboration with Japanese scientists.

The number of compounds which have been under investigation for many years is steadily decreasing. During the next contracting period, the objective will be to continue the long term carcinogenicity studies on only three compounds, cyclamate, saccharin and DDT in addition to the heterocyclic amines. It is expected that a lifetime (25-30 years) study on the carcinogenic potential of cyclamate, saccharin, and DDT will be completed in five more years.

The monkeys and the breeders are housed in an isolated facility which contains only animals committed to this project.

Support for research on retroviral pathogenesis, treatment and prevention. Recompetition of a contract held by Advanced BioScience Laboratories Inc. Total $2.3 million over four years. Project officer: Marjorie Robert-Guroff, Laboratory of Tumor Cell Biology.

This contract will provide a virus isolation capability in a suitable BL2/BL3 laboratory. This work will be complemented where required by characterization of viruses isolated by standard biochemical and immunological techniques, including immunological assessment of serologic status of the human or animal sample donors.

This contract will provide a primate stem cell culture capability for gene therapy studies. The contractor will provide stem cell cultures for in vitro and in vivo experiments, and will assess and characterize cultures following insertion of foreign genetic material. These capabilities will also be extended to tissue samples following initiation of studies in animal models.

The contract will provide the capability to purify, biochemically characterize, and provide biologically active proteins from viruses, cells for conditioned media and from bacterial or mammalian expression systems. Functional assays

will be performed to assess the effect of biologically active materials on cell growth and angiogenesis. Reagents, such as monoclonal and polyclonal antibodies, will be generated from the purified or partially purified materials and will be applied to further affinity purifications and immunologic characterizations.

The contractor will provide all laboratory support, including BL2/BL3 laboratories where necessary, and appropriately trained personnel to carry out the objectives of the contract. Virus isolations and characterizations will be performed on blood cells or tissue samples as required. Primate stem cell cultures, initially those of rhesus macaque origin, will be provided for application to the SIV system. Assessments of stem cells of either human or nonhuman primate origin carrying inserted foreign genes will be carried out routinely. Purification and characterization of bacterially expressed, biologically active tat will be a priority. Additional proteins of viral and cellular origin will be purified, characterized, and supplied as required. Functional assays, necessary for protein characterization, will be applied to assessment of cell growth and angiogenesis in the presence of modulating factors. Monoclonal and polyclonal antibodies prepared against proteins of interest will be characterized and provided.

Laboratory rodent and rabbit facility as a resource to the Laboratory of Cellular Carcinogenesis and Tumor Promotion. Recompetition of a contract held by Biocon Inc. Total $1,966,000, four years. Project officer: Henry Hennings, LCCTP.

The function of this contract is to provide space, care and technical support for the conduct of in vivo experiments. The contractor shall: 1) provide proper housing and husbandry for the maintenance of healthy intact, nude, and transgenic mice, and vitamin-deficient hamsters and mice; 2) ensure that space and equipment are dedicated to this contract; 3) monitor animal health through periodic testing for pathogenic viruses, bacteria and parasites; 4) provide a hazard-free environment to safely conduct skin carcinogenesis experiments using initiating and promoting chemicals; 5) maintain a barrier environment for nude mice to be used for homograft and xenograft experiments and tumorigenicity testing of a variety of types of cultured cells by injection or implantation; 6) feed diets for vitamin deficiency studies and monitor animal weights and other clinical signs of deficiency states; 7) conduct skin painting experiments, including application of chemicals, counting tumors and gross autopsies; 8) perform skin grafts on nude mice; 9) inoculate rabbits with antigens provided by NCI, bleed inoculated animals and collect antisera; 10) collect and preserve tissues by freezing or fixation.

The contract would provide for the care of the following numbers of animals: conventional mice, 3000; transgenic mice, 300; nude mice, 700; rabbits, 10; and hamsters, 250.

Biodosimetry for populations exposed to ionizing radiation. Recompetition of a contract held by Dept. of Energy, Lawrence Livermore National Laboratory. Total $750,000 over three years. Project officers: Ruth Kleinerman and John Boice, EBP Radiation Epidemiology Branch.

Objective of this contract is to apply simple, reliable and precise biochemical measures of radiation dose to epidemiologic studies of irradiated populations. Primarily, these populations will be Sellafield nuclear fuel workers, Chernobyl cleanup workers and x-ray technologists. There will also be several smaller feasibility studies in other populations. The aim is to measure somatic cell mutations using glycophorin-A (GPA) and to perform translocation analysis with FISH to obtain measures of biological damage and cumulative radiation dose. Such measures will be incorporated into dose assessment schemes to characterize population exposures, perform dose-response analyses, and compute estimates of radiation risk.

The contractor will perform GPA assays and translocation analysis on blood samples from irradiated populations under study by the Radiation Epidemiology Branch.

RFPs Available

RFP 282-93-0029

Title: Development and periodic updating of clinical practice guidelines for three medical conditions.

Deadline: Approximately Aug. 1

The General Acquisition Branch of the Div. of Acquisition Management, Public Health Service, on behalf of the Agency for Health Care Policy and Research, proposes to award contracts for the development and periodic updating of clinical practice guidelines, medical review criteria, standards of quality, and performance measures on: screening for colorectal cancer, management of chronic pain with special emphasis on headache pain, and nosocomial urinary tract infection.

Three awards are anticipated. The proposed awards will be set-aside for public and non-profit organizations. Anticipated award date is September 1993. The period of performance is 38 months. A closing date is tentatively set for August 1, 1993.

Requests for the RFP must be submitted in writing to: Michele Trotter, Div. of Acquisition Management, General Acquisition Branch, PHS, 5600 Fishers Ln Rm 5-101, Rockville, MD 20857.

RFP NIH-WH-93-30 E/W

Title: Additional clinical centers for the clinical trial and observational study of the Women's Health Initiative--East/West

Deadline: Approximately August 31

NIH seeks approximately 29 additional Clinical Centers for the Clinical Trial and Observational Study components of the Women's Health Initiative. The trial objectives are to test the benefit and risk of hormone replacement therapy, dietary modification, and supplementation with calcium + Vitamin D on the overall health of U.S. post-menopausal women age 50 to 79. Approximately 57,000 women will participate in the various components of the Clinical Trial.

The observational study goals are to: 1) improve risk prediction of coronary heart disease, breast cancer, fractures, and total mortality in postmenopausal women; 2) examine the impact of involuntary changes in characteristics on disease and total mortality; and 3) create a resource of data and biologic samples that can be used to unearth new risk factors and/or biomarkers for disease.

The OS cohort will be comprised of approximately 100,000 U.S. women.

The additional Clinical Centers will cooperate with a Clinical Coordinating Center, the Vanguard Clinical Centers, and the Project Officer in implementing the overall Clinical Trial and Observational Study. Each additional Clinical Center will be responsible for screening, recruitment, randomization, and follow-up of approximately 1,270 CT participants and 2,220 OS participants.

A copy of the RFP may be obtained by written request including two self-addressed mailing labels to: National Institutes of Health, WHI, Research Contracts Branch, DCG, Federal Building, Room 1C11, Bethesda, MD 20892.

RFAs Available

RFA CA-93-027

Title: **Minority enhancement awards**
Letter of Intent Receipt Date: July 14
Application Receipt Date: Sept. 22

The Comprehensive Minority Biomedical Program (CMBP) of NCI's Div. Extramural Activities invites research grant applications from investigators with access to large or predominantly minority populations to promote minority group participation in cancer research with a special focus on cancer control research.

Applications may be submitted by domestic for-profit and non-profit organizations. Applications from minority individuals and women are encouraged. Institutions are eligible if they can demonstrate the following:

1. Broad research capabilities in cancer prevention, cancer control and cancer treatment as evidenced by significant research support in these areas. This would include past and current examples of ability to design and implement strong clinical trials research programs.

2. An organizational infrastructure that promotes and sustains a strong interdisciplinary, interactive cancer research environment which links basic research effectively to research in patient and populations settings (e.g., NCI-designated Comprehensive Cancer Centers).

3. Clear access to large numbers of minorities who are representative of the minority populations in the communities and/or regions associated with the institution.

4. Demonstrated capability to work with minority populations in a research setting within communities and/or regions.

This RFA will use the NIH individual research grant (R01). Average amount of direct costs expected per award is $200,000. Funding in the amount of $1,600,000 in total costs has been set aside for the first year. Six awards are anticipated. Total project period may not exceed three years. Earliest start date for the initial awards will be April 1, 1994.

General research objectives include, but are not limited to, smoking behavior in minority youth; studies of communication strategies for presenting information to minorities about cancer and its prevention; investigations of patient perspectives of cancer risks; the design and evaluation of interventions to minimize and prevent distress of minority patients with cancer; the development of pilot studies for minority clinical prevention trials; and psychosocial studies and perception of cancer risk in minorities.

Inquiries may be directed to: Dr. Lemuel Evans, Div. of Extramural Activities, NCI, Executive Plaza North Rm 620, Bethesda, MD 20892; Tel. 301/496-7344, Fax 301/496-7911.

RFA CA-93-029

Title: **Clinical studies of systemic therapies**
Letter of Intent Receipt Date: Oct. 22
Application Receipt Date: Dec. 7

The Cancer Therapy Evaluation Program of NCI's Div. of Cancer Treatment invites Interactive Research Project Grant (IRPG) applications to perform research projects designed to conduct clinical studies of innovative systemic therapies investigating promising therapeutic approaches in a single tumor type or focused on a single class of novel compounds or a mechanism of action.

Domestic and foreign, for-profit and non-profit organizations, governments and their agencies are eligible to apply. Applications can be from single institutions and multiple institutions (collaborating institutions, consortia, cooperative groups). New and experienced investigators are encouraged to apply. Applications from minority individuals and women are encouraged.

For the purpose of this RFA, each IRPG must consist of a minimum of three investigator initiated research grant applications (R01s).

Amended applications from CA-92-25 are encouraged. An IRPG that received funding for one or more, but not all, of the applications in the original package may submit revised applications for those that were unfunded. IRPGs submitted under CA-92-25 can be submitted with less than three required independent R01s under CA-93-029.

Support of this program will be by the research project grant (R01) through the use of the IRPG program. Total cost for each IRPG (consisting of three or more R01s) is limited to $750,000 per year. The average amount of direct cost per year for each R01 will range from $140,000 to $180,000. Total project period may not exceed four years. Earliest start date will be August 1994. Approximately $2 million in total costs per year for four years will be committed to fund applications submitted in response to this RFA. It is anticipated that three IRPGs will be funded in FY94.

The aims of this RFA are 1) to provide support for translational research that brings innovative basic research findings into the clinic and 2) to foster the development of interactions between basic science laboratories of different disciplines and clinicians performing clinical trials to advance therapeutic clinical research. This RFA is soliciting applications to perform interactive research projects with the goal of developing new clinical studies involving systemic therapies with a therapeutic intent.

The interactive research project grants may have as their key focus either: 1) clinical studies investigating promising therapeutic approaches in a single tumor type or 2) the development of new clinical treatment strategies focused on a single class of novel compounds or mechanism of action.

Each project supported in the IRPG is expected to contribute to and be directly related to the common theme of the IRPG application.

The application must clearly explain how the projected integrated R01 research grants can be expected to accomplish the stated goal more efficiently and effectively than they could without the anticipated interactions. At least one clinical trial protocol must be proposed in one of the grant applications. The clinical trials should be well integrated with the laboratory studies proposed within the same R01 grant or in separate R01 grants.

Inquiries may be directed to: Dr. Roy Wu, Div. of Cancer Treatment, NCI, Executive Plaza North Rm 734, Bethesda, MD 20892; Tel. 301/496-8866, Fax 301/480-4663.

NCI Contract Awards

Title: Support services for radiation and related studies
Contractor: Westat Inc., Rockville, MD; $9,434,417.

Title: Isolation and purification of michellamine B from crude extracts at ancistrocladus SP novum
Contractor: Hauser Chemical Research Inc., Boulder, CO; $314,888.