THE CANCER LETTER

Vol. 13 No. 10
March 6, 1987

Subscription: $160 year North America, $175 year elsewhere

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White House Defers To Presssure, Gives Up Attempt To Cut NIH Budget $334 Million In '87

The White House has surrendered in its ill advised attempt to circumvent the antiimpoundment law and force NIH to delay spending $334 million appropriated by Congress for the current fiscal year until FY 1988. The white flag was waved last week by Office of Management & Budget Director James

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In Brief

FASEB Report On Diet And Cancer Mortality Available; Don Poppke AO of Nursing Center

FASEB'S "INTERIM Scientific Report on an Epidemiologic Study of Certain Dietary Characteristics and Cancer Mortality" is now available to the public. The report, compiled by the Life Sciences Research Office of the Federation of American Societies for Experimental Biology under a contract from the Food & Drug Administration, reviews data generated by a study on effects of certain dietary constituents on cancer mortality in China. This study is being conducted by Cornell Univ. and the Chinese Center for Preventive Medicine. The report may be obtained for $10 from FASEB, Special Publication Office, 9650 Rockville Pike, Bethesda, MD 20814. . . . **DONALD POPPKE**, who has been administrative officer of the Cancer Therapy Evaluation Program in NCI's Div. of Cancer Treatment, has been appointed executive officer of the new National Center for Nursing Research. **CHRISTINE LEINNEWEBER**, who has been a staff member in NCI's Financial Management Branch, is the new CTEP AO. . . . **JEAN BAUM** has moved up from chief of the Publications Branch in the International Cancer Information Center at NCI to the newly created position of Marketing Coordinator for NCI's scientific journals, PDQ, Cancerlit, Clinprot, Cancergrams, Oncology Overviews and Recent Reviews. ICIC Director Susan Hubbard announced that **ROBIN ATKISS** has been appointed chief of the Publications Branch. He has been director of publications and graphics services in the HHS Office of Human Development Services. . . . **CORRECTION**: "Cancer Journal," the name favored by NCI for its new journal which will replace "JNCI" and "Cancer Treatment Reports," is not the name of a journal "published by quackery organizations," as noted by National Cancer Advisory Board member Helene Brown (**The Cancer Letter**, Feb. 6). The publication Brown was referring to is actually named, "Cancer Control Journal."

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OMB In About Face, Directs NIH To Stop Cutting Grant Awards

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Miller in a letter to HHS Secretary Otis Bowen. Miller attempted to make it appear that the actions by HHS and NIH in cutting research grant awards was never authorized by the White House, in effect making Bowen and NIH Director James Wyngaarden the "bad guys" in the scheme to "extend the availability" of 1987 funds into 1988.

That, of course, is nonsense. When NIH learned last December that OMB was planning on cutting its 1987 budget by $334 million, and that all of that would come out of research grants, one round of grants had already been awarded. The only way a reduction of that size could be put into effect was to reduce amounts in the rest of 1987 grants, in addition to cutting the number of grants by 700. Those reductions had to be put into effect immediately, a fact well known to OMB.

The White House caved in after vehement opposition expressed by key members of Congress (**The Cancer Letter**, Feb. 20) and threats of legal action by scientific groups. Congressman William Natcher's confrontation with Bowen at the opening of the Natcher subcommittee's hearings on the 1988 budget probably pushed the secretary into demanding that OMB take a realistic view of the prospects for "extended availability."

Miller's letter to Bowen follows:

"As you know, the President's budget for the National Institutes of Health proposes to extend the availability of about $334 million in FY87 appropriated funds into FY88. In transmitting this proposal to the Congress on Jan. 5, 1987, the President assured the Congress that there would be 'no Executive Branch action to defer or otherwise restrict the funds currently available until after Congressional enactment of this proposal.'

"If, on the basis of the President's budget proposal, the Department is withholding or otherwise restricting the availability of funds, please cease such actions.

"In addition, to the extent the Department has undertaken policies which may be inconsistent with the President's assurance, please advise this agency of the facts concerning such actions and of any further steps which you believe are necessary in light of the Impoundment and Control Act."

Those "further steps" will include restoration of cuts already made.

The White House, which has made worse blunders recently, was well aware that Congress would not approve any reduction in NIH 1987 funds through the legal deferral or rescision processes. It was obvious that OMB was counting on Congress taking its time, as usual, in enacting an appropriations bill for HHS for the 1988 fiscal year. OMB also was hoping that Congress would not stir itself enough for a vote of disapproval separate from the appropriations process. Thus, disapproval of extended availability expressed in an appropriations measure passed at the end of the fiscal year, or even into the next one, would be de facto approval of it.

NCI's share of the reduction would have been $64 million, all of it out of RO1 and PO1 grants.

In a letter to members of the Coalition for Health Funding, Mindy Hatton, executive director of the Coalition, wrote:

"The reason for OMB's change of heart is not entirely clear. There are some indications that OMB's legal counsel, which is concerned about "New Haven vs. U.S. (the case striking down the legality of the deferral process) wants OMB to enter the case with 'clean hands.' Thus, fighting with Congress, the Comptroller General and others over the legality of this deferral type action would not work to OMB's advantage. Whatever, the reason, OMB has clearly conceded, at least for this year, that this is one fight that it does not wish to pursue."

Miller's letter does not actually withdraw OMB from the fight. In fact, the request for extended availability of the $334 million still remains in the budget proposal sent to Congress. HHS executives have said the request will be pursued.

But if NIH is permitted to obligate its appropriated funds under its normal schedule, all of it will be spent before the fiscal year ends, and probably before final congressional action on the 1988 appropriations bill. So, far all practical purposes, the latest White House scheme to reduce the number and size of NIH grants is dead. And one again, the biomedical research community and its friends in Congress have prevailed over an OMB that has tried repeatedly, in Democratic and Republican Administrations, to reduce budget deficits at the expense of the nation's health.

Frelick, Winding Down NCI Career, To Receive ACCC's Annual Award

Robert Frelick, NCI program director for the Community Clinical Oncology Program, will receive the Assn. of Community Cancer Centers annual award for "Outstanding Contribution to Community Cancer Care" at the association's annual meeting next week.

The award will be presented at the awards luncheon March 14. The annual meeting starts March 11.

This will be the first time ACCC has presented the award to one of its own. Frelick was one of the original organizers of ACCC when it was founded in 1974 and served as its president in 1980.

Frelick's entire career before he came to NCI in 1982 has been centered around improving cancer care for patients, particularly in communities. That effort will continue when he leaves NCI in July, to return to Delaware where he will work in chronic disease control, including cancer, with the state Dept. of Health.

But it will be primarily for his work in five years at NCI that the award will be given. CCOP could well have floundered and flopped without Frelick's brilliant management of a complicated program involving hundreds of community cancer care specialists who had little or no experience in dealing with NIH or NCI. Instead, it has developed into a smashing success that is making a major contribution to clinical cancer research. It is also contributing significantly to improving cancer care in community hospitals; the extent of that achievement is still to be measured in the evaluation process.

Frelick came to NCI from his position as chief of medicine for the three hospitals in Wilmington, a position created when the hospitals merged their management. He had spent a year in Memorial Sloan-Kettering's residency program, in 1949, before going into practice in Delaware. "I have often wondered what would have happened if I had stayed on there with David Karnofsky and Joe Burchenal," Frelick said. "But I have no regrets."

Frelick became a member of the National Surgical Adjuvant Breast Project and wrote that group's application for its first Cooperative Group Community Oncology Program award from NCI. He directed that program for NSABP, and also participated in the Delaware Breast Cancer Detection Demonstration Project and statewide breast cancer network, both supported by NCI.

During Frelick's term as ACCC president, NCI initiated the Community Hospital Oncology Program, CCOP's predecessor, a three year demonstration effort to help hospitals develop cancer programs. ACCC battled for more than the 17 CHOPs NCI awarded, but Director Vincent DeVita ended that flap when he came up with his idea for a permanent program for community hospitals, which came to be know as CCOP. He asked ACCC to help develop parameters for it, and Frelick was a member of the committee which spent months hammering out those details with NCI.

Frelick gives the late Edward Moorhead most of the credit for ACCC's part in getting CCOP off the ground. Moorhead, who died last Jan. 30 at age 50, chaired the committee which worked with NCI on CCOP.

Frelick was recruited by NCI specifically to help in organizing CCOP and to see it through its first couple of years. He had intended to return to Delaware, but was prevailed upon then, and each year thereafter, to stay "just one more year." His goal finally became to see the program through the first recompetition, which is now in process and will be wrapped up when the National Cancer Advisory Board approves the new awards in May.

"It's time to get some fresh blood into this program," Frelick said. "Not that I feel stale. But this is a fantastic opportunity for someone to become involved in an important national program." The only thing that could hold back CCOP, he said, would be lack of money. The program has only $10 million in the budget for FY 1988; it will require at least $16 million to fund close to the same number now functioning.

Frelick observed his 67th birthday Feb. 27, and is looking forward to his new job with the enthusiasm of someone half his age. He will coordinate public health and private resources for the state's chronic disease control efforts. "I hope to use some of the things I learned here. I think I have some credibility in the state and knowhow that I can bring to the job."

During the time when he had an office in a hospital where he helped manage cancer patients, Frelick also maintained a limited private practice at his home to serve the local area. Most of that involved general medicine. He still sees an occasional patient

on Saturdays, and will probably continue after leaving NCI.

Frelick and his wife, Jane, have five children and nine grandchildren.

Henderson, Weistein, Blumberg, Jukes To Present AACR Lectures

Two cancer center directors will present award lectures at the 78th annual meeting of the American Assn. for Cancer Research in Atlanta May 20-23 and another will deliver the Presidential Address. Another award lecture will be given by a member of the team whose research led to development of methotrexate, and the fourth an NCI scientist.

Brian Henderson, director of the Univ. of Southern California Comprehensive Cancer Center, will present the 11th Richard and Hinda Rosenthal Award Lecture, "Estrogens as a Cause of Human Cancer."

Thomas Jukes, Univ. of California (Berkeley), will give the Sixth Cain Memorial Award Lecture, "Searching for Magic Bullets: Early Approaches to Chemotherapy." Jukes, along with the late Margaret Belt, the late Alfred Franklin, Donna Cosulich, Martin Hultquist, Doris Seeger, James Smith and E.L. Stokstad performed the research which led to development of methotrexate at Calco Chemical and Lederle Laboratories divisions of American Cyanamid Co.

Bernard Weinstein, director of the Columbia Univ. Comprehensive Cancer Center, will deliver the 27th G.H.A. Clowes Memorial Award Lecture, "The Origins of Human Cancer: Molecular Mechanisms of Carcinogenesis and Their Implications for Cancer Prevention and Treatment."

Peter Blumberg, chief of the Molecular Mechanisms of Tumor Promotion Section of the Laboratory of Cellular Carcinogenesis & Tumor Promotion in NCI's Div. of Cancer Etiology, will present the Sixth Rhoads Memorial Award Lecture, "Protein Kinase C as the Receptor for the Phorbol Ester Tumor Promoters."

Alan Sartorelli, 1986-87 president of AACR and director of the Yale Univ. Comprehensive Cancer Center, in his Presidential Address will discuss "Role of Hypoxic Cells in the Therapeutic Response of Solid Tumors."

More than 1,800 abstracts were submitted for consideration by the AACR Program Committee chaired by Edwin Cadman of the Univ. of California (San Francisco). The committee scheduled 16 slide sessions, 57 poster sessions, 14 minisymposia and 10 poster discussion sessions. Two of the slide sessions represent an innovation for AACR: multidisciplinary sessions containing papers dealing with particular organ sites, one on breast cancer and the other on cancer of the gastrointestinal tract.

Four symposia have been scheduled:

*Cytokines: Biological status and potential clinical applications. This is being sponsored jointly with the American Society of Clinical Oncology, whose annual meeting will be held May 17-19 in Atlanta. Chairmen are Cadman and John Mendelsohn, Memorial Sloan-Kettering. Speakers include Michael Sporn, NCI; Malcolm Moore, MSK; David Goeddel, Genentech; and Warner Green, Duke Univ.

*Regulation of breast cancer development. Marc Lippman, NCI, is chairman. Speakers include Lippman; Martha Stampfer, Univ. of California (Berkeley); Angela Brodie, Univ. of Maryland; and Craig Jordan, Univ. of Wisconsin (Madison).

*Viruses in autoimmunity and human cancer. Chairman is Jay Levy, UC (San Francisco). Speakers include Abner Notkins, NCI; Gerard Orth, Pasteur Institute; Elliot Kieff, Univ. of Chicago; and Levy.

*Molecular biology of chemical carcinogenesis. Harry Gelboin, NCI, is chairman. Speakers include John Essigmann, MIT; Frank Gonzalez, NCI; Allan Balmain, Beatson Institute for Cancer Research, Glasgow; and John Knopf, Genetics Institute, Cambridge, MA.

Information on registration and other matters may be obtained from Adam Blistein or Ruth Fortson at AACR, West Bldg Rm 301, Temple Univ. School of Medicine, Philadelphia, PA 19140, phone 214/221-4565.

New Prostate Cancer Detection Group To Study Potential Of Ultrasound

The National Prostate Cancer Detection Project, a group recently established in Ann Arbor, plans to test the potential of early detection of prostate cancer in a multicenter study.

The multidisciplinary group is supported by private sources, with the two major contributors being Bruel & Kjaer, Marlborough, MA, and 3M, Minneapolis.

Cochairmen of the group are radiologist Fred Lee and urologist Gerald Murphy.

The group hopes to determine whether transrectal ultrasound has greater accuracy

in the early detection of prostate cancer than the only currently accepted means, the digital rectal examination. In this particular study, a urological examination and prostate antigen assay will be performed with ultrasound annually in 5,000 asymptomatic men between the ages of 55 and 70.

The American Cancer Society predicts that 96,000 new cases of prostate cancer will be diagnosed in 1987 and there will be 27,000 deaths from the disease. Black Americans are the population at highest risk. Institutions participating in the study will seek significant numbers of blacks.

The eight participating institutions are St. Joseph Mercy Hospital, Ann Arbor; New England Deaconess Hospital, Boston; State Univ. of New York, Buffalo; Toronto General Hospital; Ohio State Univ. Hospital, Columbus; Cook County Hospital, Chicago; St. Vincent Medical Center, Portland, OR; and M.D. Anderson Hospital & Tumor Institute, Houston.

DCT Board Okays Concepts For Three New RFAs In Radiation Research

Three new RFAs (request for applications for grant supported research) for radiation research were given concept approval by the Board of Scientific Counselors of NCI's Div. of Cancer Treatment at the Board's recent meeting. The Board also approved the concept of a new contract supported (RFP) project for prescreening compounds as potential radiosensitizers and/or radioprotectors.

One of the new RFAs possibly will rekindle a controversy that erupted last year when NCI abruptly canceled a contract with a group organized by the Assn. of American Cancer Institutes for evaluation of magnetic resonance imaging in a variety of cancer sites. That contract, awarded through the Div. of Cancer Prevention & Control (which houses NCI's Cancer Centers Program), would have cost NCI $160,000 a year. Participants for the most part were donating their time and facilities and asked only for money for data gathering and analysis.

That contract was abruptly canceled when DCPC had to cut back its budget for contracts. The participants became infuriated when almost immediately after termination of the contract, DCT released an RFA for multi-institutional imaging trials. This RFA set aside $600,000 a year to do what the AACI group felt was essentially the same thing they had been doing for $160,000. DCT contended its proposed study was broader and involved other factors, points the AACI group hotly disputed. They noted that the NCI RFA called only for studies involving prostate and lung cancer, while their study was looking at six sites.

DCT had previously budgeted in its grants pool for the MRI study (which included other imaging modalities--computed tomagraphy, ultrasound, digital radiography, positron emission tomographjy, single photon emission tomography). Although DCT also had to absorb cuts in its contracts budgets, its grants pool was left intact enough to support the new study. The NCI Executive Committee supported DCT in proceeding with the RFA while also supporting DCPC in its decision to terminate the contract with the AACI group.

The RFA went out, a number of proposals were submitted and have been reviewed. Those in the funding range will go to the National Cancer Advisory Board in May. Included in this round will be awards for an operations control center and a statistical control center.

The new action by the DCT Board will result in another RFA, this one adding colorectal, musculoskeletal and pancreas cancers to prostate and lung for evaluation of staging by imaging. Another $600,000 a year will be set aside for three years to support these awards.

There was little Board discussion of the new RFA and no reference to last year's controversy.

The Board also approved a new RFA for development, evaluation and biodistribution of chelate conjugated radiolabeled monoclonal antibodies specifically for diagnostic imaging. This RFA sets aside $500,000 a year for three years. The concept statement:

"Employment of radiolabeled monoclonal antibodies to obtain in vivo cell specific tissue characterization and diagnosis has been successfully achieved in several areas. However, much work remains to be done to refine the technology, including improvement of the specificity of the immunological response, the formulation of new radiolabled complexes and the attainment of more complete tumor visualization.

"The metal chelates have been shown to be promising agents. They are more stable than the iodinated antibodies and in addition offer opportunity for a variety of conjugated forms. The metal chelates considered

especially useful for diagnostic purposes are Tc-99m, In-111, Ga-67, Zr-87 and 89, Ru-97 and Pb-203.

"Among the features of the radiolabeled monoclonals to be evaluated, biodistribution of the antibody is of critical importance and has been largely undetermined in man. Information on the degree of uniformity of distribution of the antibodies is important not only form the standpoint of the initial diagnosis but also for planning treatment and monitoring of the response to therapy.

"SPECT would be an appropriate imaging device for the chelated radiolabeled antibodies. Further, it would allow some quantitation of antibody concentration in addition to the image itself."

Another Radiation Research Program RFA geting concept approval was for studies of anatomic and functional diagnosis before, during and following the treatment of cancer employing imaging and imaging related technology for the purpose of planning treatment and monitoring treatment response. The three year project anticipates first year awards totaling $800,000. The concept statement:

"Recent advances in imaging and imaging related technology have made possible not only more precise anatomic/pathologic diagnosis but have further provided functional information that potentially expands the capability of the diagnostic method to contribute to treatment planning and, by monitoring, to assist in management during and after treatment. The functional information provided includes evaluation of metabolism of a given area of interest by identification of various metabolites and determination of such features as pH, the tissue redox state and regional perfusion.

"Recently, as an example, it has been possible using magnetic resonance imaging to selectively image intra and extracellular sodium in brain tumors and by this means to grade neoplasms and differentiate tumor recurrence from tumor necrosis. PET studies permit a similar differentiation. Literature reports indicate that 31^{P} MRI spectra may be used to monitor therapeutic response during regional perfusion of malignant tumors in man.

"The relative applicability of the various technologies should be assessed determining what modality is most suitable in a given situation for both anatomical and functional diagnosis. For example, from the biochemical quantitation standpoint, PET is able to operate at the micromolar level whereas MRS operates at the millimolar level. Further, various combinations of modalities may prove useful."

The RFP concept, for a contract for prescreening of compounds as potential radiosensitizers and/or radioprotectors, sets aside $150,000 a year for three years. The concept statement:

"Through a series of physical-chemical tests which will include determination of compound solubility, election-affinity, partition coefficient, metabolic assays, respiratory studies and the measurement of thiol activity, a correlation will be made with the radiosensitizing activity of the test compounds. Other tests can be included to extend this prescreen to evaluating the radioprotector, chemosensitizer and chemoprotector activity of the compounds."

"NCI currently has a single contract that screens compounds as hypoxic cell radiosensitizers. The in vitro and in vivo screening provided by this contract is limited in scope because of the available funding and the work capacity of any one contractor. At present, the contractor capability of screening 300-400 compounds a year does not keep pace with the new compounds NCI receives yearly (10,000) nor make any impact on the current NCI drug inventory (500,000). The probability of finding clinically useful radiosensitizers could be increased substantially if the number of compounds screened could be increased dramatically, or the compounds sent for screening could be selected more judiciously. A system of prescreening could eliminated many undesirable compounds before they were sent to the more expensive screen.

Provision of animal facilities and performance of routine experiments and tests. Recompetition of a contract currently held by Bionetics Research Inc. Estimated annual cost, $462,000, five years. The concept statement:

The major objective of this contract is to provide a well equipped animal facility for the maintenance of mice, rats, guinea pigs, rabbits, goats and subhuman primates. The contractor will be responsible for providing adequate veterinary care and technical assistance for performance of routine procedures such as inoculation of antigens, viruses and cells, and bleeding of animals at appropriate intervals to check for antibody production. In addition, quarantine and isolation facilities for virus inoculated subhuman primates will also be necessary.

Provision of purified AIDS virus proteins and subhuman primate facilities to test immune response of the viral antigens. Recompetition of a contract held by Bionetics Research Inc. Estimated annual cost, $957,000, three years. The concept statement:

This contract is designed to be a collaborative

effort between the Dept. of Defense and NCI for studies in vaccine development against AIDS. The major objective of this contract is to provide up to 10mg each of the purified gp 120 and other viral antigens from HTLV-3 for studies of antibody response to these antigens in subhuman primates and the ability of these antibodies to protect the immunized animals against infectious virus challenge. These studies are designed towards the development of an effective AIDS vaccine.

DCT Director Bruce Chabner noted that the entire cost of this contract would come from Army funds "out of the pile of money they are getting for AIDS. They are trying desperately to find something to do with it."

Maintenance of the NCI Drug Information System. Recompetition of a contract held by Fein-Marquart Associates. Estimated annual cost, $360,000, five years. The concept statement:

The Developmental Therapeutics Program has designed and built a comprehensive information system, known as the Drug Information System (DIS), which contains all the data associated with the screening of chemicals for anticancer activity. All of the data bases in the DIS are vitally important on a day to day basis to DTP because they support the management and direction of the entire drug discovery and development effort. The DIS was originally designed to run on DEC-10 computers and it was first installed in 1983 on the DEC-10 system in NIH's Div. of Computer Research & Technology. The original design and implementation of the DIS was carried out by Fein-Marquaart Associates, who subsequently won the competition award for the maintenance of the DIS.

Since mid-1985, the DIS has been available to users for over 99 percent of the computer's service time, which is nominally 24 hours per day, seven days per week. Currency of the numerous data bases that comprise the DIS has been maximized by means of an exhaustive schedule of updates. Fault fixing has been very effective; most known problems have been remedied within 48 hours of their being reported. During the same time period, numerous enhancements to the DIS programs and capabilities have been completed. Thus, a high speed laser printer has been introduced and is now used for most of the DIS output. Elaborate multilanguage capabilities have been installed in the DIS program which writes letters to drug suppliers. Several large DIS data bases have been overhauled and subjected to extensive data checking and correction efforts, and extension of the DIS capabilities into new areas such as pharmaceutical data have been carried out.

The daily maintenance effort is to be continued, with the same emphasis on prevention of service interruption and currency of data bases. In addition, numerous minor and a few major enhancement efforts are to be undertaken during this coming contract period. Major enhancements include design and development of an online retrieval system for in vitro data, a system for the inventorying, extraction and screening of natural products, ahigh level graphics package to support the use of work stations, the development of a subsystem to deal with anti-AIDS screening data, and development of subsystems dealing with toxicology and pharmacology. With numerous major, new projects being called for, an increase in the previous funding level will be necessary. All enhancements are prioritized and then addressed in priority order at a rate which is compatible with overall funding and availability of appropriate staff. The DIS is now quite stable, at least in its central components, and it is expected that many of these major enhancements will be made during this contract.

Board member John Mendelsohn commented, "At a time when extramural people are being asked to cut their budgets, we need to make sure this increase is needed now." The estimated cost is approximately double the present size of the contract.

"Dr. Boyd is tough in cutting contract costs," Chabner responded. "No one is better. You should remember also that his program has lost a lot of money in recent years," a reference to massive cuts in the DTP budget.

Operation and maintenance of the DTP biological data processing system. Recompetition of a contract held by VSE Corp. Estimated annual cost, $1.2 million, five years. The contract was awarded for five years starting in 1985; reasons for an early recompetition are included in the concept statement:

Computer processing of the massive amounts of data derived from DTP's drug screening experiments in mice began in the early 1970s. In the 15 years of this effort, data have been accumulated into one of the larger scientific data bases in existence. Some considerable detail of the experiments is captured and stored. For example, the weight change of the mice is recorded in every experiment, as is the death pattern, the source of the mice and of the tumor inoculum.

The effort of many years under this contract and its predecessors has resulted in the creation of a very large data base which is maintained upon magnetic tape. The large IBM computers in DCRT are the machines that are generally used to manipulate these data. The normal procedure that has evolved for the capture of data involves direct connection between the screening laboratories and the NIH computers and works well. Data evaluation has generally been carried out by this contractor and also has worked well. Data retrieval, on the other hand, is still a batch process and much effort is underway to modernize this, through the creation of online access capabilities. As better online access to the data becomes available, the value of the elaborate automatic report generators diminishes. Printed reports covering some subject and routed to specific staff at regular intervals were a highly visible feature of the biological data processing system, but have, for the large part, been rendered obsolete by the appearance of online querying.

A further, very significant development has been DTP's massive shift away from in vivo screening to in vitro methods. This move has made much of the old software obsolete. The Information Technology Branch has determined that an early recompetition of this contract would be in the best interest of the government.

This contracted effort deals exclusively with the biology data which are generated and used by DTP in connection with the cancer drug development effort. This main thrust will not change, but much of the methodology used will change increasingly and perhaps rapidly, in the next five years. Some examples of such change are already clear in the in vitro screening system which was developed under this contract and which is now in use at FCRF. Much new technology will be used, including automatic sensing and reading, use of robotics and of expert systems. At the same time, it will be necessary to exploit new software and computer languages and finally, all such progress will have to be made in such a way that intersystems compatibility is not jeopardized. Within two years, it is expected that most of the drug screening will be done in vitro, with very heavy involvement of robotics. All NCI data access will be interactive and real time, use of bar codes and other microcomputer devices will become commonplace and expert systems will accomplish much of the reporting that is required. The capacity of the screening effort can be increased greatly. Computing will no longer be restricted to data processing but will be deeply involved in process control, data capture and data evaluation.

DTP computer operations support. This will be a new contract, with an estimated annual cost of $200,000 for five years. The concept statement:

The Developmental Therapeutics Program has designed and built a comprehensive information system, known as the Drug Information System, which contains all the data associated with the screening of chemicals for anticancer activity. All of the data bases in the DIS are vitally important on a day to day basis to DTP because they support the management and direction of the entire drug discovery and development effort. The DIS was originally designed to run on DEC-10 computers and it was first installed in 1983 on the DEC-10 system in NIH's Div. of Computer Research & Technology. It has served DTP well in this environment but is now threatened by impending obsolescence of the DEC-10 because it is based on a 36 bit word length. Accordingly, in 1986 DTP embarked upon on effort to rewrite the entire DIS so that it will run on any 32 bit computer. This work is well under way and consideration is now being given to the choice of a machine for future DIS use. Operating the DIS on a DCRT computer has had numerous advantages, especially during the implementation phase, but it also has some disadvantages. Chief among these are the annual billing by DCRT currently in excess of $1 million, and the contention among numerous users, DTP included, for cpu time on the NIH shared machines of this sort. The latter has led on occasion to poor response time in the DIS. To ameliorate both these problems, DTP has decided to acquire its own midsized mainframe and install DIS on it.

This computer will be purchased outright by NCI, which will also provide a satisfactory environment for it in the same building used by the Information Technology Branch. The purpose of this proposed contract is to provide support for the operation of this machine and the maintenance of much of the data and software that will reside on it. The computer must handle at least 20 simultaneous users and, more significantly, must run on a 24 hour per day, seven day per week basis because the DIS is used by scientists in Europe, and a third shift is needed in order to complete the frequent data base updates which cannot be done while production use of DIS is in progress. The third shift may be unmanned and so this contract must be able to provide staff presence and support from 8 a.m. until midnight on at least a six day per week basis. In this way, there will be 96 operator supported hours and 72 unsupported hours in every 168 hour week. The level of manpower envisaged for this contract would include a part time senior systems analyst and two full time computer operators. It is this level of staffing that underlies the proposed annual amount, above. Naturally, the personnel would have to be able to spend all their time at the USG provided site of the computer installation.

Chabner commented, "The reason we're doing this is to save money. NIH has a monopoly on large computers here, and the charges are high. Getting the supercomputer (run by NCI at the Frederick Cancer Research Facility) was a breakthrough. It has been a source of controversy."

"I support this," Schimke said. "My experience with shared computers at Stanford is that when you want to use it, it is either down or being used by someone else."

DTP staff members have groused over what they consider exorbitant charges by DCRT, and that the $1 million a year they have been paying is based on unfair and unrealistic overhead charges.

"What will you do with all that money you save?" Mendelsohn asked.

"First we have to pay for the computer," Chabner said.

Production and testing of human LAK cells. This is the recompetition of the contract held by Meloy Laboratories, at the higher level of $834,000 a year, the new figure approved by the Board for the 1987 fiscal year. The new contract will be for three years, starting in FY 1988. The concept statement:

The Surgery Branch has been intensively involved in the development of cellular approaches to the adoptive immunotherapy of cancer. This laboratory was the first to describe the lymphokine activated killer (LAK) cell phenomenon. Lympoid cells which are incubated in interleukin-2 (IL-2) will develop into lymphoid cells which are capable of lysing fresh tumor cells. It has been demonstrated that these cells, given in conjunction with IL-2, can cause the regression of a variety of established experimentally induced pulmonary and hepatic tumors in murine models.

This laboratory was the first to report the ability of IL-2 and LAK cell immunotherapy to cause the regression in a variety of patients with metastatic cancer. This new approach to cancer therapy requires a tremendous effort in the production and testing of these LAK cells. The present contract with Meloy Laboratories has helped support the Surgery Branch efforts by producing LAK cells for use in clinical investigations.

Future studies will investigate the clinical efficacy of IL-2 and LAK cell therapy. Protocols designed to examine ways of decreasing side effects and toxicity of this therapy will be initiated. Also, IL-2 and LAK given as an adjuvant treatment in patients rendered disease free surgically and yet at high risk of developing recurrent cancer has already been started in trials being conducted by the Surgery Branch. It is essential to the Surgery Branch to have a contract that continues to supply human LAK cells for clinical use.

Mendelsohn and Schimke raised the issue of whether LAK cells would be made available by NCI to other investigators. Samuel Broder, director of DCT's intramural Clinical Oncology Program, said "this is a targeted requisition for Dr. Rosenberg. We would have to come back later with an RFP for providing this material to other investigators."

"Then I will vote against it," Schimke said.

Chabner pointed out that NCI was supplying LAK cells to investigators at the six institutions where confirmatory trials are being conducted, and that they also would be given to additional investigators as the trials are expanded.

"It's going to take more than Steve's lab to do this," Mendelsohn insisted. "There are so many questions. It's important to make this available to anyone with a good idea."

Chabner noted that NCI's Medicine Branch and the Biological Response Modifiers Program are collaborating in the study. Also, "We had hoped we could get LAK cells supplied by industry." IL-2 is supplied at no charge by the Cetus Corp.

Board Chairman Paul Calabresi asked for and received a vote of approval, with the provision that the issue will be discussed further at the Board's June meeting. Schimke voted against it.

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