THE CANCER LETTER

Vol. 10 No. 38
Oct. 5, 1984

Subscription $150 year North America
$175 year elsewhere

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NCAB ASKS FOR COST REIMBURSEMENT ON PATIENTS IN CLINICAL TRIALS UNTIL MORE DATA AVAILABLE

The National Cancer Advisory Board rejected NCI staff advice and approved unanimously a motion calling on the Health Care Financing Administration to pay on a cost reimbursement basis for patients on clinical trials, at least until completion of studies on

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In Brief

NCI SEEKS BETTER WAYS TO MAKE AVAILABLE FRESH TISSUE; IVERSON HEADS CANCER CONTROL SCIENCE

ACCESS OF SCIENTISTS to fresh tissue from cancer patients has become a problem, NCI Director Vincent DeVita told the National Cancer Advisory Board last week. "We're looking at several mechanisms—grants, contracts, supplements to core grants—to set up tissue conservation units. I don't think pathologists want to become tissue brokers." Surgeons sometimes discard tissue before investigators can claim it, DeVita said. "In most institutions," NCAB Chairman David Korn said, "surgeons do not discard tissue more than once".... **DONALD IVERSON** has been appointed associate director and head of the Cancer Control Science Program in NCI's Div. of Cancer Prevention & Control. That program has been administered by DCPC Deputy Director Joseph Cullen since it was established two years ago. Iverson, 37, has been director of health promotion and disease prevention at Mercy Medical Center in Denver and assistant clinical professor at the Univ. of Colorado School of Medicine. He has a PhD in health education from the Univ. of Oregon.... **NEW APPOINTMENTS** at NCI's International Cancer Information Center: Dan Masys, presently at the Naval hospital in San Diego, will be chief of the International Cancer Research Data Bank Branch; and Mary Stram, presently with the U.S. Dept. of the Treasury, will be chief of the Computer Communications Branch.... **ROBERT GOOD**, former president of Sloan-Kettering Institute and more recently at the Oklahoma Medical Research Foundation, has been appointed professor of pediatrics and graduate research at the Univ. of South Florida and physician in chief and chairman of the USF Dept. of Pediatrics at All Children's Hospital. Good plans to develop a 10 bed bone marrow transplant unit at the hospital.... **JOHN HISSERICH**, deputy director of the Univ. of Southern California Cancer Center, has assumed additional duties there as director of development.... **GEORGE KLEIN**, Karolinska Institute, will deliver the Charles Heidelberger Memorial Lecture Nov. 16 at USC. The lecture, honoring the late director for basic research at USC who died of cancer in 1983, will be part of an international sym-posium Nov. 16-17 on lymphoproliferative diseases which will be held at Mayer Auditorium on the Health Sciences Campus.

KATTERHAGEN SAYS STUDIES SO FAR SHOW PROTOCOL PATIENTS COST MORE

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patient care cost of clinical research. The Board's action last week followed the recommendation of its Committee on Cancer Control & the Community, chaired by Gale Katterhagen.

The committee, meeting the night before the meeting of the full Board, had approved unanimously the following resolution:

"To remove the disincentive against clinical trials research produced by the prospective payment system, the National Cancer Advisory Board urges that a cost based reimbursement mechanism be implemented for National Institutes of Health approved clinical trials."

Jerome Yates, director of the Centers & Community Oncology Program in NCI's Div. of Cancer Prevention & Control, designated by Director Vincent DeVita to head NCI's handling of the issue, repeated his oft stated position that it would be premature to recommend any change from the current DRG regulations until completion of various studies looking at patient care costs involved in research protocols.

Board member Helene Brown suggested a modification of the resolution which, with further rewriting by Katterhagen and other Board members, was approved as follows:

"National Institutes of Health approved clinical trials are an important mechanism whereby the latest advances in biomedical research can be evaluated for their applicability to direct patient care. The trials, based at major medical centers and community hospitals, are of critical importance as part of the Year 2000 goals of the National Cancer Institute to reduce cancer deaths by 50 per cent.

"The relationship of these clinical trials to the DRG reimbursement system is of vital concern to the NCAB. The DRG system may have an unintended, harmful effect on clinical trials. We understand that studies identifying all relevant cost factors and issues are now being undertaken. Until completion of these necessary studies, which may indicate that adjustments are in order, it may be prudent to continue to fund these patients on a cost reimbursement basis.

"The NCAB recommends this proposal to the Secretary, HHS, and urges its consideration by the Health Care Financing Administration."

Katterhagen's committee had made its recommendation following a presentation by John Yarbro, president of the Assn. of Community Cancer Centers which is pushing for a new DRG category ("DRG 471") for clinical research. Yarbro summarized results of four published studies which found that patient care cost for those on research protocols does exceed that for nonprotocol patients. "These studies were done in four different hospitals in four different parts of the country using different techniques. It is highly unlikely that the overall conclusion that clinical trials are associated with an excess cost is in error. The only reasonable question remaining is the exact amount of that excess cost and the variation between different clinical trials," Yarbro said.

"Clinical trials cases cost more when all trials cases are compared with all cancer cases," Yarbro continued. "They cost more when trials patients are case matched with nontrials patients. They cost more when cases are compared within the same DRG. They cost more in hospitals before DRGs were implemented, just after DRGs are implemented, and after DRGs have been in effect for two years, at least in New Jersey.

"This is not really a surprising result for two reasons. People who actually do clinical trials and deliver conventional therapy at the same time on a day to day basis know that clinical trials cost more than conventional therapy. It is the people who never write orders who are uncertain. Second, new technology may save money in the long term, but testing it in the short term costs more. Conceptually, it is clear that if we limit clinical trials only to those that cost less in the short term we will impede development of any new technique that costs more for initial hospital treatment, even if it saves money in the long run."

Waiting too long to deal with the problem could erode the research base or set a precedent that will allow third party payers other than Medicare to "dodge their responsibility to pay the legitimate patient care costs of patients on clinical trials," Yarbro said. He mentioned several possible solutions:

"Can we pay these excess costs by a grant mechanism as though they were research costs? Not really. A DRG payment is a statistical value unrelated to individual patient costs. It would be impossible in each case to determine the amount of the excess.

"Can we pay on a formula basis? This is possible in theory because we can calculate the excess retrospectively for each protocol and each DRG. It would be very difficult to do in practice, however, and even then only possible retrospectively. Such funds for patient care would then have to be added to NIH research budgets and would compete with other research expenditures.

"Can we pay the hospital costs of clinical trials as we now pay for patients in NIH Clinical Center beds? This is what I think HCFA rather naively imagines is the best solution. This would be a major

drain on already limited research funds. If the excess costs represent about 20-25 per cent of the total costs as the limited data of Hughes et al suggest, then the estimate of total excess costs of about $50 million baloon to $250 million and all from NIH sources (the $50 million was a total excess cost estimate of which half would come from third parties other than Medicare). I do not believe that it is a realistic solution to pay all care costs for clinical trials patients as we do for NIH Clinical Center patients.

"I believe we are left with the creation of a new DRG. This can be done under the existing law, rapidly, administratively by HCFA, and at a cost so low that it will not even be noticed. If HCFA will do this, as other third parties go to the all payers system, clinical research will be protected. Since under DRGs the hospitals will have an incentive to use real cost figures instead of the fictional cost shifted figures in use today, we will be assured that only true costs are being paid. Furthermore, if the DRG is limited to NIH approved clinical trials we will have a guarantee against abuse."

Although NCI's position has been to wait until more data are in, senior executives are leaning toward the position that excess patient care costs of clinical trials are the responsibility of the funding institutions—namely, NIH and NCI in the case of cancer clinical trials. That position assumes that Congress would agree to add the required amount of money to NIH and NCI appropriations to cover those costs. Staff members have argued privately that either way, DRG 471 or payment through NCI, would require congressional action and that the latter might be more acceptable since it would not be seen as tinkering with the DRG system.

ACCC has taken the position that HCFA could create DRG 471 administratively without further congressional authorization. HCFA has responded that it is prohibited by existing Medicare legislation from reimbursing research costs. ACCC is committed to getting DRG 471 approved, by new legislation if that is the only way.

Yarbro responded to NCI's approach, as he perceived it to be from the NCAB committee discussion:

"ACCC had never asked for new money. We had only asked that HCFA pay the same costs they paid last year for clinical trial patients. The mechanism to accomplish this through cost reimbursement is already set up at HCFA and in every hospital in the country."

Paying for excess clinical trials costs through NCI would require a new mechanism to disburse those funds, Yarbro said. Also, "in a time of fiscal constraint, a request for additional funds from NCI is not likely to be as successful as a request that HCFA continue to pay the costs they have been paying all along (Medicare reimbursement is paid from entitlement funds and do not require annual congressional appropriations). Even if NCI does have its budget augmented to pay the patient care costs previously paid by HCFAh, it is likely that the budget increase will be substantially less than the request. Furthermore, half of all the new dollars going to NCI in the past few years have been allocated for RO1 and PO1 research grants and the basic science community is unlikely to appreciate that these new funds are in reality a kind of transfer of responsibility from HCFA to NCI. In short, it is my judgment that there is a low probability that the clinical trial budget, now approximately $47 million, will be augmented by $50 million. These kinds of changes simply do not occur.

"What then will happen? NCI will have already admitted that there are excess patient care costs associated with clinical trials because these data will be used to justify the increase of funds. Investigators, using NCI's own data, will then demand to be reimbursed for the excess costs which HCFA no longer has an obligation to pay.

"This will require that NCI establish a new bureaucracy to quantitate, validate and reimburse these patient care costs. In all probability, this would lead to a reduction in the number of institutions involved in clinical trials. Funds now supporting research costs of clinical trials would be diverted to pay patient care costs; and institutions inadequately reimbursed for their costs or frustrated by the new level of bureaucracy would drop out of the clinical research program."

Katterhagen, in presenting the committee's recommendation to the Board, said, "I personally feel the present HCFA policy on reimbursement will lead many hospital CEOs to dump a loser, clinical trials, and that this would significantly damage our ability to achieve our Year 2000 goals."

Board members Brown and Geza Jako, who had been present at the committee meeting, indicated they felt the Board should wait for more information. "I wonder if we aren't being premature in presenting this resolution without all the data," Brown said.

Board member Ed Calhoon disagreed. "There certainly is a disparity. I think we need to take some action on this," he said.

"My concern is that the discussion (at the committee meeting) was not balanced," Yates said. "We should hear from the cooperative group chairmen (who are conducting their own cost study). There are two levels to this problem. Are DRGs as constituted appropriate for each disease. There is a problem with leukemias and lymphomas. HCFA is aware of this.

Are DRGs adequate for state of the art care? Second, are DRGs adequate to reimburse for clinical research? Dr. (Paul) Carbone has presented some data from his institution (Univ. of Wisconsin Clinical Cancer Center) where protocol patients are not costing more.

"There is a problem with methodology," Yates continued. "HCFA is addressing these issues. The National Center for Health Services Research is looking at relative costs of matched patients at 50 institutions. This blanket approach (the committee resolution) is premature."

"Are you urging us to table this motion?" Board member Victor Braren asked.

"I think we should hear from others, and wait for the data," Yates said. "Another aspect of this is that we are trying to develop a cooperative relationship with HCFA."

"This motion doesn't say to selectively overpay but to obviate a disincentive that exists," Board member William Powers said. "The only data I heard (at the committee meeting) was presented by Dr. Yarbro. The rest was a wish list. Clinical trials patients represent advances in scientific research. We're not asking for anything extra."

"The issue is, is it costing hospitals to do research?" Katterhagen said. "The only published data says it is. There is a clear indication that those patients are costing a significant amount of money. There is a crisis here. There is a need for more data, but my feeling is that further studies will continue to show this, and two or three years from now the horse will be out of the barn and into the next village."

"Hospital administrators are going to force the referral of patients they are losing money on, whether they are on protocols or not," Yates said.

"The data show they lose more money on protocol patients than those not on protocol," Katterhagen said. "HCFA's policy now is to continue ratcheting payments down. I don't share your benevolent attitude toward HCFA."

"If there is not a difference, this (the motion) won"t have any effect," Powers argued. "If there is, all this does is call the problem to the attention of those studying DRG adjustments."

"I disagree," Brown said. "What Dr. Yates is talking about is trying to avoid a confrontation with another agency, give them a chance."

"This is a bland motion," Breren said. "There is nothing confrontational about it."

Board Chairman David Korn suggested that the motion be modified to include acknowledgement that more data is needed; "that preliminary data show for at least some kinds of cases, there is reason for concern. This is a strong signal, that we don't want to wait until the horse is out of the barn."

KORN TAKES CHARGE, REVAMPS NCAB COMMITTEES, NAMES NEW CHAIRMEN

With David Korn taking charge as chairman, the National Cancer Advisory Board last week had what some members and NCI observors said was one of its best meetings in years. The five new members including Korn; the sixth 1984 appointee, Roswell Boutwell, reappointed to a full term while on a two year assignment in Hiroshima; and all the holdover members were present. They participated in spirited and (for the most part) intelligent discussions on the issues in the open sessions and handled with dispatch and competence review of grants in the closed session.

Korn demonstrated that he had taken charge when he presented his appointments to Board committees. Three of the new members were named chairmen of committees; he replaced the influential and sometimes controversial William Powers as chairman of the Organ Systems Committee with holdover member Robert Hickey (**The Cancer Letter**, Sept. 28); and in what Korn said was the most important substantive change, he combined Cancer Control & Community and the Cancer Control & Minorities committees into one. The two chairmen of those committees, Gale Katterhagen and LaSalle Leffall, respectively, will serve as cochairmen of the new committee now named "Cancer Control for the Year 2000."

The new members named as committee chairmen are Gertrude Elion, Planning & Budget; Louise Strong, Environmental Carcinogenesis; and Enrico Mihich, Special Actions (which is the committee of the whole that reviews grants). Holdover member Richard Bloch will chair the committee that reviews the budget and contract concepts for the NCI Office of the Director; Boutwell will head the Construction Committee; and Ed Calhoon was reappointed chairman of the Innovations in Surgical Oncology Committee.

Korn appointed himself as chairman of the Activities & Agenda Committee, which will include the entire Board and have its meetings during the Board's regular sessions.

Korn said he was influenced in his decision to combine the Katterhagen and Leffall committees by the discussions at the meetings of the President's Cancer Panel in Los Angeles and San Francisco. In Southern California, he noted, the discussion at the Panel meeting indicated "a lack of effective interaction among centers in an area of great diversification. It was emphasized that these centers were not quite getting through to underserved groups."

In San Francisco, by contrast, the Panel found the Northern California Cancer Program, a consortium, "to be a very unusual program. There is a tremendous amount of outreach, community action and interaction. It serves a host of diverse groups. It

occurred to me there is a real area of need essential to achieving our Year 2000 goals. If we are going to maximize cancer control efforts and deal with the range of underserved groups, the Board will have to play a contributing role, interacting closely with the President's Cancer Panel, and try to get to that mass of people outside the system."

Describing the charge to the committee, Korn said:

"This committee is interested in factors which influence the effectiveness of the Institute's cancer control program (prevention, detection, treatment and rehabilitation) in reducing cancer incidence, morbidity and mortality and increasing survival in all population groups.

"Issues considered may include: barriers to access to service—economic, racial, cultural and geographic; social patterns and behaviors influencing incidence in different populations and areas of the country; effectiveness and appropriateness of NCI public and professional information and education, especially that directed at minorities; minority access to research and training opportunities.

"The committee may study and make recommendations regarding these and other issues particularly as they affect minority and underserved populations and attainment of the goals for the Year 2000."

Board members supported Korn's initiatives enthusiastically, except for his decision to abolish the committee for the Frederick Cancer Research Facility. That committee had been established, Korn said, "when Frederick was in a state of change. Now there is a chartered advisory committee for Frederick which basically is equivalent to a board of scientific counselors. It is a very distinguished group. I don't see why we need another committee. NCAB members are invited to attend those meetings. There is no intent to diminish Board participation in Frederick discussions."

"Part of your information is not quite correct," Powers said. "The NCAB committee was initiated after the new contracts were awarded (recompetition of the contract split into five separate awards in 1982). We were concerned about whether a solution was possible. It was never intended that our committee would serve as a board of scientific counselors."

Korn said he would be happy to receive any advice on the matter. "I assure you I would treat it with care and respect, but I would have to be convinced that a need exists."

"I choose not to give you some advice," Hickey said. "But would you accept some counseling? I have no objection to your suggestion. That is a very good group appointed to oversee Frederick. But I have a feeling that that group feels isolated from the NCAB."

Peter Fischinger, NCI associate director whose responsibilities include FCRF, responded to Bloch's question of whether he feels an NCAB committee is needed. "I feel it is important to have as wide a group of advisors as possible," Fischinger said. "The chartered committee does that, and we have always asked that one or two members of this Board attend the meetings.

"The feeling about Frederick," Fischinger continued, "is that it is stabilized. People there are very excited about their work. Previously, we had constantly talked with congressional representatives, the press, and others about our problems. Now, I almost feel lonesome. Frederick is a happy place today."

"What has the NCAB committee done since the contracts were awarded?" Board member Rose Kushner asked.

"Nothing," Fischinger said. "It hasn't met."

That ended the discussion.

SURVEY TO INCLUDE ALL INSTITUTIONS WITH $200,000 OR MORE NCI SUPPORT

The group advising CDP Associates in the cancer research facilities survey sponsored by Armand Hammer and the American Cancer Society has decided that all institutions receiving $200,000 or more a year in NCI support will have the opportunity to participate in the survey.

The plan originally was to conduct only a representative sampling of institutions involved in cancer research, but the advisors felt that the survey results would have more validity with a complete survey of all institutions which are eligible to apply for NCI construction funds. The cutoff at $200,000 might eliminate some which could be eligible but probably would not be expected to compete for construction/renovation grants in the near future. CDP estimated that questionnaires will be sent to about 250 institutions.

A final draft of the questionnaire is being prepared by CDP to include recommendations by group members. CDP plans to have the questionnaire in the hands of the participating institutions by Nov. 1, with a response time of three to four weeks. The group will meet in January to review results and assist with the analysis. CDP is aiming for submission of the complete report to Hammer and ACS by Feb. 1 so that they may provide it to NCI Director Vincent DeVita in time to include in his budget presentations to Congress. NCI has asked for $23.8 million in the 1986 fiscal year for construction grants.

Members of the advisory group are Emmett Barkley, director of the NIH Div. of Safety; Richard Cooper, director of the Univ. of Pennsylvania Cancer Center; Harry Eagle, director of the Cancer Research

Center at Albert Einstein College of Medicine; Jane Elchlepp, Dept. of Pathology, Duke Univ. Medical Center; Jay Goldman, chairman of the Dept. of Industrial Engineering at the Univ. of Missouri; Richard Harrington, St. Jude Children's Research Hospital; Russell King, King & King Architects; Carlos Kruytbosch, coordinator for the interagency academic research facilities survey being conducted by the National Science Foundation; Salvador Luria, director of Massachusetts Institute of Technology; and Steven Pakes, Div. of Comparative Medicine, Univ. of Texas Health Sciences Center.

NCI RESTRUCTURES AIDS EFFORT; NEW RESEARCH THRUSTS OKAYED BY ADVISORS

NCI has restructured its organizational handling of research on AIDS following the spectacular developments in etiology of the syndrome reported earlier this year, with a new research thrust in etiology encompassing and integrating efforts in the entire area of biological carcinogenesis.

The old NCI AIDS Task Force has been abolished, and the new associate director for biological carcinogenesis in the Div. of Cancer Etiology, now being recruited by DCE Director Richard Adamson, will have primary responsibility for both intramural and extramural AIDS research.

NCI Director Vincent DeVita told the National Cancer Advisory Board last week that five companies have been licensed to produce AIDS diagnostic tests. They are Abbott Laboratories, Electro-Nucleonics Laboratories, Litton Bionetics, Travenol/Genentech Diagnostics, and Dupont/Biotech Research Laboratories.

DeVita also said that the antiparasitic drug suramin has been approved for clinical trials against AIDS at the NIH Clinical Center. The drug is not commercially available in the U.S., but the Center for Disease Control Parasitic Disease Drug Service holds an IND on it; NCI cross filed on that IND.

Other AIDS INDs "are rolling into FDA," DeVita said.

An AIDS subcommittee consisting of DeVita, Hilary Koprowski of the DCE Board of Scientific Counselors, Dani Bolognesi of the Div. of Cancer Treatment Board of Scientific Counselors, and NCI staff members Robert Gallo, Samuel Broder and Peter Fischinger met recently to review progress and consider new areas of emphasis. Excerpts from that report follow:

NCI has been mandated by the Dept. of Health & Human Services to be the lead group to develop research which will lead to a safe HTLV III based vaccine preparation for AIDS. NCI has the proven capacity for large scale HTLV III and/or antigen production and has extensive intramural expertise in retroviruses. The major area where these activities will be performed will be through the NCI Frederick Cancer Research Center contracts, principally the Program Resources Inc. contract. A rapid mechanism exists for the extension of these activities by dedicated funds from PRI to outside subcontractors with unique resources and skills. To optimize this process, a concept review as well as a technical assessment of individual brief proposals can be performed by the subcommittee of outside advisors, who are also members of the boards of scientific counselors of the involved divisions. The report of the meeting back to the full BSCs and the endorsement of the concepts by those boards makes this approach compatible with other contract decision processes.

Vaccine development was considered to be closely contingent on the advances in etiopathogenesis. The most important areas discussed and resulting conclusions were:

1. AIDS continues to spread rapidly in the known at risk groups in the U.S. The rate of accrual of new cases is slower in New York, but is unabated elsewhere. Evidence for transmission to heterosexual partners was reinforced. Evidence for possible nonsexual transmission by body fluid is also being considered with the finding of HTLV III in saliva in a number of antibody positive members of at risk groups. Heterosexual transmission is known in Africa, and female to male transmission probably occurs. Background HTLV/LAV positive antibody occurs in selected African populations 7-21 per cent. HTLV III antibody was detected in sera of children in Africa before the current AIDS outbreak.

2. First available positive data on primate inoculations are being reported. Several agencies have inoculated chimpanzees with AIDS and LAS patient material. In one case, two thirds of the chimpanzees seroconverted in 14 weeks; one came down with LAS in 24 weeks, which then cleared spontaneously. Several of the CDC animals are said to have seroconverted and are releasing virus. The spectrum of animal responses will be followed closely to develop the best and the least demanding test system for vaccine preparation evaluation.

3. An assessment of up to date data on the HTLV III positive antibody has been made in the AIDS, pre-AIDS and controls from the available worldwide studies. What is critical is that the "well" members of at risk groups have had a high degree (55-75%) of exposure to HTLV III which occurred only recently. At this time, the predictive value of an HTLV III antibody positive test in a normal individual is unknown. The time factor may be important because of the known possibility of a very long incubation period (>4 years). Are some antibody individuals "cured", or at least protected from, or do they

control the virus? This is critical to determine because they will define the specificity of the natural protective antibody which will have to be elicited by any vaccine preparation. Up to now, the p24 core and the gp41 presumed envelope reactivities are diagnostically important but not protective since terminal AIDS patients are still positive for these antibodies. A key issue will be to develop an antigen detection assay. This can be based on several techniques including a competitive radioimmune assay or an in situ hybridization test with cloned proviral HTLV III DNA.

4. Data from Africa have to be extended. The NCI report from eastern Zaire will have to be integrated with the Belgian-CDC-NIAID reports from Kinshasa. There seems to be a high AIDS attack rate in several of the major equatorial African cities which exceed those in New York. Contacts should be made with members of the Rockefeller Foundation and the International Health Foundation for further information on sample accrual from various areas because of their extensive contacts. Additional input and special sample and patient data from Africa may be available from Karolinska Institut.

Action items at FCRF

Production of HTLV by PRI should continue at 250L per week. A concentrate from 100m L should go to Gallo's laboratory on a weekly basis for further research. Gallo could also continue to avail himself of some support services of PRI. The remainder of virus is to be frozen for future vaccine development. A characterization of antigens and the determination of immunogenicity in a variety of hosts should be attempted. Because mouse T lymphocytes may be susceptible to an in vitro infection with HTLV III, a number of normal and other mouse strains which may be relatively more susceptible to immune deficiency will be inoculated with HTLV III in P3 containment facilities.

Other NCI intramural efforts which could be supported in LMO:

*HTLV III envelope gene expression vectors, and COP testing of drugs for biological and biochemical transcriptase inhibitor studies prior to trials in humans.

*The activities within FCRF will extend also to Litton Bionetics' basic research program. Notably, the protein identification and sequencing skill of Dr. S. Oroszlan should be brought to bear on this problem, with virus and reagent support.

A number of resources and contributors will be needed to implement the basic vaccine development program at NCI-FCRF. These involve generally unique resources and skills not readily available. A review of concepts and options was performed in several categories. The following concepts from a number of proposals were reviewed and singled out for support:

1. California Regional Primate Center at Davis. This unit has a dedicated, isolated P3 containment area for potential HTLV III inoculations into various species of primates. A number of old and new world primates will be inoculated with concentrated HTLV III. Pretesting in vitro of stimulated lymphocytes from each species for HTLV III infection is planned to determine the level of susceptibility within a given species.

2. New England Regional Primate Center. A significant strength is the close collaboration with Max Essex who will interact with them on experimental protocols. He also will be involved in the species lymphocyte pretesting for susceptibility to HTLV III. Stress will be put on a number of species unique to this primate center.

3. Cornell Univ. Veterinary School. This group has had the most expertise in intervention approaches to lelukemias and sarcomas in the cat. Treatment with various antiviral antibodies has been shown to be successful in prevention of feline leukemia and sarcoma virus induced disease.

4. Memorial Sloan-Kettering Cancer Center. The antibody profile of an individual who might have overcome HTLV III infection is not known. Our present assessment of p41, putative envelope, and p24 core antigen reactivities has to consider the fact that these antibodies are not protective in man. To develop proper immunogenic preparations, one has to interrelate an antigenic complex and various antiviral antibodies. One such basis is the development of immunoabsorbent columns (at FCRF) with large quantities of selected high titer patient sera. Dr. B. Safai (at MSK) has the capability for serum accrual, especially from sources such as normal positive controls, long term LAS patients, and the rare multiyear survivors of AIDS.

5. New England Deaconess Hospital/Harvard. This clinical group has also been preeminent in identifying human models for AIDS pathogenesis. They will study and attempt to identify those individuals in these groups and their consorts who may have achieved a status of protection. The selected antigen and antibody documented sera will be made available for the vaccine development effort.

Univ. of Glasgow. In a search for unique approaches to HTLV III vaccine development, this group, previously successful in deriving membrane fraction vaccine for FeLV, has extended its approaches to the generation of retroviral antigens at the infectious recombinant virus level. Earlier observations have shown that an inserted gene from various pathogenic agents into an infectious vaccinia virus can be expressed and induce specific protective antibody to the introduced gene product. Because vaccination had already occurred in the high risk population for AIDS, the efficacy of such

constructs may be limited. An alternative approach is to use one of the >30 human adenovirus strains as a vehicle for the genes of interest. The model is being developed at Glasgow using a canine adenovirus vehicle (cause of hepatitis) with the introduced FeLV envelope genes as passenger. This can now be extended to the HTLV III gene. The advantage here is that the dog system can serve as an experimental model to determine the levels of induced HTLV III envelope specific antibody. Further work will involve molecular design of human adenovirus strains with powerful promoters for the expression of those HTLV III antigens which will mediate protection.

Other discussions at the subcommittee meeting included:

*A working meeting on HTLV originally planned for November will be combined with a meeting on HTLV etiopathogenesis in December.

*B. Moran of Uppsala, Sweden, presented a state of the art assessment of using viral membrane glycoproteins as immunogens in various formats. The discussion centered on advances in "iscoms" which are artificial glycoside immune stimulating complexes in the structure of micelles which present the antigen in a more effective way. A 10 fold higher antibody titer was achieved if iscom micelles were used over the natural membrane-glycoprotein aggregates.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-47689-09

Title: Operation and maintenance of the Developmental Therapeutics Program data processing system

Deadline: Approx. Jan. 4

NCI will make available to interested contractors a request for proposals for data processing services. The government will supply all the necessary mainframe computer time. The successful bidder shall furnish all necessary personnel, labor, materials, supplies, equipment and facilities (except as furnished by the government) to operate and maintain the various subsystems of the Drug Information System (DIS), and shall provide data processing support and services for related programs of the Developmental Therapeutics Program. NCI screens approximately 10,000 chemical substances annually for antitumor activity. This results in about 50,000 compound registration rounds per year and 13,000 testing transactions per fortnightly update cycle. Nearly 500,000 substances have been tested in the 20 years of testing in the program. This has resulted in a data base of some 9.1 million records (1.9 billion bytes). The operation and maintenance of the subsystems of the DIS shall be performed so as to provide data processing functions on a regular schedule requiring timely completion of data input and output, using prescribed media, including prescribed forms for input of data from five screening laboratories within the U.S. and Europe, and formats for reporting.

The contractor will also be responsible for establishment and maintenance of procedures for data preparation, reporting and control, and documentation for either newly written or modified programs.

The current DIS is an on line biological, chemical and management information system for acquisition and management of data collected in connection with NCI's program for screening potential antitumor agents. It consists of approximately 12 subsystems of the DIS. Data are transferred automatically between subsystems of the DIS to support queries and generate upon request. The chemical names file, which contains 227,000 entries, is one such subsystem and the supplier name and address file with 8,500 records is another. The computer facilities of the NIH Div. of Computer Research & Technology are to be used for the majority of data processing activities performed under this contract with file preparation on the IBM 370, and searching and report generation on the DEC 10. Due to the dynamic nature of the systems, inmputs and outputs, as well as the programs, are subject to change.

A document viewing room will be available by appointment for interested parties and will contain the present documentation of the system. This will include program documentation, input/output formats, record layouts, and program run instructions. A preproposal conference will be held. The locations and dates of the documentation viewing room and the preproposal conference will be announced in the RFP. One award is anticipated as the result of this RFP. The anticipated award will be for a five year incrementally funded period of performance. The government estimates the level of effort to be 1.7 staff years for each of the five years.

Contracting Officer: William Roberts
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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.