THE CANCER LETTER

Vol. 7 No. 32

Aug. 7, 1981

Subscription $125.00 per year

P.O. Box 2370 Reston, Virginia 22090 Telephone 703-620-4646

DCT BOARD APPROVES CONCEPT OF PLANNING GRANTS FOR NEW PARTICLE THERAPY EQUIPMENT DEVELOPMENT

NCI's position that it would not support further new particle therapy equipment development, beyond the existing contracts for neutron facilities, has been relaxed somewhat, although it could be years before such support might be available.

(Continued to page 2)

In Brief

PETER GREENWALD A LEADING CANDIDATE FOR ONE OF THREE TOP NCI JOBS REMAINING TO BE FILLED

PETER GREENWALD, director of the Div. of Epidemiology in the New York State Health Dept., is one of the leading candidates for one of the three top positions still open at NCI—deputy director, director of the Div. of Cancer Cause & Prevention, director of the Div. of Resources, Centers & Community Activities. . . . **CORRECTION**: It was the Ewing's Sarcoma Intergroup Study, not the Rhabdomyosarcoma Intergroup Study (as reported in ***The Cancer Letter*** July 10) which had been disapproved on a split vote by the Clinical Cancer Investigation Review Committee. The latter was approved with a high priority. The CCIRC voted 10-7 to disapprove the Ewing's study, but that was following a review without a site visit. NCI staff felt that some issues which bothered the CCIRC might have been addressed in a site visit and asked the National Cancer Advisory Board to set aside the disapproval and refer the study back to the CCIRC for another review. The NCAB agreed, and a site visit has been scheduled for September, with review by CCIRC in November. . . . **VINCENT DEVITA**, on investigator compliance with submission of annual reports to FDA: "When I say we'll be up to date on annual reports, I mean we will be. Frequently, when our staff has called up and asked for data, the response has been that 'we're too busy.' From now on, if the data are not in on schedule, no more drugs will be supplied. There will be no flexibility on that." . . . **ANOTHER SWORDS** to ploughshares spinoff: Clinical trials have started with the drug WR-2721, synthesized by **THOMAS JOHNSTON** and **J. ROBERT PIPER** of Southern Research Institute. They had developed the drug for the Army under a contract to find something to protect soldiers from effects of radiation after a military attack. Its potential usefulness as a radioprotector was established at Walter Reed. It is absorbed readily by most normal tissues and increases their tolerance toward radiation; solid tumors absorb only barely detectable quantities. Phase 1 studies are under way at the Univ. of Pennsylvania and at a limited number of institutions under the auspices of the Radiation Therapy Oncology Group. The drug also seems to offer some protection for normal cells against antitumor agents, and phase 1 trials to test that possibility also have started.

DOOR OPENED SLIGHTLY FOR SUPPORT OF PARTICLE THERAPY EQUIPMENT

(Continued from page 1)

The Div. of Cancer Treatment Board of Scientific Counselors agreed at its last meeting that planning grants for new facilities, including pion, heavy ion, and proton equipment, should be considered for funding if they receive high priority scores.

The DCT Board approved the concept of developing four new clinically dedicated neutron radiation facilities in October, 1978. Contracts were awarded to the Univ. of Pennsylvania, Univ. of Washington, UCLA, and M.D. Anderson. The decision was made then not to fund any further equipment grants or contracts having to do with equipment development. "That was the price," NCI Director Vincent DeVita said, for DCT's commitment of $9 million to the four neutron contracts.

"We did get one grant application, which received a very high score, but we did not fund it," DeVita told the DCT Board. "We have to review that policy, and decide whether to open it up again."

"The time has come to take off the freeze," Board member Theodore Phillips said. "If we don't, we may fall behind the state of the art."

"I think we should support good high priority studies, like any others," Board member Carlos Perez added.

"We're supporting $40 million a year in radiation biology grants," DeVita said. "What I mean is, if someone applies for a grant to develop a pi meson facility, that's a big project and would come to this Board. The issue is, do we still not purchase any heavy equipment?"

"There have been a lot of changes since 1979," Board member Sharon Murphy said.

"I would be reluctant to support more heavy machinery development at this time," commented David Pistenma, chief of DCT's Radiation Therapy Development Branch.

Board Chairman Samuel Hellman, summarizing the discussion, said, "It is the sense of the Board that we are open to planning grants (for new particle therapy equipment)," and Board members agreed.

The previous policy had been interpreted by some to mean that NCI would not support clinical trials with neutron radiotherapy other than at the four institutions with the facility development contracts. That is not the case, and the Board reaffirmed that NCI support for clinical trials could be extended to any institution with access to the proper equipment, subject to competitive factors and availability of funds.

Pistenma said that the neutron facilities at M.D. Anderson and Fox Chase/Univ. of Pennsylvania would be operational late in 1981, the Univ. of Washington and UCLA in late 1982 or early 1983. Characteristics of the equipment and facility at each of those institutions:

- Fox Chase/Univ. of Pennsylvania—D-T generator designed for clinical use; isocentric treatment capability; 14 MeV neutrons from D-T reaction; located in Fox Chase Cancer Center.
- M.D. Anderson—Cyclotron therapy system designed for clinical use; one isocentric treatment beam and one horizontal beam; 42 MeVp-Be.
- UCLA—Cyclotron therapy system designed for clinical use; one isocentric treatment beam and one horizontal beam; 42 MeVp-Be; to be in the Wadsworth VA Medical Center.
- Univ. of Washington—Cyclotron therapy system designed for clinical use; one isocentric treatment beam and one horizontal beam; 48 MeVp-Be (variable energy 32-48 MeV); to be in the University Hospital.

Other particle beam therapy facilities now in existence were all designed for physics research, which makes their application to cancer treatment somewhat difficult. Pilot studies conducted there, despite those difficulties, provided the rationale for development of clinically dedicated facilities. Those neutron therapy facilities are located at Lewis Research Center, supported by NASA and operated by the Cleveland Clinic Foundation; Fermi National Accelerator Laboratory, Batavia, Ill.; and the Univ. of Washington, in Seattle, which will be closed to clinical use when the new facility becomes operational.

A proton therapy facility at Massachusetts General Hospital is operated by Harvard Univ. It consists of a physics cyclotron; 160 MeV protons; range of approximately 15.9 cm in water; two horizontal treatment beams.

The negative pi-meson (pion) therapy facility at Los Alamos, N.M., probably is the best known of the particle beam operations. It consists of a physics proton linear accelerator; vertical pion beam; pion range up to 28 cm in water.

Helium and heavy ion therapy facilities are located at Lawrence Berkeley Laboratory, operated by the Univ. of California. The helium facility includes physics synthocyclotron; range of approximately 26 cm in water; 930 MeV helium ions; horizontal treatment beam. The heavy ion facility includes a physics machine (combination of a heavy ion linear accelerator and a synchrotron); high energy beams with approximate ranges in water of ^{12}C-26 cm, ^{20}Ne-24 cm, ^{28}Di-20 cm, ^{40}Ar-16 cm; two horizontal treatment beams.

Pistenma listed disease sites most suitable for particle beam studies:

Neutrons, primary emphasis—advanced head and neck cancer, stage 3 and 4 A carcinoma of the cervix, inoperable or recurrent salivary gland cancer, bladder cancer, and non-oat cell lung cancer. Secondary emphasis—malignant gliomas, soft tissue sarcomas, malignant melanoma, pancreatic cancer, and in-

operable cancer of the rectum.

Charged particles, primary emphasis—advanced head and neck cancer, stage 3 and 4 A carcinoma of the cervix, salivary gland cancer, and bladder cancer. Secondary emphasis—sarcomas of the skull base and trunk, prostate cancer (boost), cancers of the pancreas and stomach, esophageal cancer, and malignant gliomas.

Pistenma suggested that selection of patients for charged particle beam trials would involve these considerations:

- Dose localization advantage—bladder (boost), prostate (boost), head and neck (entire treatment or boost), salivary gland (recurrent and unresectable), para-aortic lymph nodes, soft tissue sarcomas of the trunk, retinoblastoma, choroidal melanoma, and base skull tumors (chordoma). The last three offer less of an advantage for pions, Pistenma said.
- Biological advantage possible (pions and heavy ions)—bladder (advanced), brain (grade 3 and 4 gliomas), cervix (advanced), esophagus, head and neck (advanced), lung, pancreas, prostate, rectum (localized or recurrent), and stomach. All except brain and cervix also would have dose localization advantages, Pistenma noted.

FERMILAB TREATS 1,000TH NEUTRON PATIENT, RESULTS ARE "ENCOURAGING"

The Neutron Therapy Facility at the Fermi National Accelerator Lab last week announced that it had registered its 1,000th patient, only the second in the world to have treated that many cancer patients. The other is Hammersmith Hospital in London, which has been treating patients with neutrons for 12 years.

Frank Hendrickson, director of the Fermilab NTF, said the rapid growth of Fermilab's NTF is an "indication of the outstanding cooperation and support we have received from the medical community for our research program. It's also a measure of our ability to respond to the health care needs of our community and to interact with our patients in a manner that inspires their confidence."

The Fermilab NTF has the highest energy neutron beam in the world for treating patients (66 million electron volts). It can reach deeper into tissues than less powerful beams.

"Our experience in the five years we have been treating patients here," said Hendrickson, "has shown us clearly that we can treat them safely. Safety, of course, is extremely important and is one of our highest priorities. We also know that some selected rare tumors and some of the common tumors respond better to treatment with neutrons than to the more conventional treatments."

The NTF director said that treatment of salivary gland cancers, for example, "really seems to go better with neutron therapy when compared to the traditional methods." He added that "we think some of the other carcinomas respond more readily to this treatment, but we're not sure. We're still doing research in these areas."

Hendrickson and others are conducting extensive research on how well neutrons will eradicate or at least brind under control a variety of tumors. It is premature for them to make precise evaluations, but Hendrickson did note that "we are excited and encouraged by what we are finding.

"We want to make our research available to more patients than we have seen so far," Hendrickson continued. "There are about 300 diseases that physicians call cancer. They are different from one another, require different treatments, and have different prognoses. We still need to do research on many of these cancers. What we learn about one cancer, we believe we can apply in general to the treatment of other cancers. But we need to do considerably more research."

LOMBARDI CENTER TO PROVIDE TREATMENT, CONSULTATION TO U.S. VIRGIN ISLANDS

The Georgetown Univ. Vincent Lombardi Cancer Research Center has entered into an agreement with the government of the U.S. Virgin Islands to provide oncologic consultation and treatment to the cancer patients there.

Under the affiliation agreement, the Lombardi Center provides outpatient and inpatient oncologic consultations and treatment by assigning physicians to serve in the oncology clinics of the Virgin Islands.

"Approximately 20 percent of the residents of these islands will develop a malignancy during their lifetime, requiring varying degrees of sophisticated cancer treatment," said Lawrence Hill, program coordinator of the project and associate director of radiation oncology at the center.

Virgin Islands Commissioner of Health Roy Schneider pointed out that while surgical oncology is well represented on the islands, there is a serious shortage of medical and radiation oncologists. Consequently, most cancer patients have been flown to Puerto Rico and the continental U.S. for treatment.

"This arrangement not only presents a great cost to our government," Schneider said, "but it is also unsatisfactory in that it provides the patients with little continuity in medical care and forces them to leave their families for long periods of time while seeking treatment."

Since fall 1980, eight physicians from the Lombardi Center have served a one to two month tour of service as consultant oncologists. The consulting physicians have established an ambulatory care program for both St. Thomas and St. Croix, providing consultations and chemotherapy treatments.

Consultative services also are available for hospi-

talized patients in the islands, along with those referred by private physicians. In the event that a patient's case cannot be appropriately handled on the islands, the patient is treated at the Lombardi Center.

To ensure continuity of medical care for these patients, Lombardi Center physicians are working under the direction of Hill. If a specific case requires additional review, the oncology consultant has available a 24-hour telephone consultation service with the members of the center's fulltime staff.

"We are pleased with this cooperative arrangement with the U.S. Virgin Islands," said John Potter, director of the center. "The patients on these islands are able to participate in research protocols of the Lombardi Center, providing us with the opportunity of helping these patients as well as expanding the clinical population of our research programs."

Patients also have access to anticancer agents not commercially available, but which are accessible through the affiliation with the center, one of the national comprehensive cancer centers.

On-island radiation therapy services, including interstitial and intracavitary radiation therapy, are being developed by Schneider and Hill, with the cooperation of Alfred Goldson, director of radiation therapy at Howard Univ. In the interim patients have access to the radiation services of the Lombardi Center, including the intraoperative radiation therapy available through the Howard Cancer Research Center.

In addition to these services the oncologic consultants are expanding teaching opportunities to the physicians of the islands by establishishing a tumor board to discuss difficult diagnostic and management problems. The conslultants are also organizing a continuing education program, including weekly lecture series, and are compiling an oncology reference library.

Virgin Island physicians are welcome to visit and attend educational programs of the Lombardi Center and are eligible for joint faculty appointments at the university and the center.

HUMAN PROTEIN INDEX STIRS NCAB, NCI INTEREST; WOULD COST $150 MILLION

Human Protein Index.

That term may represent the next major advance in human biology, with strong implications in the diagnosis and treatment, and perhaps even prevention, of cancer. It also could be the rallying cry for an effort to sell Congress on a big increase in funding for biomedical research. And it might be describing a new and bloody battleground as scientists and their allies fight over priorities and allocation of resources.

HPI already has caught the attention of a prospective congressional sponsor, namely Alan Cranston of California, the No. 2 Democrat in the Senate. Cranston, who participated in last year's International Symposium on Research Frontiers in Aging and Cancer where he became aware of HPI and its ramifications.

Estimates on the number of different proteins in human cells range from 20,000 to 50,000. Norman Anderson of the Argonne National Laboratory and his son, Leigh, have done much of the groundwork for cataloging those proteins. In their view, a Human Protein Index "would fulfill for molecular biology the role that sky maps do for astronomy or even the periodic table for chemistry. It represents the kind of systematic cataloging of basic subject matter which is the hallmark of a mature discipline."[1]

HPI would be "a comprehensive roster of every variety of protein in the human body. When completed, its compilers hope, it will list not only all our proteins, along with their functions and locations in the body, but also the genes that dictate their manufacture, and perhaps even the locations of those genes on specific chromosomes. The index should prove enormously useful to medical science, since virtually every disease is involved in some way with proteins."[2]

Anderson believes that HPI would make possible the deciphering of the entire genetic program of human differentiation and development and lead to discovering causes of genetic diseases. "The misprogramming of genetic expression in cancer, perhaps the key piece of missing knowledge, could be resolved. Damaged tissues could be identified through the protein leakage that occurs in nearly every variety of disease and injury. New replacement therapies might be devised for missing proteins. Diseases could be more precisely typed and the efficacy of therapies measured or even predicted."[2]

Cranston was so intrigued that he called for a meeting in his office last August to review the prospects for HPI. That led to establishing a Human Protein Index Task Force, with Norman Anderson as chairman and including Robert Stevenson, American Type Culture Collection; Vincent Abajian, Electro-Nucleonics Inc.; Leigh Anderson; Irving Johnson, Eli Lilly Co.; Edwin McConkey, Univ. of Colorado; Walsh McDermott, Robert Wood Johnson Foundation; James Neel, Univ. of Michigan; Stephen Thomas, Foundation for Integrated Biomedical Research; and Edwin Whitehead, Technicon Corp.

The Task Force went to work and produced a report in December, describing briefly the process, possible uses, interrelations with other technologies, technical development requirements, types of support and collaboration required, organizational requirements, and funding requirements.

That last item—funding requirements—is the one that gets everyone's attention—$150 million over an eight-10 year period.

The task force report summarizes:

"Recent technical advances make it feasible to begin to construct a Human Protein Index which

would be a library of information about all human proteins, and would enable us to identify among the entries those proteins causally related to each of the thousands of human diseases. The key to this effort is a new procedure, two dimensional gel electrophoresis (2-D gel) that makes possible the simultaneous measurement of charge, mass and quantity of a thousand or more proteins from a single sample of body cells or fluids.

"When combined with techniques of genetic engineering, monoclonal antibody production and automated clinical testing, this advance makes the HPI possible. Assocation of specific protein changes with human diseases can be deduced as well as strategies, products and procedures for the prompt diagnosis and treatment of them.

"While the completion of the index will take some years, sets of proteins that behave most reproducibly can be defined at the outset for immediate use.

"A program to accomplish these goals is suggested and crucial to it is a central coordinating activity that takes advantage of existing scientific research mechanisms but also requires cross compatibility of data between laboratories; development and provision of standards of purity and identity; acquisition and sharing of data by common computer program; collaboration on technical improvements; and adoption of common terminology.

"Not only should the new information be of incalculable benefit to our understanding of normal and disease states, but also could lead to a new family of commercial products and services such as enhanced diagnostic and treatment modalities and more sensitive and meaningful tests for the monitoring of environmental and toxicological effects of chemicals.

"This program initiative could be accomplished with funding in the range of $150 million over an eight to 10 year period and in our opinion ranks as an outstanding and affordable opportunity."

Norman Anderson appeared at the most recent meeting of the National Cancer Advisory Board in an effort to stir up interest among those involved in the National Cancer Program—especially NCI with its funding capabilities. He was not asking that NCI pick up the entire $150 million tab.

"I wonder if this is one of those square ideas which must fit into a round system," Director Vincent DeVita commented after Anderson made his presentation. "Do you have any suggestions on what the Cancer Institute can do? I think this is a very exciting new area."

"We don't have the staff for biological work," Anderson said. "The Dept. of Energy (which supports Argonne) will continue technology support... This is the atomic cable for your chemists. I would suggest that some interagency arrangement be worked out."

The Dept. of Energy will continue to provide major support for the program, Anderson said, along with significant contributions from industry, since HPI will have profound impact on development of synthetic fuels and new plant strains. DeVita acknowledged that this might allow development of the biomedical spinoffs at a bargain price.

DeVita suggested that HPI would have applications involving at least three of NCI's divisions and that the question of NCI support be presented to the respective boards of scientific counselors. NCAB Chairman Henry Pitot summarized the discussion by referring the issue to one or more of those boards.

The Div. of Cancer Treatment Board of Scientific Counselors may consider a proposal to collect samples from a wide variety of tumors for entry into the indexing project. Anderson is tentatively scheduled to discuss the project at the Board's Oct. 1-2 meeting.

Anderson told ***The Cancer Letter*** that he has never had any NIH funding. He has presented the idea to NCI before, he said, with no results.

The task force felt that HPI development might require an entirely new agency which would cut across all existing agencies, Anderson said. "The national laboratories are probably the only ones which can do this work.... What we really need is a center for biotechnology."

The key technical advance which makes HPI possible is the 2-D gel electrophoresis which was developed in 1975 by Patrick O'Farrell, a young molecular biologist at the Univ. of California (San Francisco). This makes possible simultaneous measurement of 1,000 proteins. It is a two step procedure which makes use of the fact that different proteins will move at different rates in response to an electric field. The separations are carried out on thin sheets of a jelly like material, acrylamide. Data provided by this technique take the form of a pattern of spots, each of which represents a protein. These patterns can be converted to computer manipulable forms for analysis and storage in a data bank.

Anderson, in an attempt to generate a reaction from the scientific community, sent copies of the task force report to the first 325 members of committees listed in the publication, "NIH Public Advisory Groups." Letters that stimulated, and Anderson's responses to those letters, were compiled by him in a publication, "Molecular Anatomy Program."

Responses ranged all the way from, "I agree that the Human Protein Index ... is of great potential import.... I support this ambitious undertaking," by E.C.C. Lin, professor of microbiology and molecular genetics at Harvard, to "I really believe that the rather expensive project you are suggesting certainly is not the optimal way to spend research money at this time. I do not have time to go into all the reasons that are involved in my having this opinion," from Rosalyn Yalow, Nobel Prize winner with the

Veterans Administration. Selections from other comments Anderson received:

Anthony Miller, director of the National Cancer Institute of Canada's Epidemiology Unit and a member of the Board of Scientific Counselors of NCI's Div. of Resources, Centers & Community Activities—The HPI proposal "puts into specific focus the problem that faces NIH . . . in developing criteria that would enable priority decisions to be taken in relation to expenditure on different areas of research. . . . The problem is that scientists are not equipped to make the sort of unbiased decisions that are necessary in order to allocate resources to different areas. . . . We are not equipped to make cross discipline comparisons. . . . I do believe that your battle really has to be extended into the political arena and that Congress will have to make the final decision."

Howard Temin, McArdle Laboratory—"I am not convinced of the necessity for a large crash program at this time. The development of an enormous mass of new data at great expense does not seem warranted at the present time. We need better ways to handle the data generated now, as well as new methods for focusing on minor components. Certainly, work should continue on this project at present speeds."

Anderson's response—"The point is that it is now perfectly feasible to follow some 2,000 proteins in human lymphocytes, to switch on and off over a dozen gene sets experimentally, to begin to classify different types of leukemia, and to get directly at the problem of drug resistance. Central to all of this is standardization and automation of the analyses (we have run over 35,000 2-D gels thus far) and really first class state of the art image analysis and data reduction. We spend about a million a year now. None of it from NIH. Part of the work is done abroad with NATO support. If we go through NIH we are in a mill of endless proposals, reviews, and schedules that stretch out forever. A better approach is to bypass all of this completely and go directly for commercial clinical use through our collaboration with industry and clinical laboratories. Fortunately the same mapping systems are applicable to the problem of developing new strains of plants for the biomass energy program and part of the synfuels program. So the idea is to use funds from such sources (major oil companies for example), build the systems ultimately required, and then hit the cancer problem in concert with the community of pathologists and clinical chemists."

John Costanzi, director of the Univ. of Texas Medical Branch Cancer Center, Galveston—"The idea of indexing human proteins on a computer basis and making it relevant to clinical medicine is very admirable and worth the task. However, the approach in the report emphasizes the 2-D O'Farrell system almost exclusively and I do not think it is a satisfactory way to go. There is too much protein microheterogeneity and polymorphism in the population to resolve satisfactorily this one method. This is a simplistic approach to an ambitious project. A multimethodological approach together with a 2-D system may be worthwhile but a lot of planning would be needed."

Anderson agreed and noted that he has developed other systems, including a centrifugal fast analyzer. "However, there has to one central reference analytical system for all of this with the highest resolution. No other method approaches the Stegeman-Klose-Scheele-O'Farrell system."

David Baltimore, Massachusetts Institute of Technology Center for Cancer Research—"My reaction to your proposal is one of great skepticism. I do not believe the two dimensional gel system is likely to require an enormous investment in order to reap its benefits. In general I am not impressed with the results of very large scale programs and I would rather see the scientific community develop this kind of analytic tool using the normal mechanisms of grant support."

Anderson's response—"In an academic environment it is better not to know the true cost of things, whether it is the exploration of reverse transcriptase as a cancer marker, the production of interferon, the development of zonal and vaccine centrifuges, CAT scanners (the greatest advance in cancer in a decade), centrifugal fast analyzers, or high resolution 2-D electrophoresis carried all the way to clinical use. One new drug brought to the drugstore shelf now costs $50 million. Clinical instrumentation, with new regulations, does not lag far behind. American industry thus far views what we are doing as having too high a basic and developmental research cost, while most government groups view it as too applied. Thus it falls in the class of things successfully done by the Japanese. The total cost of health care in the U.S. is now over $200 billion per year. Unless we revise some of our policies and strategies, we will repeat in health our experiences with automobiles."

Ernest Beutler, chairman of the Dept. of Clinical Research at Scripps Clinic & Research Foundation—"I must confess to feeling some skepticism regarding the wisdom of making as large a commitment as your task force report suggests. Within the context provided by the level of support of basic biomedical research, $150 million, even spread over an eight-10 year period, is a very large sum of money. Large investigator initiated biomedical research programs generally are funded at a cost of well under a million dollars a year. It is such investigator initiated programs which have provided us with the most exciting advances in theoretical and applied biomedicine over the past two decades. In contrast, large planned multidisciplinary programs costing several million dollars a year have contributed meagerly to biomedical pro-

gress. I am not at all sure that this technology is sufficiently advanced to justify so large a commitment. Many of the spots which you observe may represent various stages of normal processing of proteins which may differ from individual to individual without clinical consequences. There will be no doubt many mutations irrelevant to the disease state being studied in every pattern. Thus the effort to diagnose disease, on the one hand, or to detect the cause of disease, on the other, would be carried out against an enormous background of variability."

Anderson's response—"The Dept. of Energy has now spent some $2 billion on research on the biological effects of radiation, and spends $56 million per year preparing impact statements. The HPI project grew from the notion that, while tens of millions of dollars are now spent on large scale animal studies largely with the intent of extrapolating the effects to man, very little was being spent on studies which could, for example, measure the background mutation rate in man to see whether it has been altered. The meager results now coming out of the studies at Hiroshima suggest that human and mouse sensitivities may differ by a factor of as much as five. . . . It would be rather fun to follow up on your comments on large vs. small projects. The way to do that would be to pick completely at random NIH grants adding up to the HPI budget each year and then systematically evaluate the payoff."

Mary Edmonds, professor of biological sciences at the Univ. of Pittsburgh—"This systematic approach to human protein classification has merit and I am impressed with the depth of the planning that has gone into the proposal. . . . However, for a number of reasons having largely to do with allocation of federal dollars for research, I would not like to see this project receive any large increment in federal funding. I'm unconvinced of the urgency to complete it on some arbitrary time table (10 years for example). I would prefer to spend $150 million in the next 10 years on research grants to talented young investigators; this sum could support 150 researchers at $100,000 a year for 10 years. The amount of new innovative research generated by this expenditure would certainly be significant and more importantly would sustain a cadre of young scientists into their mature productive years. It is significant that the 2-D gel electrophoresis technique was brought into the realm of every day laboratory practice by a graduate student, Patrick O'Farrell. At this moment young researchers newly appointed to our faculty are waiting for NIH funds or for projects with highest priority scores."

Anderson's response—"I completely agree with you on the overriding importance of funding for for young investigators. However, this depends on convincing the public that such support is worthwhile and that the results will be carried into use. The present perception, as I sense it, both in the general public and in Congress, is that there is no active bridge between the basic individual investigators and the patient user in this country. . . . I tend to the view that if it were plainly evident that U.S. basic research were funneling directly into industry and the health care system, the level of grant support would at least double."

In a letter to T. Ming Chu, director of diagnostic immunology research at Roswell Park (who supported the project), Anderson wrote—"The chief concern (of the NIH advisors who responded to the task force report) is that funding for the effort would come out of grants. There has never been any plan to do that. . . . We now feel that the next step should be to scale up the present effort by a factor of approximately 10, which would bring it up to about 40 percent of the size of Frederick Cancer Research Center. Other comments concern the evils of large projects, often from researchers who were active in the Special Virus Cancer Program, and fears that genetic variation would mask the differences we seek to investigate (which it doesn't).

"I am left with a few observations of my own. Nearly every other branch of science has mastered the art of attacking difficult problems which require an integrated multidisciplinary approach. This includes nuclear physics, computer sciences, chemistry, and space. Biomedical research has by far the most complex problems to solve, and is largely conducted as a cottage industry. That may be necessary (and more fun) at the outset. However, I rather think that the time has come for a mix of a few carefully chosen larger scale projects with many small ones."

1. **Science**, Jan. 2, 1981.
2. **Science 81**, Jan-Feb.

RFPs AVAILABLE

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

RFP N01-CP-15786-71

Title: *Bioassay reports (small business setaside)*
Deadline: *Oct. 5*

The National Toxicology Program is interested in obtaining support for preparation of technical reports on a series of chronic and subchronic bioassays for carcinogenesis and other toxic effects.

This project requires a scientific team with expertise in a broad range of toxicology specialties, as well as an experienced technical editor. Reports are to be

prepared according to formats supplied by NTP. Preparation of reports shall be a cooperative effort involving participation of both Program Staff and contractual support.

A task order contract for a three year duration is anticipated. Multiple awards may be made under this solicitation.

This RFP incorporates two minimum requirements (1) availability of word processing equipment compatible with the Xerox 860 currently in use at NTP and (2) an operational office within a 50-mile radius of the NIH campus, Bethesda, Md.

Contract Specialist: Susan Hoffman
RCB Blair Bldg., Rm. 2A01
301-427-8774

RFP NCI-CM-27494

Title: *Establishment and operation of rodent production centers for inbred and hybrid rodents*

Deadline: *Approximately Sept. 11*

The animals will be produced under maximum barrier and modified conventional environmental conditions. NCI is seeking organizations with the capability and facilities for producing and supplying rodents primarily for hybrid mouse production and as hosts for maintaining experimental tumor lines.

To be considered for award of a contract, respondents must meet the following criteria: (1) Have existing facilities for maximum barrier and/or modified conventional environmental conditions. (2) Principal investigator must have experience with rodent production, inbreeding procedures and maximum barrier and/or modified conventional environmental conditions. (3) Organizational experience in the production of high quality laboratory animals.

A total of eight tasks is anticipated which will include cage levels of 2,000, 4,000, 7,000, and 8,000 cages. One task will include the requirement of a physical location so that truck delivery is available to the NIH, Bethesda, Md. area. Still another task will include a requirement of access to an international airport which can expedite animal shipments to the Philippine Islands, Japan and other Far Eastern areas. Finally, still another task will include the requirement for access to an international airport which can expedite shipments to Western European areas.

Multiple awards will be made as the result of this RFP; awards will be for three year incrementally funded period of performance.

Contract Specialist: Charles Lerner
RCB Blair Bldg. Rm. 232
301-427-8737

RFP N01-CP-11021-76

Title: *Preparation of antisera to oncogenic or potentially oncogenic viruses*

Deadline: *Approximately Sept. 18*

NCI has a requirement for the preparation of antisera to oncogenic or potentially oncogenic viruses. In part A the offeror will inventory, maintain and distribute existing government owned antisera and replenish supplies of these reagents, including purification of the necessary antigens.

It is estimated that no more than 10 liters of antisera to these agents or their subviral proteins will be needed per year, and the necessary virus will be supplied by the government until supplies are exhausted, (note, no spleen cell focus forming virus is available from the government).

In part B the offeror will prepare hybridomas producing monoclonal antibodies directed against (a) protein kinase cacade proteins (PKF, PKL, PKM, and PKS); b) spleen cell focus forming virus glycoprotein; and c) the active sites of murine virus polymerases. It is estimated that 500 ml per year of each of these antisera will be sufficient to satisfy program needs. Provision of the antigens for production of these hybridomas will be the responsibility of the offeror.

In part C the offeror will, from time to time, be directed to produce ascites derived monoclonal antibodies utilizing hybridomas provided by NCI. It is estimated that no more than 10 hybridomas per year will be submitted for this procedure, and approximately 300 ml of antibody containing ascites fluid will be required in each case.

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

NCI CONTRACT AWARDS

Title: Statistical support for the Gastrointestinal Tumor Study Group, continuation
Contractor: Emmes Corp., Potomac, Md., $1,791,278.

Title: Cancer Information Dissemination and Analysis Centers (Cidacs) covering virology, immunology and biology
Contractor: Franklin Institute, Philadelphia, $921,119.

Title: Incorporation of several alteration/renovation/maintenance/upgrading projects at Frederick Cancer Research Center, two modifications to the existing contract
Contractor: Litton Bionetics Inc., $762,041 and $882,448.

The Cancer Letter _Editor Jerry D. Boyd
Published fifty times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter.