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## TURNOVER IN IMMUNOLOGY CONTRACTS TO FREE UP SUBSTANTIAL SUMS; POSSIBLE NEW RFPs LISTED

NCI's Immunology Program, with $16.1 million in contracts it supports each year, is going through its first major "turnover" since the program was started in 1972. The program will have little if any new money (funds in excess of the amount it had in FY 1976) for fiscal 1977. But from one-third to one-half of the program's 175 contracts will be allowed to expire when their three-year commitments have been fulfilled, freeing substantial sums for funding new contracts.

Three advisory committees have generated lists of research topics from which NCI staff will select those it decides to develop into RFPs. Each committee is responsible for a program area—immunobiology, immunotherapy, and immunodiagnosis.

Director William Terry discussed his program with the National Cancer Advisory Board, explaining the problem he has with assuring quality scientific advice in both the initiation of RFPs and review of

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*In Brief*

## FORD DECIDES AGAINST ASKING FOR RECISION OF NCI FUNDS AFTER CONGRESS OVERRIDES VETO

**PRESIDENT FORD** will not ask Congress to rescind any of the $819 million that is in HEW appropriations for NCI for FY 1977. Ford made that decision after Congress overrode his veto of the appropriations bill, with votes of 312-93 in the House and 67-15 in the Senate. This means that 1977 money will be available "very soon," Director Frank Rauscher told the President's Cancer Panel. In recent years, vetoes, recision requests and congressional delays have resulted in holding up NCI grant and contract disbursals well into the fiscal year, sometimes only a month before the end of the year. With the start of the fiscal year now Oct. 1, funds will be available only a few weeks or even a few days into the year. . . . **THE TOTAL** for NCI is $819 instead of $815, the figure included in the appropriation bill, because when Congress approved the 4.7% pay raise for most government employees, it appropriated extra money to cover it rather than requiring the agencies to pay the increase out of their regular funds. . . . **RAUSCHER'S SUCCESSOR** may not be appointed until after the election, or even after the inauguration in January, depending on who wins Nov. 2. The job is a Presidential appointment, with no fixed term; the director serves at the pleasure of the President. Some prospects might hesitate to accept the job from Ford, fearing that if Carter wins he might want someone else. There was speculation around NCI that an attempt might be made to gain in advance Carter's assurance he would retain the new director, which of course should be the most unpartisan appointment any President could make. If no appointment is made before Rauscher leaves Nov. 1, Deputy Director Guy Newell probably will be named acting director.

## NEW IMMUNOLOGY RFP POSSIBILITIES LISTED FOR AWARD IN FY 1977

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proposals. The field of immunology is still so limited that those scientists best qualified to serve on his advisory committees are also those most likely to compete successfully for contracts.

Terry avoids permitting those on his committees of gaining significant advantage over others in developing contract proposals by permitting the committees to draw up only very general statements of suggested areas for research. The committees come up with 20 or more suggestions each, from which Terry and his staff will choose two or three for development into RFPs (with multiple awards for each a possibility). The committees will not be further involved in writing the scope of work.

When the proposals come in, they go to the appropriate committee for peer review. However, when a member of a committee submits a proposal which normally would be reviewed by that committee, it either is sent to one of the other committees, when appropriate, or an ad hoc committee is put together to do the review.

In FY 1976, the $16.1 million was broken down this way:

Immunobiology–57 contracts totaling $3.6 million.

Immunodiagnosis–40 contracts totaling $3 million.

Immunotherapy–63 contracts totaling $6.6 million.

Fifteen support contracts, primarily for the program's intramural operations, accounted for the rest of the $16.1 million.

The biology contracts averaged about $63,000 each. Diagnosis averaged about $13,000 more, Terry said, because of the large amounts of tissue culture and the clinical work required. The therapy contracts cost the most, averaging $106,000 each, because they involved so much clinical work. Those dealing entirely with clinical research averaged as much as $135,000, Terry said.

Here are the suggestions developed by the Immunobiology Committee:

1. Develop or initiate techniques to produce monoclonal antibody of known specificity and restricted heterogeneity in large quantity using cell hybridization or other suitable techniques.

2. Expand hybridization techniques to develop homogeneous T cell populations in large quantity.

3. Biophysical and/or biochemical approaches to study the mechanisms whereby immunocompetent cells kill other cells.

4. Preparation of antisera to differentiation antigens on T cells, null cells and/or macrophages. Include provisions for distribution.

5. Production of large quantities of antisera to Ly-1 and 2 with appropriate quality control. Responses must include indication of how the necessary animals will be obtained or produced and how much antiserum will be produced. In addition, proposers should include attempts to produce these antisera in heterologous species.

6. Isolation and chemical characterization of lymphokines of defined biological activity. Proposers must have a quantitative assay for the activity of the lymphokine and be prepared to characterize this material only after it has been purified to homogeneity.

7. Production and distribution of mutant congenic strains of mice: major histocompatibility variants; mainly mouse but other mammalian species, with justification; include characterization.

8. Genetic control of susceptibility and/or immune response to tumors–determine number of genes involved, and do linkage studies; mechanism of susceptibility/response to tumors.

9. Animal models for bone marrow transplantation–factors controlling susceptibility or resistance; mode of stem cell differentiation to immune competent cells; immunologic reactivities in chimeric state.

10. Characterization of immune effector mechanisms in Marek's disease–nature of immune response; in vivo and in vitro immunologic parameters; define antigens involved.

11. Antisera to viral antigens and reactions with human tumors–antisera to C type oncorna virus should be studied for reactivity against human tumors in an attempt to define antigens in or on human tumor cells that are cross reactive with oncorna virus antigens; look at viral induced leukemias (antiviral antibodies to characterize human leukemic cells; attempt to block reactions using a tumor specific antigen.

12. Classification of human lymphomas on basis of reagents which detect cell surface antigens or other properties or functional activities. Proposals utilizing new or previously little used techniques will be given preference–leukemias also?

13. Role of suppressor cells in tumor bearing and other patients–effect on induction of immune responses in vitro or on lymphocute or other blood cell differentiation.

14. Study of in vitro induction of functional differentiation of T cells in systems relevant to tumor immunology–using tumor associated antigens as stimulus; consider role of soluble factors; thymic epithelium; human and murine.

15. Isolation and chemical characterization of antigen-binding T cell receptors–molecular and chemical characterization, polypeptide chain structures, associated proteins; leave broad, stress imaginative approach.

16. Investigate the nature and function of immune related cells in tumor masses.

17. Serology of human tumors. Proposals should attempt to utilize serologic techniques to identify

tumor associated antigens on human tumor cells. Preliminary evidence will be required.

18. Do embryonic/fetal antigens serve as transplantation rejection antigens?—Not CEA or α-fetoprotein.

19. Immunobiology of metastases—immunologic characterization of metastases; role of immune system in biology of metastases; distinguishing metastatic from primary tumor—characteristics.

20. Determination of in vivo biological significance of antibody-dependent cell-mediated cytotoxicity.

21. Characterization of preneoplastic cells—cell populations in preneoplastic states; neoplastic transformation models.

22. Alpha heavy chain disease research—abdominal lymphoma: alpha heavy chain fragments in serum and urine; animal model; determine region of molecular defect; detection of abnormal alpha heavy chain.

**Here are the research suggestions developed by the Immunotherapy Committee:**

—Immunotherapy of melanoma recurrent in lymph nodes using BCG by scarification (Repeat of M.D. Anderson).

—Comparison of FAC with FAC plus BCG by scarification in metastatic breast cancer (Repeat of M.D. Anderson).

—Comparison of post thoracotomy BCG plus INH versus INH in stage I lung cancer (Repeat of McKneally).

—Comparison of no further therapy versus BCG by scarification versus BCG plus 5-FU in Duke's C colon cancer (Repeat of M.D. Anderson).

—Comparison of DIC versus DIC plus BCG in metastatic melanoma (Repeat of M.D. Anderson).

—Comparison of intravesical BCG versus intravesical chemotherapy in bladder cancer (Repeat of Morales & Eidinger).

—Use of "intensive" immunotherapy with either BCG or intravenous C. parvum combined with optimal chemotherapy and/or radiotherapy compared to chemotherapy and/or radiotherapy alone in treatment of small cell carcinoma of the lung.

—Use of intrahepatic arterial infusions of immunotherapeutic agents in the treatment of hepatic metastases from G.I. malignancies or malignant melanoma.

—Regional administration of BCG immediately following surgical removal of cancers with known poor prognoses.

—Use of immunotherapy before, during or after radiotherapy used to treat locally recurrent breast cancer in patients failing chemotherapy.

—Immunochemotherapy versus chemotherapy in patients with disseminated malignant disease.

—Phase I trials of intravenous immunotherapeutic agents other than C. parvum.

—Immunotherapy prior to conventional therapy in patients with "early", clinically nondisseminated cancer.

—Immunotherapy prior to conventional therapy in patients with disseminated cancer.

—Use of intratumoral immunotherapy in "early", clinically nondisseminated cancer. For example, intralesional BCG in primary melanoma lesions before surgery.

—Studies of animal model systems in which immunotherapeutic agents cause enhancement (increased rate of tumor growth) in an attempt to define the mechanisms responsible.

—Studies of adoptive immunotherapy in animals and attempts to define mechanisms in systems that work.

—Studies of adoptive therapy in man.

—Obtain evidence for human tumor associated antigens by performing tests for humoral and/or cell-mediated immunity to autochthonous tumors and showing increased immune responses after in vivo or in vitro immunization with autochthonous tumor. Define nature of effector cell in cell-mediated responses.

—Obtain evidence for cross-reactive human tumor associated antigens by performing tests for humoral and/or cell-mediated immunity to autochthonous tumors and showing increased immune responses after in vivo or in vitro immunization with allogeneic tumors. Define nature of effector cell in cell-mediated responses.

—New approaches to immunotherapy.

—Effects of immunotherapeutic agents on the reticuloendothelial system of animals or man studied in vitro or in vivo.

—Immunization of cancer patients with weak immunogens (e.g., synthetic polypeptides) in combination with a series of adjuvants to determine the relative strengths of different adjuvants.

—Immunotherapy of tumors in animals using active or adoptive methods designed to ablate the organ of origin by immune reactions directed against organ specific antigens.

**Suggested areas for research developed by the Immunodiagnosis Committee were not available at press time and will appear next week in *The Cancer Letter*.**

Terry emphasized that these are very general suggestions and that only a relatively few actually will be worked up into RFPs this year.

NCAB member Frank Dixon asked Terry if the questions asked in the RFPs can be "tied up and answered in three years. Are they definitive enough so that you expect to get it done that fast?"

"No. Obviously they will vary, but the broad themes over a three to five-year period remain the same," Terry said.

Panel Chairman Benno Schmidt commented, "Obviously, you like the program, better than you would if you would take the same amount of money and put it into the grant program for immunology. Right?"

"Wrong," Terry answered. "I don't think that's a

fair way to put it. What is fair to say is that the institute has available two funding mechanisms to support good biomedical research in cancer. One is the grant mechanism in which the investigator picks his best shot, comes in with it and asks a study section to approve it. The other mechanism, the one I'm associated with, is one in which a group of his peers get together and define areas that they think are of importance and which they think are not being adequately funded through the grant mechanism, for one of a number of very good reasons, and where they feel it would be worthwhile to solicit proposals for that area."

"I'll put it another way," Schmidt said. "Do you like what you're doing with this $16 million better than adding this amount to grants for immunology?"

"There would be a trade off," Terry said. "The real benefit in having this $16 million invested this way is that we are getting things we would not otherwise get."

## CHANGES IN LABELING OF ANTICANCER DRUGS SUGGESTED; RESPONSE IS SLOW

The Food & Drug Administration Oncologic Drugs Advisory Committee earlier this year recommended changes in the package insert instructions for 20 anticancer agents, but members of the committee hit the ceiling when they discovered six months later that only "two or three" manufacturers had responded to letters notifying them of the proposed changes.

The committee based its proposed changes on information developed since the labels were originally written. For some, it had been years since they were updated. Most of the changes dealt with toxicity, efficacy, indications and dose schedules.

Stanley Balcerzak, committee member from Ohio State, said he was "very disturbed" that pharmaceutical firms appeared to be dragging their feet on the suggested changes, "some of them very important."

Committee member Charles Moertel, Mayo Clinic, said, "These are pertinent to patient safety. The actions [of the manufacturers] are not consistent with public safety."

But Leo Collins, FDA compliance officer, insisted that "it's not as bad as you may think." He said that most of the manufacturers were working on the proposed changes, searching the literature to substantiate them.

Robert Young, FDA group leader for oncology, had told the committee he had seen only two or three responses from the manufacturers. Collins said he thought there were more than that.

The recommended changes were derived from the committee's extended and sometimes rambling discussions of labeling of a number of antitumor agents at its meeting last March. Young went over the transcript of the meeting for weeks, pulling out the recommendations. Letters were sent May 27 to each manufacturer over the signature of William Gyarfas, director of the Div. of Oncology & Radiopharmaceutical Drug Products, notifying them of the suggested changes.

Following the expressions of displeasure by committee members at their next meeting, Gyarfas sent another letter:

"We are now placing added emphasis on these changes which affect safety and efficacy in use," Gyarfas wrote. "We would be pleased to have either your definitive response or an acknowledgement together with your estimate of the time requested to complete the definitive reply."

Committee members discussed steps FDA could take to enforce package insert updating. Young explained that the only real club FDA has is to threaten to withdraw permission to market the drug, if it is determined that the labeling does not reflect the drug's effects.

Melvin Krant, committee consultant from Tufts Univ., suggested that FDA grant approval for marketing of drugs for two-year periods, with renewals subject to review. Philip Paquin, chief of FDA's General Regulations Branch, said he was not sure the Act governing drug regulation would permit that. Balcerzak pointed out that manufacturers do not sell enough of some drugs to encourage them to continually respond to FDA requirements, yet those drugs may be very valuable to many patients.

Committee Chairman Michael Shimkin said he favored limiting the use of some drugs to certain physicians, "those qualified to use them. But I'm told there are no provisions in the law for that."

Krant noted that the committee had decided "some package inserts are no longer pertinent, some are dangerous, and yet there has been little or no reaction from industry. We need some mechanism for review after a period of time of drug use. The drug industry has not responded to the advice of this committee. We need some mandatory procedure."

Committee members argued with Paquin over FDA's reluctance to include literature references in the package inserts. Paquin said the intention is to include "explicit information" on the labels, that "labeling is not intended to be a treatise."

"That seems to imply that someone has made a judgment," Krant said. "The physician has to trust someone's judgment, not his own . . . Your philosophy is that the physician need not know how your judgment was arrived at . . . Do you simply tell someone, do this, use that, or do you provide him with some arsenal for thought, assist him to use his expertise and training and ability to reach that decision?"

"Many of us believe that the most valuable information in an insert would be a limited and selected bibliography," Shimkin said. "When you say, this is our judgment, accept it, is not acceptable to us. The problem is, which references. You can't use them all.

but only a few key ones. FDA lawyers say that citing a reference in the literature implies that everything in the article is approved. We reject that forcefully. To give further leads for reading is the most valuable thing you can do."

"You [FDA] assume a role you don't want to assume," Krant said. "Give the physician the opportunity to be part of the decision making process. Allow him to use his intellect to help."

Moertel defended FDA's position on this point. "Physician education is not a function of the insert," he said. "He uses his background to help reach a decision even before he buys a drug. The insert is a poor educational vehicle. To review the literature on an insert becomes subjective. It is difficult to do without being arbitrary. Medical schools, books, even pharmaceutical company brochures are far better places and ways to educate physicians about drugs."

"My information is that most physicians get information on drugs from drug company detail men," Krant said. "Education is reinforcement, repetitive."

"Most inserts wind up in waste baskets without being read," Moertel said.

"Unfortunately, a lot of physicians do use package inserts," said committee member John Whitaker, who is in private practice with the Capital Medical Clinic in Austin, Texas. "They use it blindly. They pull out an insert that says here's how to use this drug, then they overdose or underdose. Thousands of patients are getting drugs that their doctors know little about."

Whitaker said physicians use inserts primarily for dose schedules, but that instructions in inserts frequently are difficult to interpret.

"If we have inserts, they should be complete and clearly written," Whitaker later told *The Cancer Letter*. "The insert for 5-FU is an example. The dose schedule it lists is too high, and it has killed patients."

Moertel commented that "Dr. Whitaker has told us how practitioners with no prior experience with a drug do use the package inserts. We looked at them and found some very out of date. For those 20 letters to go out, with only three or four responses, is no effective mechanism to protect the public. Patient safety is clearly a responsibility of FDA."

Stanley Crooke, a representative of Bristol Laboratories who attended the meeting, said his form has started reviewing package inserts on antitumor agents every year. "We need some changes on the legalities of package inserts. There was much information we wanted to include on adriamycin that we couldn't because of limits on research information."

Shimkin recommended that FDA "set up some mechanism by which essential changes in inserts are carried out in a predetermined time frame."

Moertel added that yearly review of package inserts should be mandatory. "It's not that much of an effort. We need also to make them more readable." He suggested a summation at the top of each to include important features—indications, common side effects, important cautions, dosage recommendations.

**The drugs and recommended changes:**

**Adria Laboratories**

Adriamycin—The term "antiblastic agent" is not in general use and should be changed. A discussion of the interaction of the drug and irradiation to produce a more severe mucositis than that produced by either alone. Deletion of the indication of bronchogenic carcinoma unless there is evidence that the drug has significant activity in this disease.

**Burroughs Wellcome**

Alkeran (melphalan)—The adjective "abnormal" should be removed from the warnings section. The use of melphalan in combination should be discussed. The use of the drug in carcinoma of the ovary should be included. The drug's effect on fertility and its carcinogenic, mutagenic, teratogenic and immunosuppressive potentials should be discussed.

Thioguanine—Removal of the recommendation of use during period of thrombocytopenia induced by other therapy. Revision of the description section with a discussion of the mechanism of action of the drug, and clinical pharmacology. Revision of dosage to a lean body mass basis or equivalent basis. A discussion of the use of the drug as part of a combination.

Leukeran (chlorambucil)—Clarification of "abnormal" depressions of the bone marrow. Therapeutic ratio relationship to other agents is overstated. Indications—use in polycythemia vera and ovarian cancer.

Imuran (azathioprine)—The discussion of the drug's hepatotoxicity should be revised and expanded. Hepatocellular necrosis has been reported to occur with use of this drug. Increased prominence of the allopurinol azathioprine interaction.

**Dome Laboratories**

DTIC (dacarbazine)—Reference should be made to the other commonly used names of DTIC. Delete the benefit to risk statement in the box warning. Delete the reference to combination chemotherapy unless data to support such usage can be presented. Reconsider the use of food and water restriction and barbiturates as measures to manage the drug-induced nausea and vomiting.

**Eli Lilly**

Oncovin (vincristine sulfate)—Discussion of urinary retention and paralytic ileus particularly in elderly patients. Box warning regarding extravasation of the drug. Revision of the classification of lymphomas. Discussion of the usefulness of the drug in pediatric tumors and in combination with other agents. Updating of references.

Velban (vinblastine sulfate)—Include a discussion of the use of this drug as part of a combination. Revise the dosage in terms of lean body mass or an equivalent basis. Provide a more exact statement as to remission length. Revise the names and classifica-

tion of lymphomatous diseases to conform to presently accepted systems. Revise the bibliography. Drop neuroblastoma as an indication. Revise the recommendations for maintenance therapy. A statement that neurotoxicity often lasts longer than 24 hours. Include a discussion of the drug as part of a combination for Hodgkin's disease and embryonal cancer.

**Hoffmann-La Roche**

Fluorouracil—Is hospitalization necessary for safe use of this drug? A guide to dosage and adjustment and evaluation of the drug's effect (Precautions). Timing and duration of wbc nadirs. Special measures for alopecia? Dosage recommendations in terms of lean body mass dry weight. Is this drug indicated as a single agent in breast cancer? Definition of "carefully selected" patients.

FUDR (fluorodeoxyuridine)—Must patients be hospitalized for safe use of the drug? The indications section is broadly written. The committee suggests: adenocarcinomas, gastrointestinal metastatic to the liver. Where there is no evidence, remove certain adverse reactions. A discussion of the drug's hepatotoxicity including jaundice and hepatic coma. A discussion of the clinical efficacy of FUDR in relationship to 5-FU.

Matulane (procarbazaine)—Revise the indications section and discuss the usefulness of the drug in combination. Dosage should be recommended on a lean body mass or equivalent basis. Edema, ascites, effusions, cough and other respiratory symptoms have not been causally linked with the drug.

**Lederle**

Thiotepa (thiophosphoramide)—Malignant lymphomas and bronchogenic carcinoma should be dropped as indications. Recommendation of antimicrobial prophylaxis. Explanation of usage guidelines in terms of granulocyte levels. Discussion of the drug's mutagenic and carcinogenic potential. Dosage on a body surface or lean body mass basis. Discussion of intratumor administration of the drugs. Recommendation of use in bladder cancer. Revise indication based on clinical data to support such use.

**Merck Sharp & Dohme**

Hustargen—Box warning on extravasation of the drug. Amplification of the mutagenic and carcinogenic potential of the drug. Amplification of the reproductive effects on the drug such as on spermatogenesis, amenorrhea and sterility. Discussion of the immunosuppressive potential of the drug. Discussion of the impairment of host defenses as regards infection. The recommendation that barbiturates alleviate nausea and vomiting associated with the administration of this drug.

**E.R. Squibb & Sons**

Hydrea (hydroxyurea)—As the proposed mechanisms for radiosensitizing activity have over the past several years not been established, and clinical experience has suggested that this drug is not a radiosensitizer, delete the paragraph discussing such an interaction. Revise the paragraph on changes in laboratory values which can be found in the warnings section. Reference to the usefulness of the drug in combination with irradiation should be deleted unless adequate data exists to support such use.

**Upjohn**

Uracil mustard—From the indications section, drop Hodgkin's disease and adjunctive treatment of carcinoma of the ovary and lung. Revise the classification of lymphomas to conform to current classification standards. Drop the claim that uracil mustard is well tolerated clinically. Revise dosage recommendations in terms of lean body mass or an equivalent basis. Include a discussion of the mutagenic and carcinogenic effects of the drug.

Cytosar (cytarabine)—Revise preclinical discussion. Include a discussion of the clinical pharmacology of the drug. Indications should also include the treatment of CNS leukemia, with instructions for reconstitution. A discussion of the use of Ara C with other agents in the combination chemotherapy of leukemia, including modifications of dosage when so used. Update of efficacy tables. Stability recommendations of reconstituted solutions. "Precautions" concerning bone marrow toxicity to imply that the therapeutic efficacy (bone marrow) of the drug should govern the extent of drug therapy. Hospitalization may not be an absolute necessity for safe use of the drug. A discussion of the immunosuppressant properties of the drug.

*Contract Awards*

## SOUTHWEST, CHILDREN'S COOPERATIVE GROUPS LAND CONTROL CONTRACTS

NCI's Cancer Control Program has awarded the first in a series of contracts to Clinical Cooperative Groups to assist them in extending their research into community hospitals. The first two awards went to the Southwest Oncology Group, for $2 million, and to the Children's Cancer Study Group, for $1.5 million. Those amounts will be spread over three years.

Another contract will be awarded within two weeks to the Eastern Cooperative Oncology Group. Also, the proposal submitted by the Gynecologic Oncology Group has been approved and will be awarded as soon as some revisions are made in the business details.

The proposal submitted by the Primary Breast Cancer Therapy Group did not make it through the peer review process; it is being revised and will be resubmitted. The Southeastern Cancer Study Group's proposal was returned with suggestions for resubmission. And a proposal is still being worked up by the Radiation Therapy Oncology Group.

Other contract awards:

Title: Structure-activity studies among anticancer agents
Contractor: Mayo Foundation, $1,108,562.

Title: Operation of a facility for the storage and distribution of clinical drugs
Contractor: Flow Laboratories, $653,060.

Title: Coordination of mammography education programs
Contractor: American College of Radiology, $186,929.

Title: Incorporation of three new alteration/renovation projects at the Frederick Cancer Research Center
Contractor: Litton Bionetics, $450,155.

Title: Biochemical analysis of human breast cyst fluid and its correlation with development of human carcinoma
Contractor: Memorial Sloan-Kettering, $157,830.

Title: Influence of repeated low dose irradiation on mammary gland carcinogenesis in estrogenized rats
Contractor: Alton Ochsner Medical Foundation, $476,405.

Title: Development and validation of an in vitro mammalian cell mutagenesis system for carcinogenesis screening
Contractor: Litton Bionetics, $384,770.

Title: Maintenance and scheduled sacrifice of guinea pigs
Contractor: Univ. of Illinois, $105,209.

Title: Development and validation of an in vitro mammalian cell mutagenesis system for carcinogenesis screening
Contractor: Stanford Research Institute, $404,496.

Title: In vitro cultivation of normal, epithelial, human, prostatic cells
Contractor: Univ. of Colorado, $392,069.

Title: Validation and utilization of microbial mutagenesis systems as prescreens for chemical carcinogens
Contractor: Stanford Research Institute, $181,427.

Title: Current awareness services for nitrosamine program of DCCP
Contractor: Franklin Institute, $26,050.

Title: Study of oncogenesis and other late effects of cancer therapy
Contractor: Children's Hospital of Philadelphia, $96,276.

Title: Markers for evaluation of preneoplastic lesions in the respiratory tract
Contractor: Univ. of Chicago, $452,560.

Title: Implementation for a cervical cancer screening program
Contractors: Hawaii State Dept. of Health, $429,133; and Vermont Dept. of Health, $200,016.

Title: Clinical oncology program
Contractor: Institute for Medical Research of Santa Clara County, Calif., $310,940.

Title: Resource for microscopic and autoradiographic technology
Contractors: Basic ordering agreement, Litton Bionetics and Experimental Pathology Laboratories Inc., Herndon, Va.

Title: Prototype comprehensive network demonstration project in head and neck cancer
Contractor: Illinois Cancer Council, $749,500.

Title: Training programs for maxillofacial prosthedontists and maxillofacial dental technicians
Contractors: New York Univ., $42,335; and Memorial Hospital, $34,967.

Title: Production and supply of one kilogram of daunomycin
Contractor: Parke Davis, $92,154.

Title: Study of the distribution, disposition, and metabolism of antineoplastic agents
Contractor: Univ. of Southern California, $384,119.

Title: Supramolecular organization of normal and tumor cell surfaces and their relationship to escape from immune surveillance and growth control
Contractor: Salk Institute, $146,212.

Title: Evaluation of thermography in mass screening for breast cancer
Contractor: Jefferson Medical College, $433,694.

Title: Studies on the viral etiology of malignant lymphoma in rhesus monkeys
Contractor: Univ. of California (Davis), $32,980.

Title: Production of sarcoma and leukemia viruses
Contractor: University Laboratories Inc., Highland Park, N.J., $333,853.

## SOLE SOURCE NEGOTIATIONS

***Proposals are listed here for information purposes only. RFPs are not available.***

Title: Breast cancer detection demonstration project
Contractors: Pacific Health Research Institute; Wilmington Medical Center; St. Joseph Hospital; St. Vincent's Medical Center, and Albert Einstein Medical Center.

Title: Preparation and characterization of antisera to oncogenic viral antigens
Contractor: Huntingdon Research Center, Brooklandville, Md.

Title: Production of oncogenic or potentially oncogenic viruses
Contractor: Electro-Nucleonics Laboratories Inc.

Title: Studies of tumor viruses in nonhuman primates
Contractor: Rush-Presbyterian-St. Luke's Medical Center.

## 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. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology & Diagnosis Divisions are located at: NCI, Landow Bldg., NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise noted.***

## SOURCES SOUGHT

### RFP NO1-CP-65862-59

**Title:** *Studies of chemical carcinogenesis on human tissues in culture*

**Deadline:** *Jan. 7*

NCI is interested in organizations having both the technical capability and the interest to study various aspects of chemical carcinogenesis in specific human tissues. These studies involve: 1) obtainment of noncancerous viable human tissues from patients with and without cancer; 2) the isolation of viable epithelial cells suitable for culture as well as for biochemical studies; 3) long- and short-term in vitro maintenance of these tissues as both explants and dispersed epithelial cells; and 4) xenotransplantation of these tissues and of epithelial cells into immune deficient animals. The development of model systems, as outlined above, for esophagus, stomach, uterus, pancreatic duct and prostate are of special interest.

Since this area of research requires human tissues obtained at surgery and/or autopsy, thorough knowledge of the medical, legal, and ethical aspects of human experimentation is necessary. Resumes of experience and capabilities should cover:

1. Scientific medical and experimental research personnel to serve as staff for the project.
2. Technical and professional experience and capability in experimental and clinical research.
3. Constant and reliable source of viable noncancerous human tissues; specifically pancreatic duct, esophagus, stomach, large intestine, bladder, bronchi, uterus and/or prostate.
4. Knowledge and facilities for the safe handling of both human tissues and chemical carcinogens.
5. Willingness to participate in a collaborative program with other institutions (universities, private laboratories, federal agencies, etc.).

This is not a request for proposal. Ten copies of the resume of experience and capabilities must be submitted to Daniel Longen, Contracting Officer, Research Contracts Branch, NCI, Blair Bldg., Room B-16, Bethesda, Md. 20014. All inquiries must be directed to Linda Waring or Melvin Hamilton at 301-427-7957.

### RFP NCI-CB-74115-35

**Title:** *Development of alternatives to conventional mechanical collimators and detector systems for use with non-positron emitters*

**Deadline:** *Dec. 17*

NCI is interested in establishing a contract to develop a suitable system to replace mechanical collimators for use with non-positron emitters in the nuclear medicine imaging techniques employed for detection and localization of cancer lesions.

### RFP NCI-CB-74114-35

**Title:** *Study of innovative techniques to facilitate passage of colonoscope to the cecum*

**Deadline:** *Dec. 17*

NCI is interested in establishing a contract to design, fabricate and test new colonoscope systems with greater ease of passage.

### RFP NCI-CB-74112-35

**Title:** *Development of large area solid state image receptors for x-ray imaging*

**Deadline:** *Dec. 17*

NCI is interested in establishing a contract for the study of the development of a large area solid state image receptor which would convert the radiologic image into electronic signals with the purpose of facilitating storage retrieval and data processing in the field of diagnostic radiology.

### RFP NCI-CB-74113-35

**Title:** *Development of a compact cyclotron for medical use*

**Deadline:** *Dec. 17*

NCI is interested in establishing a contract to develop a cyclotron sufficiently compact in size to allow its installation in existing facilities of an average nuclear medicine department.

**Contract Specialist for the above four RFPs:** Catherine Baker
Biology & Diagnosis
301-496-5565

**The Cancer Letter**—*Editor* JERRY D. BOYD

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